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

April 9-11, 2002

Final Meeting-24 Highlights

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

INTRODUCTION

George Rusch, NAC/AEGL Chair, opened the meeting with brief remarks and along with AEGL Program Director, Roger Garrett, welcomed the committee members and guests. Thanks were expressed to George Cushmac for continued hosting of the NAC/AEGL meeting at the Department of Transportation. Roger Garrett briefly discussed his health situation and offered his continued commitment to the AEGL Program.

George Rusch made the following administrative announcements:

- The current emphasis of the AEGL Program is to work closely with NAS/COT and publish as many TSDs as possible in 2002. Therefore, we are seeing many recycled TSDs in this meeting instead of new TSDs.
- To facilitate the process of meeting highlights preparation, the Chemical Manager along with the ORNL scientist, will capture the essence of the discussions and forward the results to Po-Yung Lu in two weeks. Po-Yung can then integrate the information and distribute the highlights to NAC/AEGL members in a timely manner.

Bob Snyder inquired about the accessibility of the meeting recording tapes. These are available upon request through Paul Tobin.

The highlights of NAC/AEGL-23 held December 3-5, 2001, in San Antonio were reviewed; two minor revisions will be made. They were : "There was discussion on the appropriateness of product presentations to the committee and the limitations on short term detection tubes." and " Revisions were made to the discussion and vote on methanol." A motion was made by John Hinz and seconded by David Belluck to accept the aforementioned draft meeting highlights. The motion passed unanimously. The revised highlights of NAC/AEGL-23 are attached (Appendix A). The highlights of the NAC/AEGL-24 meeting are presented below along with the meeting

agenda (Attachment 1) and the attendee list (Attachment 2). Ballots were taken during the meeting and are incorporated into the appropriate chemical specific section as Appendices.

Publication Status/TSDs Review by NAS/COT (Feb. 2002)

George Rusch reported to NAC/AEGL that the preparation of volume three of TSD documents is under way and publication by the NRC should take place in summer. This volume will include HFC-134a, HCFC- 141b, Otto Fuel, HCN and Phosgene. He also summarized the status of Interim TSDs submitted to NAS for review. An impressive number of TSDs, a total of 17, were reviewed by the NAS/COT AEGL subcommittee during the February 6-8, 2002, meeting at Irvine, California. These chemicals are listed in Attachment 3. The NAS formal report on these chemicals will be available in early May. In addition, George Rusch provided the NAC/AEGL with a list of TSDs that are available for presentation to the COT Subcommittee at the July and October 2002 meetings (Attachment 4).

In a separate presentation, George Rusch reported on the status of the G-Nerve agent (GA, GB, GD, and GF) and VX AEGLs which were presented to the COT Subcommittee at the February 2002 meeting (Attachment 5). In order to expedite the review of these compounds, the TSD authors were asked to submit their responses to the COT Subcommittee concerns prior to publication of the COT's formal report. The TSD's responses were provided to the COT Subcommittee on March 15, 2002 and are currently under review.

Upcoming Conference Event Pertinent to AEGL Program

Bob Snyder announced an upcoming conference jointly sponsored by UMDNJ-Robert Wood Johnson Medical School and Rutgers University. The conference, entitled "Preparing for Biological & Chemical Terrorism: A New Jersey Perspective," will be held on June 6-7, 2002 at the Environmental and Occupational Health Sciences Institute, Piscataway, NJ. The conference will discuss some of the "lessons learned" as well as the current research on biological and chemical terrorism. It will be a synthesis of public health, basic research and emergency preparedness issues. Bob welcomed and encouraged all NAC/AEGL members and guests to attend since several AEGL features will be discussed during the conference. Conference brochures were distributed (Attachment 6).

REVIEW OF PRIORITY CHEMICALS FOR 10-Minutes AEGL VALUES

AMMONIA
CAS Reg. No. 7664-41-7

Chemical Manager: Larry Gephart, Exxonmobil
Staff Scientist: Kowetha Davidson, ORNL

A discussion on derivation of 10-minute values was initiated by Larry Gephart, noting that the TSD is SOP compliant. Kowetha Davidson presented the proposed 10- minute AEGL values for ammonia (Attachment 7). The same data and approach used to derive the 5-and 30-minute values, and 1-, 4-, and 8-hour values was recommended to derive the 10-minute values. Following the discussion, NAC/AEGL decided to use irritancy rather than odor as the primary endpoint for the AEGL-1. The 10-minute AEGL-1 value, 25 ppm, was made equal to the other proposed AEGL-1 values. The 10-minute values for AEGL-2, 270 ppm, and AEGL-3, 2700 ppm, were time-scaled using a calculated value of n = 2. A motion to accept the values was made by Loren Koller and seconded by Ernest Falke. Each level was voted on separately. AEGL-1 (YES:22; NO:0; Abstain:0); AEGL-2 (YES:21; NO:2; Abstain:0); AEGL-3 (YES:23; NO:0; Abstain:0) (Appendix B).

FLUORINE
CAS Reg. No. 7782-41-4

Chemical Manager: Ernie Falke, EPA
Staff Scientist: Sylvia Talmage, ORNL

The data base on fluorine was reviewed by Sylvia Talmage prior to establishing 10-minute values (Attachment 8). In response to the suggestion by the COT Subcommittee that accommodation to irritant gases occurs at low concentrations, the AEGL-1 values for fluorine were all set equal. The 15-minute no-effect exposure of human subjects to a concentration of 10 ppm was divided by an intraspecies uncertainty factor of 3 and a modifying factor of 2 (based on a limited data base). The resulting value of 1.7 ppm was applied across all AEGL-1 exposure durations. The 10-minute AEGL-2 and AEGL-3 values were both time-scaled from the previously-approved values. Because the previously-approved time-scaled 8-hour values for the AEGL-2 and AEGL-3 appeared low in light of the human experience and because the 8-hour AEGL-2 value conflicted with the 8-hour AEGL-1 value, the 8-hour values were set equal to the respective 4-hour values. An AEGL category graph developed by Ernie Falke demonstrated the appropriateness of setting the 8-hour values equal to the 4-hour values. It was moved by Mark McClanahan and seconded by Loren Koller to accept the revised values. Separate votes were taken for the 10-minute values and for the AEGL-2 and AEGL-3 8-hour values: AEGL-1, 2, & 3 for 10-minutes values (YES: 21; NO:3; Abstain:2); AEGL-2 for 8 hours (YES:21; NO:0; Abstain:3); AEGL-3 for 8-hours (YES:21; NO:0; Abstain:3) (Appendix C). The NAC-approved values appear below:

SUMMARY OF AEGL VALUES FOR FLUORINE (ppm)						
Classification	**10-minute**	**30-minute**	**1-hour**	**4-hour**	**8-hour**	**Endpoint**
AEGL–1	1.7	1.7	1.7	1.7	1.7	No sensory irritation - human
AEGL–2	20	11	5.0	2.3	2.3	Mild lung congestion - mouse

AEGL–3	36	19	13	5.7	5.7	Severe lung congestion - mouse

NITROGEN DIOXIDE
CAS Reg. No. 10102-44-0
&
NITRIC ACID
CAS Reg. No. 7697-37-2

Chemical Manager: Loren Koller, OSU (retired)
Staff Scientist: Carol Forsyth, ORNL

Loren Koller led the discussion on development of 10-minutes AEGLs as outlined in Attachment 9. The NAC/AEGL questioned the information used for development of the nitric acid AEGL-2 [Diem (1907), cited in Henschler (1991)] in that the exposure involved a single human subject. Furthermore, the information was from a secondary source. Mark Ruijten commented that the study by Gray et al. (1954), selected for the AEGL-3 value of nitric acid, has problems with the reporting as well as the interpretation of the data. Mark indicated that the exposure was to a mixture but that the results are reported as nitrogen dioxide. The NAC/AEGL directed the TSD Development Team to reexamine the Gray manuscript (Attachment 10) to confirm his comments. If the data cannot be used, another study should be selected for development of AEGL-3 values.

There were also some questions about the Henschler et al. (l960) data used for the AEGL-2 and the Henry et al. (1969) paper used for the nitrogen dioxide AEGL-3. Again, the TSD Development Team was directed to confirm the quality of the data and reevaluate the available data for deriving AEGLs. Tom Sobotka agreed to search for FDA information on nitrogen dioxide (nitric oxide) for inclusion in the TSD development. The entire TSD of nitric acid and nitrogen dioxide should be reevaluated at a later time.

REVISION OF PRIORITY CHEMICALS

ETHYLENIMINE
CAS Reg. No. 151-56-4
&
PROPYLENIMINE
CAS Reg. No. 75-55-8

Chemical Manager: Mark McClanahan, CDC
Staff Scientist: Kowetha Davidson, ORNL

The NAS/COT/AEGL Subcommittee requested the NAC/AEGL to consider deriving AEGL-1 values for these chemicals. At the December 2001 meeting Mark McClanahan presented AEGL-1 values based on dividing the AEGL-2 values by two. This factor was the average for the ratio of AEGL-3 divided by AEGL-2 for the time 10-, 30- and 60-minutes as these were the only

AEGL-1 values proposed. Values for 4- and 8-hours would be below the odor detection threshold. At the December meeting NAC/AEGL members raised the question about the AEGL ratios for similar chemicals. A check of the chemicals the NAC/AEGL has approved showed the committee had evaluated no other imines and had approved only three amines. The AEGL ratios from these three amines provided no useful insight. Between the December 2001 meeting and the April 2002 meeting Mark McClanahan compiled the AEGL-3/AEGL-2 and AEGL2/AEGL-1 ratios for all the chemicals approved by the NAC/AEGL (List compiled by Paul Tobin dated January 18, 2001.) Mark presented the results of the ratio analysis in the following table. The results show that for the 8-hour data the ratio of the geometric means for the two ratios, AEGL-3/AEGL-2 and AEGL-2/AEGL-1 for the approved chemicals is one. This ratio for the 30-minute data is 2.2.

RATIO AEGL-2 TO AEGL-1				
time	number of chemicals	geometric mean	multiplicative standard deviation	range
30-minute	40	8.85	3.70	1.50 to 1066.67
8-hour	40	3.61	3.05	1.30 to 566.67
RATIO AEGL-3 TO AEGL-2				
30-minute	72	3.97	1.94	1.67 to 36.40
8-hour	73	3.62	2.00	1.33 to 40.77
RATIO OF AEGL-1/AEGL-2 TO AEGL-3/AEGL2				
30-minute	NA	2.2	NA	NA
8-hour	NA	1.0	NA	NA

Mark presented proposed AEGL-1 values for 10- 30- and 60-minute of 11, 3.3, and 1.5 ppm respectively (Attachment 11). The basis for these was the Carpenter et al. (1948) study in guinea pigs. Animals exposed to 25 ppm for 3 hours experienced extreme respiratory difficulty while animals exposed to 10 ppm for 4 hours did not. The 10 ppm, 4-hour exposure was the basis for the AEGL-2 derivation as a no-effect level for AEGL-2 type symptoms. To estimate the threshold for AEGL-1 effects (notable discomfort, irritation, or certain asymptomatic, non-sensory effects) a factor of 3 was used to adjust to the less severe effects defining level one. The NAC/AEGL has occasionally derived AEGL-2 values by dividing AEGL-3 values by 3, however, it did not believe the available data warranted development of AEGL-1 values for ethylenimine. Because the AEGL values for propylenimine are based on its chemical similarity and relative acute toxicity (one-fifth) to ethylenimine, the NAC/AEGL also chose not to develop AEGL-1 values for it.

George Rusch, Chair, will take the result from NAC/AEGL discussion not to develop AEGL-1 values for ethylenimine and propylenimine to the next NAS/COT/AEGL meeting in July.

METHYL MERCAPTAN

Chemical Manager: Doan Hansen, BNL
Staff Scientist: Cheryl Bast, ORNL

Doan Hansen pointed out that methyl mercaptan is one of the older chemicals on the first AEGL priority working list. Because originally there had not been agreement on the role that odor should play in setting AEGL-1, it had been difficult to finalize the AEGL values. The document had been tabled at that time, pending development of the SOP.

Cheryl Bast lead the discussion of new data that potentially affected existing AEGL-2 and -3 levels (Attachment 12). The new data resulted in new AEGL-2 and -3 values as shown below. The Committee was about to address AEGL-1, with no new data, and with presentation and discussion of the odor Level of Annoyance (LOA) concept still to take place at the next meeting. However, rather than engage in an unproductive discussion, the results of which might be changed after the LOA discussion, the Committee decided to table methyl mercaptan for one or two more meetings. It is hoped that consensus will be more easily reached on AEGL-1 at that time.

AEGL-2 values were based on shallow breathing and hypoactivity in mice exposed to 258 ppm methyl mercaptan for 6 hours (Elf Atcohem, 1996). An intraspecies uncertainty factor of 3 was applied and is considered sufficient due to the steepness of the lethal response curve which implies limited individual variability. An interspecies uncertainty factor of 3 was also applied. Although an interspecies uncertainty factor of 10 might normally be applied due to limited data, AEGL-2 values calculated utilizing a total UF of 30 would yield values that are inconsistent with the total data base. Temporal scaling was performed using the default values of n=3 when extrapolating to shorter time points (30-minutes, 1-hour, and 4-hours) and n = 1 (8-hours) when extrapolating to longer time points using the $c^n \times t = k$ equation. The 30-minute AEGL-2 value was also be adopted as the 10-minute AEGL-2 value due to the added uncertainty of extrapolating from a 6-hour time point to 10-minutes. It was moved by Ernest Falke and seconded by Bob Benson to adopt the proposed AEGL-2 values. The values were accepted: (YES:19; NO:2; Abstain:0) (Appendix D).

AEGL-3 values were based on the LC_{01} (430 ppm) for rats exposed for four hours (Tansy et al., 1981). An intraspecies uncertainty factor of 3 was applied and is considered sufficient due to the steepness of the lethal response curve. An interspecies uncertainty factor of 3 was also applied. Although an interspecies uncertainty factor of 10 might normally be applied due to limited data, AEGL-3 values calculated utilizing a total UF of 30 would yield values that are inconsistent with the total data base. Temporal scaling was performed using n=3 when extrapolating to shorter time points (30-minutes, 1-hour, and 4-hours) and n = 1 (8-hours) when extrapolating to longer time points using the $c^n \times t = k$ equation. A motion to accept the AEGL-3 values was made by Steve Barbee and seconded by Nancy Kim (YES:21; NO:1; Abstain:1) (Appendix D).

Summary of Proposed AEGL Values for Methyl Mercaptan [ppm]						
Classification	**10-minutes**	**30-minutes**	**1-hour**	**4-hour**	**8-hour**	**Endpoint (Reference)**
AEGL-1	_	_	_	_	_	TABLED
AEGL-2	59	59	47	30	19	Shallow breathing and hypoactivity in mice (Elf Atochem, 1996)
AEGL-3	120	86	68	43	22	LC_{01} in rats (Tansy et al., 1981)

PHOSPHORUS TRICHLORIDE
CAS Reg. No. 7719-12-2

Chemical Manager: Tom Hornshaw, IEPA
Staff Scientist: Bob Young, ORNL

Bob Young presented a re-visit of the AEGLs for phosphorus trichloride (PCl3), for which the NAC/AEGL has previously accepted Proposed AEGL-3 values (Attachment 13). This re-visit was prompted by the submission of an unpublished study conducted by Hazelton Laboratories that suggested that the proposed AEGL-3 values may be too low.

Bob presented an overview of the Hazelton study, in which rats were exposed to 0, 0.5, 3.4, and 11.0 ppm (analytical concentrations) for 6 hr/d, 5 d/wk, for 4 weeks. This study reported no deaths or treatment-related clinical signs, hematological or clinical chemistry changes, or effects on body or organ weights. The only adverse effects reported were from histopathological findings of respiratory (mainly nasal) lesions. The NOAEL and LOAEL for these lesions were 3.4 and 11.0 ppm, respectively.

Based on these new study results, Bob suggested that the current AEGL-3 values (1.1, 1.1, 0.88, 0.56, and 0.28 ppm for 10 min, 30 min, 60 min, 4 hr, and 8 hr, respectively) may be too low since the Hazelton study rats survived 4 week exposures to 11 ppm. He also suggested that the Hazelton study might be used as the basis for developing the AEGLs 1 and 2. Regarding an approach for adjusting the current AEGL-3 values, Bob suggested that the new data could support a reduction in the interspecies uncertainty factor used with the guinea pig LC_{50} from 10 to 3, since it appears that the guinea pig is more sensitive than rats; this is supported by occupational reports (albeit of relatively poor quality) that workers exposed to 14-27 ppm for 2-6 hours experienced only irritation (Sassi, 1953). Regarding an approach for the AEGLs-1 and 2, he suggested that the Hazelton study NOAEL and LOAEL could be the basis for developing these values, although the data are from a repeated dose study.

To begin the discussion, it was noted that the rat nose more efficiently protects the lungs than the guinea pig nose, which may account for the disparity in the rat and guinea pig results. It was

asked if the AEGL values for hydrogen chloride could provide help in deriving new values for PCl3, since 3 molecules of HCl are generated from the rapid reaction of PCl3 with water. Since the AEGL-3 values for HCl are about 2 orders of magnitude greater than the current PCl3 AEGL-3 values, and phosphoric, phosphonic, and pyrophosphonic acids and significant heat of dissociation are also generated in the reaction with water, it was decided that comparison to HCl AEGLs would not be beneficial. It was then suggested that the occupational data from Sassi (1953) might be used as the basis for the AEGLs-1 and 2, but Bob reminded the NAC/AEGL that these data are taken from an abstract of an article, which is all that is available to the Committee. As a result, it was decided that the Sassi study could be no more than supporting information for AEGL development.

After further discussion, it was suggested that the rat 4-hr LC_{50} of 104.3 ppm (Weeks et al., 1964) could be used as the basis for the AEGL-3 values, using one-third of this concentration as the threshold for lethality, inter- and intraspecies uncertainty factors of 3, and the default values of n. The intraspecies UF of 3 is unchanged from the current AEGL-3 values. It was argued that an interspecies UF of 3, instead of the current value of 10, is supportable because the guinea pig is not a good model for deep lung irritants, and the occupational data suggest that humans can survive exposures to concentrations similar to those that only cause nasal lesions in rats upon repeated exposure. A motion for AEGL-3 values of 7.0, 7.0, 5.6, 3.5, and 1.8 ppm for the 5 AEGL time periods was made by Larry Gephart and seconded by John Hinz. The motion passed (YES:20; NO:1; Abstain:0)(Appendix E).

It was then argued that the LOAEL of 11.0 ppm from the Hazelton study could be the basis for the AEGLs-2, being the highest dose not causing AEGL-2 effects, and the NOAEL of 3.4 ppm could be the basis for the AEGLs-1, being the highest dose not causing AEGL-1 effects. Inter- and intraspecies uncertainty factors of 3 were again suggested, using the same reasoning as for the AEGLs-3, and the occupational data were cited as supportive of the appropriateness of using the Hazelton study for developing the AEGLs-1 and 2. Using the default values of n, AEGL-2 values of 2.5, 2.5, 2.0, 1.3, and 0.83 ppm for the 5 AEGL time periods were proposed by Bob Benson and seconded by Richard Thomas. The motion passed (YES:21; NO:0; Abstain:0). A motion to accept AEGL-1 values of 0.78, 0.78, 0.62, 0.39, and 0.26 ppm was made by Bob Benson and seconded by Mark McClanahan. The motion passed (YES:13; NO:5; Abstain:3).

SUMMARY OF AEGL VALUES FOR PHOSPHORUS TRICHLORIDE (ppm)						
Classification	**10-minute**	**30-minute**	**1-hour**	**4-hour**	**8-hour**	**Endpoint**
AEGL–1	0.78	0.78	0.62	0.39	0.26	NOAEL for nasal lesions - rat
AEGL–2	2.5	2.5	2.0	1.3	0.83	LOAEL for nasal lesions - rat
AEGL–3	7.0	7.0	5.6	3.5	1.8	One-third of 4-hour LC50 - rat

RESPONSES TO *FEDERAL REGISTER* COMMENTS ON THE PROPOSED AEGL VALUES

(A). Comments from the *Federal Register Notice* of May 2, 2001, on the proposed AEGL values for acrylic acid were received and discussed. The NAC/AEGL deliberation of these chemicals are briefly summarized as the following:

ACRYLIC ACID

Comments were received from the Basic Acrylic Monomer Manufacturers, Inc. (BAMM) regarding the proposed AEGL-1, -2 and -3 values; the comments addressed the selection of end points, the selection of key studies, and the time scaling and completeness of the considered data by the NAC/AEGL. Initial discussion took place in September, 2001 (NAC/AEGL-22). At that time, Clay Frederick, Rohm and Haas Company, indicated that a recent report would be made available for NAC/AEGL evaluation. Two reports were subsequently distributed to NAC/AEGL by BAMM via Elizabeth Hunt (dated November 9 and December 31, 2001) prior to the April (NAC/AEGL-24) meeting.

This is a continuation of the discussion of acrylic acid from NAC/AEGL-22 which focused the discussion on the new information provided by BAMM. Tipton Tyler, Health Studies Management & Consulting, presented comments on acrylic acid to the NAC/AEGL on behalf of BAMM (Attachment 14). BAMM asked the committee to consider basing the AEGL-1 on irritation rather than odor. They felt that value(s) between 5 and 10 ppm would be justified if irritancy rather than the odor threshold was used as the critical end-point. BAMM felt odor was not an appropriate end-point for acrylic acid as the chemical is “data rich” and concentrations that produce direct effects on the nasal mucosa of rodents and primates have been well established. BAMM asked the Committee to consider basing the AEGL-2 value on impairment of avoidance of escape and felt that values between 60 and 75 ppm were justified on the basis of involuntary eye closure in rabbits. Finally, BAMM expressed concern over the low values selected by the Committee for AEGL-3 (51 ppm to 470 ppm for times ranging from 8 hours to 10 minutes). BAMM felt the large gap between the Committees proposed values and lethal levels in laboratory animals (up to 2000 ppm for 4 hours without lethality) could compromise the credibility of the AEGL-3. A lack of credibility in the AEGL values could possibly lead to their being ignored in life-threatening situations.

Dr. Gundert-Remy also presented the AEGL Development Team’s responses to these issues and concerns (the detailed responses from the acrylic acid TSD Development Team are found in Attachment 15). The AEGL Development Team explained its view that AEGL values cannot be derived directly from existing workplace exposure limits or other limit or guideline values, because these values are derived for other purposes, subpopulations, exposure times and exposure frequencies and are derived using methodologies different from the AEGLs Standing Operating Procedures. Workplace monitoring and health surveillance data may, in principle, be used in the AEGL derivation, however, evaluation of the data provided by BAMM was difficult because the medical examination was not performed in correlation with exposure measurement, which was

seen as critical for slight irritative effects. Moreover, the exposure data of BAMM and BASF indicated that for most of the time actual workplace concentrations are far below the limit values. The NAC/AEGL committee decided to change the endpoint for the AEGL-1 derivation from the odor threshold to irritation without changing the actual AEGL-1 values. Acceptance of the present AEGL-1 values with a change of endpoint was shown by a unanimous show of hands (Appendix F).

With regard to AEGL-2, the AEGL Development Team considered a level of 75 ppm as an adequate threshold for an AEGL-2 effect because at higher concentrations, clinical effects occurred in animals (tearing and blepharospasm) that could impair the ability to escape, and because olfactory tissue destruction which increases with the exposure concentration is increasingly likely to result in permanent damage of the olfactory epithelium. The available animal data clearly demonstrate that the degree of olfactory epithelium damage increases with increasing exposure time and, thus, argue against using the same exposure concentration as the AEGL-2 value for all relevant periods of time. The AEGL Development Team suggested incorporation of the monkey study into the TSD. This study, together with the histopathological analysis was considered an adequate basis for a further reduction of the interspecies factor to 1. At the same time, this study strengthens the rationale for reduction of the default interspecies factor. For the AEGL-2 derivation, the monkey study will be used as an additional key study. The motion to accept the revised AEGL-2 values was made by Bob Snyder and seconded by Steve Barbee. The motion passed (YES:17; NO:4; Abstain:0) (Appendix F).

With regard to AEGL-3, the aerosol data from the study of Hagan and Emmons (1988) were considered a better basis for the derivation of AEGL-3 values because, in contrast to the vapor exposure part of the study, three different exposure times were used providing information on the time-dose-response relationship. Also, this study used a considerable higher number of animals. The monkey study on histopathological effects on the nasal mucosa was not considered an adequate rationale for a further reduction of the interspecies uncertainty factor. The AEGL Development Team referred to the AEGL Standing Operating Procedures for more information on the derivation of the exponent for time scaling. The Committee found no compelling reasons or data to change the values or rationale for the AEGL-3 at this time. It was moved by George Rodgers and seconded by Dave Belluck to keep the present AEGL-3 values. The motion passed (YES:20; NO:0; Abstain:1) (Appendix F).

Further more, a motion made by Steve Barbee and seconded by Ernest Falke, the acrylic acid values were raised to Interim status (YES:21; NO:0; Abstain:1 or 0) (Appendix F). The new AEGL-2 values appear below.

SUMMARY OF AEGL-2 VALUES FOR ACRYLIC ACID (ppm)						
Classification	**10-minute**	**30-minute**	**1-hour**	**4-hour**	**8-hour**	**Endpoint**
AEGL–2	68	68	46	21	14	Threshold for clinical effects and permanent olfactory epithelium damage

(B). No comments from the *Federal Register Notice* of February 15, 2002, on the proposed AEGL values for boron trifluoride, HFE-7100, and uranium hexafluoride were received. Therefore, these chemicals were elevated to Interim status as indicated below.

BORON TRIFLUORIDE

No comments were received from the *Federal Register Notices* of February 15, 2002. A motion to move the chemical from proposed to interim status was made by Mark McClanahan and seconded by Richard Thomas. The motion was approved unanimously by the NAC/AEGL (Appendix G).

HFE-7100

No comments were received from the *Federal Register Notices* of February 15, 2002. A motion to move the chemical from proposed to interim status was made by Mark McClanahan and seconded by Richard Thomas. The motion was approved unanimously by the NAC/AEGL (Appendix H).

URANIUM HEXAFLUORIDE

No comments were received from the *Federal Register Notices* of February 15, 2002. A motion to move the chemical from proposed to interim status was made by Mark McClanahan and seconded by Richard Thomas. The motion was approved unanimously by the NAC/AEGL (Appendix I).

REVIEW OF PRIORITY CHEMICALS FOR AEGL VALUES

TRICHLOROETHYLENE
CAS Reg. No. 79-01-6

Chemical Manager: Bill Bress, ASTHO
Staff Scientist: Marcel van Raaij, RIVM

Marcel van Raaij discussed the available toxicity data on trichloroethylene (TCE) (Attachment 16). The data base includes controlled human studies, human metabolism studies, narcosis information, and rat neurobehavioral studies. Marcel suggested a "weight of evidence" approach to development of AEGL-1 values. The AEGL-1 was based on a 2-hour NOAEL of 300 ppm for neurobehavioral effects in a study with humans volunteers (Vernon and Ferguson 1969); additional studies with human volunteers were cited as supporting data. For extrapolation across time a human PBPK model supplied by Boyes et al. (2002) was used. An intraspecies uncertainty factor of 3 was used because the mechanism of action for general CNS depression is not expected

to vary greatly among individuals. It was moved by Bill Bress and seconded by John Hinz to accept the proposed numbers. The motion passed (YES:24; NO:0; Abstain:1) (Appendix J). The AEGL-2 was based on effects seen at 1000 ppm for 2 hours in the study by Vernon and Ferguson (1969). These effects included dizziness, light-headedness and lethargy. These effects were considered to be below a level for an AEGL-2 endpoint, i.e., the highest level not showing any AEGL-2 effects. For extrapolation across the various time periods, the human PBPK model of Boyes et al. (2002) was used. For inter-individual variation among humans an intraspecies factor of 3 was used (the mechanism of action for general CNS depression is not expected to vary greatly among individuals. It was moved by Bob Benson and seconded by John Hinz to accept the proposed values (YES:17/18; NO:7; Abstain:0) (Appendix J).

The 30-minute to 8 hour AEGL-3 values were based on a NOAEL for mortality in mice of 4600 ppm for 4 hours. An uncertainty factor of 3 was applied. A value of 1.5 was used for time scaling (n) based on a rat mortality study of Adams et al. (1951). The 10-minute number was kept at a maximal level of 10,000 ppm based on the experience with trichloroethylene as an anesthetic agent. At concentrations above 10,00 ppm, cardiac arrhythmias may occur in humans (Orth and Gillespie, 1945; Pembleton, 1974). It was moved by Robert Snyder and seconded by Richard Thomas to accept the values (YES:19; NO:5; Abstain:0) (Appendix J).

SUMMARY OF AEGL VALUES FOR TRICHLOROETHYLENE (ppm)						
Classification	**10-minute**	**30-minute**	**1-hour**	**4-hour**	**8-hour**	**Endpoint**
AEGL–1	260	180	130	84	77	NOAEL for neuro-behavioral effects in humans
AEGL–2	960	620	450	270	240	Neurobehavioral effects in humans
AEGL–3	10,000	6100	3800	1500	970	Cardiac sensitization; threshold for lethality-mouse

RESPONSE TO NAS/COT/AEGL COMMENTS

TOLUENE
CAS Reg. No. 108-88-3

Chemical Manager: Larry Gephart, Exxonmobil
Staff Scientist: Sylvia Talmage, ORNL

Sylvia Talmage distributed the COT Subcommittee's review comments on the toluene AEGLs. The COT Subcommittee felt that, based on extensive human data, the toluene AEGL values were unrealistic. New values were proposed (Attachment 16), but the NAC suggested that further research into the data available for modeling, particularly for the longer-term AEGL-2 values, be

pursued. It was suggested that a comparison could be made between the AEGL-2 values modeled for the xylenes and AEGL-2 values for toluene.

ALLYL ALCOHOL
CAS Reg. No. 107-18-6

Chemical Manager: Mark McClanahan, CDC
Staff Scientist: Claudia Troxel, ORNL

The NAS/COT Committee reviewed the allyl alcohol document during its August 2001 meeting and made the following recommendation:

> *Because available data do not clearly indicate the extent to which the AEGL-3 value should exceed the AEGL-2 value, the subcommittee recommends that the AEGL-3 and AEGL-2 values be identical.*

Mark McClanahan summarized the AEGL values approved by the NAC/AEGL at the October 2000 meeting for allyl alcohol (Attachment 18). The basis for the AEGL-2 values was a 7-hour exposure repeated 60 times in which 10 rats/group experienced reversible lung irritation at 40 ppm. Time scaling for AEGL-2 used an n of 3 going to shorter times and an n of 1 going to longer times. AEGL-3 values were based on a one page summary from Union Carbide (1951) in which no rats exposed to 200 ppm for 1-hour died and was taken as the threshold for lethality. Time scaling for AEGL-3 values use an n of 3 going to short times and an n of 2 going to longer times. The use of an n of 2 was necessary to avoid producing AEGL-3 values essentially equal with the AEGL-2 value for 4-hours and smaller than the AEGL-2 value at 8-hours.

The revised TSD provided the following as support for the suggestion of setting AEGL-3 values equal to the AEGL-2 values:

- Study used for AEGL-3 is very weak - database does not provide good background for assessing acute lethal concentrations. Really is no clear indication of how much AEGL-3 value should exceed AEGL-2 value. Conversely, decent support for the AEGL-2 value, which is the level for "action."

- Would eliminate the inconsistency observed during the time scaling of the AEGL-2 and AEGL-3 values.

Thus, the proposed values for allyl alcohol, modified according to the suggestion by the NAS/COT are presented in the following table.

SUMMARY OF PROPOSED AEGL VALUES FOR ALLYL ALCOHOL (ppm)

Level	10-minute	30-minute	1-hour	4-hour	8-hour
AEGL-1	1.8	1.8	1.8	1.8	1.8
AEGL-2	9.6	9.6	7.7	4.8	3.5

AEGL-3	9.6	9.6	7.7	4.8	3.5

The NAC/AEGL disagreed with the idea of making AEGL-2 and AEGL-3 values equal. Ernest Falke suggested that data from Table 3, "Summary of Acute Lethal Inhalation Data in Laboratory Animals," are available to calculate an n value for time scaling rather than using the default value. Thus, NAC/AEGL directed the TSD Development Team to use all available data to set a value for n and recycle the TSD.

FURAN
CAS Reg. No. 110-00-9

Chemical Manager: George Rodgers, AAPCC
Staff Scientist: Claudia Troxel, ORNL

George Rodgers presented the status of furan as follows (Attachment 19). At its August 2001 meeting the COT reviewed the AEGL TSD on furan. Claudia Troxel presented the document at that time. The COT Subcommittee made many specific comments about the TSD. Most of these were editorial and have been addressed by Claudia. The one issue needing NAC discussion relates to the total uncertainty factor used to calculate the AEGL-2 and AEGL-3 values. We have never proposed AEGL-1 values because of the total lack of usable data. The furan database contains only one study suitable for derivation of AEGL-2 or-3 values. This study was done in rats by Terrill et al. in 1989. Groups of 10 rats (5 male and 5 female) were exposed for 1 hour to three different concentrations of furan. Surviving animals were sacrificed 14 days after exposure. No animals died at the two lower concentrations and 9/10 died at the highest concentration. A 1-hour LC_{50} was calculated to be 3466 ppm. In our initial consideration of furan, interspecies and intraspecies uncertainty factors of 10 and 3, respectively, were used. An additional modifying factor of 3 was used for a total uncertainty factor of 100. The COT has suggested a higher modifying factor because of the extremely poor data set. After discussion the NAC voted to change the modifying factor to 5 for a total uncertainty factor of 150. The values appear below. A motion to accept the revised values was made by Tom Hornshaw and seconded by George Rodgers. The vote was (YES:13; NO:5; Abstain:1) (Appendix K)

SUMMARY OF AEGL VALUES FOR FURAN (ppm)						
Classification	**10-minute**	**30-minute**	**1-hour**	**4-hour**	**8-hour**	**Endpoint**
AEGL–1	NR	NR	NR	NR	NR	Insufficient data
AEGL–2	12	8.5	6.8	1.7	0.85	Threshold for adverse effects - rat
AEGL–3	35	24	19	4.8	2.4	Threshold for lethality - rat

NR = Not recommended.

REVIEW OF CHEMICALS WITH ISSUES FROM

PREVIOUS MEETINGS

Sylvia Talmage presented the chronology on development of AEGL values for HCN and the studies used as "weight of evidence" for development of the AEGL-1 (Attachment 20). As of January, 2002, The HCN AEGL values/TSD have been accepted as final by NAS/COT. John Morawetz brought up points of disagreement with the description and use of some of the studies and values used for AEGL-1 development (Attachment 21). George Rodgers, the Chemical Manager, also disagreed with a statement taken from a NIOSH document. In order to resolve these issues, George Rodgers will rewrite the justification for the AEGL-1.

In addition, John Morawetz also passed out a handout that he prepared on the issues of AEGL applications to occupational settings (Appendix 22).

SECOND AEGL CHEMICAL PRIORITY LIST

Paul Tobin distributed the draft second AEGL chemical priority list to NAC/AEGL (Attachment 23). In addition, he described briefly how the priority list was put together from inputs provided by the participating agencies and interested stake holders. This list comprised 137 high priority and 236 low priority chemicals for AEGL development. He also explained the value of a chemical classes approach for AEGL development. Any comments on the draft priority list should be addressed to Paul Tobin.

Administrative Matters

1. George Alexeeff would like to discuss the inconsistency in endpoints used in development of AEGL values. This subject will be addressed at the June meeting.
2. John Morawetz handed out a memo in which he discussed the application of AEGL values to the occupational setting. The memo calls for a clear distinction to be made between occupational guidelines such as ACGIH and OSHA and AEGLs (Attachment 22).

The next meeting, NAC/AEGL-25, has been set for June 17-19, 2002, in Piscataway, N.J. (Rutgers University, hosted by Bob Snyder). More information about the lodging will be provided soon by Po-Yung Lu. The tentative NAC/AEGL-26 meeting is proposed for September 10-12, 2002, in Washington, D.C.

The meeting highlights were prepared by Po-Yung Lu and Sylvia Talmage, Oak Ridge National Laboratory, with input from the respective chemical managers.

LIST OF ATTACHMENTS

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

Attachment 1. NAC/AEGL-24 meeting agenda
Attachment 2. NAC/AEGL-24 attendee list
Attachment 3. TSDs reviewed at February NAS/COT/AEGL meeting
Attachment 4. TSDs Candidates for review at July/October NAS/COT/AEGL meetings
Attachment 5. COT/ Review Status of G-series Nerve Agents and VX
Attachment 6. Conference Flyer- Preparing for Biological & Chemical Terrorism: A New Jersey
Attachment 7. Data Analysis of Ammonia
Attachment 8. Data Analysis of Fluorine
Attachment 9. Data Analysis of Nitric acid and Nitrogen Dioxide
Attachment 10. Reference, Acute inhalation toxicity of white fuming nitric acid by ten Berge
Attachment 11. Data Analysis of Ethylenimine and Propylenimine
Attachment 12. Data Analysis of Methyl mercaptan
Attachment 13. Data Analysis of Phosphorus Trichloride
Attachment 14. BAMM handout on Acrylic Acid
Attachment 15. TSD Development Team Responses Federal Register Comments on Acrylic acid
Attachment 16. Data Analysis of Trichloroethylene
Attachment 17. Data Analysis of Toluene
Attachment 18. Data Analysis of Allyl Alcohol
Attachment 19. Data Analysis of Furan
Attachment 20. Chronology of HCN TSD Development
Attachment 21. Morawetz HCN discussion
Attachment 22. Issue: Applications of AEGLs to Occupational Settings
Attachment 23. AEGL Second Priority List

LIST OF APPENDICES

Appendix A. Revised meeting highlights of NAC/AEGL-23
Appendix B. Ballot for Ammonia
Appendix C. Ballot for Fluorine
Appendix D. Ballot for Methylmercaptan
Appendix E. Ballot for Phosphorus Trichloride
Appendix F. Ballot for Acrylic Acid
Appendix G. Ballot for Boron Trifluoride
Appendix H. Ballot for HFE-7100
Appendix I. Ballot for Uranium Hexafluoride
Appendix J. Ballot for Trichloroethylene
Appendix K. Ballot for Furan

National Advisory Committee for Acute Exposure Guideline Levels for Hazardous Substances

NAC/AEGL-24
April 9-11, 2002

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

AGENDA

Tuesday, April 9, 2002

10:00 AM	Introductory remarks and approval of NAC/AEGL-23 Highlights (George Rusch, Roger Garrett, and Paul Tobin)
10:15	NAS/COT/AEGL review status (Roger Garrett, Ernie Falke, and George Rusch)
10:30	AEGL 10-minutes values for Ammonia, Fluorine, Nitric acid, and Nitrogen dioxide (Larry Gephart/Kowetha Davidson, Ernie Falke/Sylvia Talmage, Loren Koller/Carol Forsyth)
12:00 PM	Lunch
1:00	AEGL 10-minutes values (continued)
1:30	AEGL-1values of Ethyleneimine and Propyleneimine (Mark McClanahan/Kowetha Davidson)
3:00	Break
3:15	Response to NAS/COT/AEGL comments: Toluene (Larry Gephart/Sylvia Talmage)
4:45	Status report of NAS/COT/AEGL comments: G-agents and VX (George Rusch)
5:00	Adjourn for the day

Wednesday, April 10, 2002

8:00 AM	Review of Trichloroethylene (Bill Bress/Marcel Raaij)
10:15	Break
10:30	Revision of Methylmercaptan (Doan Hansen/Cheryl Bast)
11:45	Lunch
12:45 PM	Revision of Phosphorus trichloride - new study (Tom Hornshaw/Bob Young)
2:00	Review of AEGL-1 of HCN (George Rusch, John Morawetz, George Rodgers/Sylvia Talmage)
2:30	Break
2:45	Review of comments received from February 15, 2002, *Federal Register Notice* - Boron trifluoride, Carbon tetrachloride, Chlorine, Chlorine dioxide, HFE-7100, Propylene oxide, and Uranium hexafluoride.
4:30	Administrative matters
5:00	Adjourn for the day

Thursday, April 11, 2002

8:00 AM	Review of comments received from May 2, 2001, *Federal Register Notice* - Acrylic acid (Ursula Gundert-Remy/Ernie Falke)
10:00	Break
10:15	Response to NAS/COT/AEGL comments: Allyl alcohol (Mark McClanahan/Claudia Troxel)
11:15	Response to NAS/COT/AEGL comments: Furan (George Rodgers/Claudia Troxel)
12:15 PM	Review of Second AEGL Priority Chemical List and Chemical Categories (Paul Tobin)
12:45	Adjourn meeting

NAC/AEGL-24
April 9-11, 2002

Attachment 2

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Taylor Tyler	HSMEC	trtyler@att.net

Chemicals Reviewed at February NAS/COT/AEGL Meeting

- HF
- HCl
- Phosgene
- Hydrogen Sulfide
- Diborane
- cis & trans Crotonaldehyde
- Perchloromethylmercaptan
- Iron Pentacarbonyl
- Nickel Carbonyl
- Allyl Amine
- Cyclohexylamine
- Ethylenediamine
- G Nerve Agents (GA, GB, GD, and GF) and VX

Attachment 3

Chemicals For Review at July and October NAS/COT/AEGL Meetings

- Methyl Isocyanate
- Toluene Diisocyanate
- Chlorine Trifluoride
- Furan
- Allyl Alcohol
- Chlorine Dimethyldichlorosilane
- Methyltrichlorosilane
- Boron Trichloride
- Boron Trifluoride
- HFE-7100
- Uranium Hexafluoride
- Chloromethylmethyl Ethers ✓
- Tetranitromethane ✓
- Toluene ✓
- Fluorine
- 1,2-Dichloroethene
- Phosphine
- Hydrazine
- Carbon Tetrachloride
- Chloroform
- 1,1,1-Trichloroethane
- Propionitrile
- Isobutyronitrile
- Methyl Acrylonitrile
- Ethylenimine
- Propylenimine
- Tetrachloroethylene

Attachment 4

COT Subcommittee on AEGLs (9th Meeting); Review of Interim Values for the G-series Nerve Agents (GA, GB, GD, GF) and Nerve Agent VX

6-7 Feb 2002

The National Academies/Beckman Center

Irvine, CA

Attachment 5

Presentation of Technical Support Documents

- Overview and Statement of National Need--Glenn Leach, Chemical Manager for Agent VX
- Nerve Agent Issues Analysis--Robert Young, AEGL Development Team
- Decision Logic for Estimating AEGLs--Annetta Watson, AEGL Development Team

COT Subcommittee Reviewers

- Ed Bishop, Lead Reviewer; Program Manager, Parsons Engineering Science, Inc.
- John Doull; Professor Emer., Dept. Pharmacology & Toxicology, Univ. Of Kansas Med. Ctr.
- Frederik de Wolff; Professor and Chair, Dept. of Toxicology, Leiden University Med. Ctr., Netherlands
- Franz Oesch; Prof. Pharmacology & Toxicology, Director of Toxicology Inst., Univ. of Mainz, Germany
- Dave Gaylor; Sciences International, Inc.
- Dan Krewski, Subcommittee Chair; Professor of Medicine, Epidemiology & Community Medicine, Univ. of Ottawa

Status

- COT Subcommittee review in-progress
- In keeping with broad support for expedited review of these compounds, TSD authors' response to Subcommittee concerns expressed at Beckman Center meeting provided to Kulbir Bakshi, COT Project Director, on 15 Mar 02
- TSD authors' response currently under consideration by Subcommittee Reviewers
- Subcommittee Interim Report expected May 02

Preparing for Biological and Chemical Terrorism: A New Jersey Perspective

June 6 and 7, 2002

at

the Environmental and Occupational Health Sciences Institute (EOHSI)* Piscataway, NJ

Sponsored by:
EOHSI
Rutgers University
UMDNJ-Center for BioDefense
University of Medicine and Dentistry of New Jersey

* EOHSI is a jointly sponsored program of UMDNJ-Robert Wood Johnson Medical School and Rutgers, The State University of New Jersey.

BACKGROUND

Since the events of the past year, biological and chemical terrorism has become an increasing threat to all Americans. New Jersey was in the spotlight during the anthrax episodes in 2001 and has experienced what many fear first hand. This conference will discuss some of the "lessons learned" as well as the current research on biological and chemical terrorism. It will be a synthesis of public health, basic research and emergency preparedness.

Program

7:30am **Registration and Continental Breakfast**

8:20 **Welcome**
Robert Snyder, PhD, Director, EOHSI
Keith Cooper, PhD, Cook College, Rutgers University
Nancy Connell, Ph.D., UMDNJ

8:35 **Nature of Biological and Chemical Terrorism Threats in New Jersey and a Review of Recent Biological Terrorism Incident(s) in New Jersey**
Captain Kevin J. Hayden, NJ State Police, Acting Commander, Emergency Management Section

9:20 **Biological Terrorism Agents: Basic Science and Basic Policy**
Nancy Connell, PhD, UMDNJ-NJMS Dept. of Microbiology and Molecular Genetics and the UMDNJ Center for BioDefense

10:05 **Chemical Terrorism Agents: Basic Science and Basic Policy**
Robert Snyder, Ph.D., EOHSI and *Member, National Advisory Committee for Acute Exposure Guideline Levels for Hazardous Substances, National Academy of Sciences*

10:45 **Break**

11:15 **Keynote Address: Emergency Preparedness in The Netherlands - Similarities with New Jersey**
Marc Ruitjen, PhD, Centrum Voor Epidemiologisch Onderzoek bij, the Netherlands

12:15 **Lunch**

1:30 **Symptoms, Health Effects, and Medical Response to Biological and Chemical Agents**
Michael Gochfeld, MD, PhD, EOHSI and UMDNJ-Robert Wood Johnson Medical School and

Attachment 6

Iris Udasin, MD, EOHSI and UMDNJ-Robert Wood Johnson Medical School

2:15 **New Jersey's Response to Mass Casualty/Mass Exposure Events**
George DiFerdinando, MD, MPH, Deputy Commissioner, Public Health Services, NJ Dept of Health and Senior Services

3:00 **Break**

3:30 **Community Exposure and Contaminant Modeling**
Paul Lioy, Ph.D., EOHSI and UMDNJ-Robert Wood Johnson Medical School and *Panos Georgopoulos, PhD, EOHSI and UMDNJ-Robert Wood Johnson Medical School*

4:15 **Sampling Techniques to Detect Airborne Bioaerosols**
Gediminas Mainelis, PhD ,EOHSI and Cook College

5:00 **Discussion**

5:15 **Adjourn**

<u>June 6, 2002 - Evening Program</u>
7:00pm - 9:00pm Public Forum
This "town meeting" type forum will provide an open exchange between the public and public health and policy experts.
Invited Speakers:
Senator Jon Corzine (invited); Congressman Rodney Frelinghuysen (invited); Leonard Cole, Ph.D., Rutgers University

<u>June 7, 2002</u>

8:00am **Continental Breakfast**

9:00 **Keynote Address: Current State of Emergency Preparedness in New Jersey**
Clifton Lacy, M.D., Acting Commissioner, New Jersey Department of Health and Senior Services

10:00 **Chemical Terrorism Agents: Determination of Exposure Limits to Chemical Agents**
George Rusch, PhD, Honeywell Corp. and *Chair, National Advisory Committee for Acute Exposure Guideline Levels for Hazardous Substances, National Academy of Sciences*

10:45 **Break**

11:15 **Public Health Surveillance: Applications to Biological and Chemical Terrorism**
William Halperin, MD, UMDNJ-New Jersey Medical School

12:00 **Lunch**

1:15 **Public Policy and Public Health Issues**
Michael Greenberg, PhD, EOHSI and Associate Dean, Edward J. Bloustein School of Planning and Public Policy, Rutgers University

1:45 **Breakout Demonstration**
Brendan McCluskey, UMDNJ-NJMS, University Hospital Emergency Medical Services

2:15 **Breakout Sessions: Table Top Exercises* - Mock Biological and/or Chemical Terror Incidents in New Jersey. Sessions Include:**

- Agriculture and Food Supply
- Analysis and Detection
- Business and Industry's Role in Emergency Planning and Response
- Ecological Considerations
- Economic Impact
- Emergency Response- Police and Law Enforcement
- Emergency Response- Fire, EMS, and Haz Mat
- Emergency Management
- Health Care Considerations
- Impact on Schools
- Media and Public Information Considerations
- Mental Health Considerations
- Post Event Surveillance
- Public Health and Public Policy
- Use of Epidemiological Data in Real Time Decision Making
- Worker Protection and Personal Protective Equipment

3:45 **Breakout Reporting**

5:15 **Wrap Up**

5:30 **Adjourn**

* The Table Top Exercise will simulate a biological and/or chemical terror incident in New Jersey and will ask participants to address specific aspects of the incident.

REGISTRATION FORM

Preparing for Biological and Chemical Terrorism: A New Jersey Perspective

Name _____
(First) (M.I.) (Last)

Affiliation _____

Address _____

Phone Number _____

Fax Number _____

E-Mail _____

Breakout Sessions

Please list your top three choices in order of preference. We will attempt to put you in your first choice, however, breakout space is limited and will be filled on a first come first serve basis.

_____ Agriculture and Food Supply
_____ Analysis and Detection
_____ Business and Industry's Role in Emergency Planning and Response
_____ Ecological Considerations
_____ Economic Impact
_____ Emergency Response- Police and Law Enforcement
_____ Emergency Response- Fire, EMS, and Haz Mat
_____ Emergency Management
_____ Health Care Considerations
_____ Impact on Schools
_____ Media and Public Information Considerations
_____ Mental Health Considerations
_____ Post Event Surveillance
_____ Public Health and Public Policy
_____ Use of Epidemiological Data in Real Time Decision Making
_____ Worker Protection and Personal Protective Equipment

REGISTRATION DEADLINE - May 10, 2002

[ ] $75 **Registration**
Includes Conference Materials and Meals

[ ] $25 **Student Registration (a current student ID should be submitted with registration form)**
Includes Conference Materials and Lectures Only

[ ] $0 **I plan on attending the evening public forum on June 6th.**

Amount Enclosed $_____
(Make Checks Payable to EOHSI - Biological/Chemical Terrorism Conf.)

Mail completed form with check to:
Candace E. Botnick, M.S., Public Affairs Manager
EOHSI, 170 Frelinghuysen Road, Piscataway, NJ 08854
For additional information contact:
Candace Botnick at 732/445-0206 or botnick@eohsi.rutgers.edu.

Preparing for Biological and Chemical Terrorism: A New Jersey Perspective

EOHSI
170 Frelinghuysen Road
Piscataway, NJ 08854

ACUTE EXPOSURE GUIDELINE LEVELS FOR AMMONIA

(10-MINUTE VALUES)

PRESENTED BY
KOWETHA DAVIDSON, ORNL, TOXICOLOGIST

LARRY GEPHART, CHEMICAL MANAGER

NAC/AEGL MEETING, WASHINGTON, DC
APRIL 9-11, 2002

Modifying Factor: 1
Animal to Human Dosimetric Adjustment: not applicable
Time Scaling: The AEGL-1 values for a odor detection were not changed across time because odor detection is not expected to change with time except for olfactory adaptation.
Data Adequacy: Several reports stated that the odor detection level for ammonia is between 5 and 53 ppm. Sufficient data were available for a fairly accurate documentation of the irritation threshold, which is slightly higher than the AEGL-1 level.

AEGL-1 VALUES FOR AMMONIA (CAS No. 7664-41-7)					
5 minutes	10 minutes	30 minutes	1 hour	4 hours	8 hours
25 ppm	25 ppm	25 ppm	25 ppm	25 ppm	25 ppm

Reference: MacEwen, J.D.; Theodore, J; Vernot, E.H. 1970. Human exposure to EEL concentrations of monomethylhydrazine, AMRL-TR-70-102, paper no 23. In: Proc. 1st Ann. Conf. Environ. Toxicol., September 9-11, 1970, Wright-Patterson AFB, OH. pp-355-363.

Pierce, J.O. 1994. Ammonia. In: Patty's Industrial Hygiene and Toxicology, 4th ed., Vol. II, Pt. A (Toxicology), G.D. Clayton and F.E. Clayton, Eds. John Wiley & Sons, Inc, New York. pp. 756-782.

Verberk, M.M. 1977. Effects of ammonia on volunteers. Int. Arch. Occup. Environ. Health. 39:73-81.

Test Species/Strain/Sex/Number: Humans

Exposure Route/Concentrations/Durations: Inhalation

Effects: Odor perception.

Endpoint/Concentration/Rationale: Odor perception. The range of odor detection for ammonia is from 5 to 53 (Pierce 1994). The value of 25 ppm was chosen as a midpoint to the reported ranges of perception. For example, Verberk 1977 found that humans exposed to 50 ppm found the odor to range from just perceptible to nuisance. MacEwen et al., 1970 reported that at 30 ppm ammonia was perceived as moderately intense to highly penetrating.

Uncertainty Factors/Rationale:
Total uncertainty factor: 1
Interspecies: not applicable
Intraspecies: 1 - most people should detect the odor at 25 ppm, concentration is below that causing irritation if irritation occurred it would be mild and confined to the nasopharyngeal region because of scrubbing efficiency.

AEGL-2 VALUES FOR AMMONIA (CAS No. 7664-41-7)					
5 minutes	10 minutes	30 minutes	1 hour	4 hours	8 hours
380 ppm	270 ppm	160 ppm	110 ppm	110 ppm	110 ppm

Reference: Verberk, M.M. 1977. Effects of ammonia on volunteers. Int. Arch. Occup. Environ. Health. 39:73-81.

Test Species/Strain/Sex/Number: Humans, mixed sex; 8 expert and 8 nonexpert subjects

Exposure Route/Concentrations/Durations: Inhalation; 50, 80, 110, or 140 ppm for durations up to 2 hours

Effects:
50 ppm: just perceptible to offensive odor; no sensation to nuisance eye, nose, and throat irritation; no sensation to distinctly perceptible urge to cough, chest irritation and general discomfort
80 ppm: just perceptible to offensive odor; no sensation to offensive eye, nose, throat and chest irritation and urge to cough; no sensation to nuisance general discomfort
110 ppm: distinctly perceptible to offensive odor; no sensation to offensive eye, nose, throat, and chest irritation, urge to cough, and general discomfort
140 ppm: just perceptible to offensive odor; just perceptible to unbearable eye irritation; no sensation to offensive nose, throat, and chest irritation, urge to cough, and general discomfort
severity ratings: 0 = no sensation, 1 = just perceptible, 2 = distinctly perceptible, 3 = nuisance, 4 = offensive, and 5 = unbearable

Endpoint/Concentration/Rationale: 110 ppm for 1 hours; respiratory tract and eye irritation and urge to cough ranged from no sensation to nuisance or offensive during the first hour of exposure. The range of responses at 2 hours was very similar to that at one hour. The non-experts considered the effects to be near the maximum response (offensive), whereas the expert responses were always of a lesser degree.

Uncertainty Factors/Rationale:
Total uncertainty factor:1

Interspecies: not applicable

Intraspecies: 1- AEGL based on response of most sensitive individual (responses ranged from just perceptible to offensive); the effects involved primarily the eyes and upper respiratory tract and asthmatics would be unlikely to respond differently, atopic subjects responded similarly to non-atopic subjects to a brief nasal exposure to ammonia; exercising subjects showed only a small equivocal decrease in pulmonary function, and the effects were less serious than those defined by the AEGL-2 level.

Modifying Factor: 1, values based on controlled exposure to human subjects

Animal to Human Dosimetric Adjustment: not applicable

Time Scaling: $C^n \times t = k$ where n = 2 based upon an analysis of empirical mouse and rat lethality data in which the times of exposure ranged from 10 to 60 minutes (ten Berge et al., 1986). Values for 4 and 8 hours are the same as the 1-hour AEGL value because the responses of the subjects did not change between 1 and 2 hours. In addition, the use of time scaling past 1 hour would drive AEGL-2 values into a range which humans are expected to tolerate for extended periods of time.

Data Adequacy: The AEGL-2 values were based on a study using human subjects but the effects were somewhat less serious than those defined by AEGL-2 level. Studies of long-term or irreversible effects in humans with exposure estimates were not available in the literature. In addition, adequate animals studies also were not available for deriving AEGL-2 values.

Endpoint/Concentration/Rationale: Lethality; LC_{01} = 3374 ppm (I) and 3317 ppm (II) for one hour are the estimated thresholds for lethality derived by probit analysis of the data. Both numbers when divided by an uncertainty factor of 3 give the same result when the AEGL value is expressed to 2 significant figures.

Uncertainty Factors/Rationale:
Total uncertainty factor: 3

Interspecies: 1, The mouse was unusually sensitive to ammonia. Applying a UF of 3 would yield a 30 minute AEGL-3 value of 480 ppm (in combination with a intraspecies UF of 3, the total UF would equal 10). In addition, humans can tolerate exposure to ammonia at 500 ppm for 30 minutes. Therefore, a lower UF of 1 is used.

Intraspecies: 3, A larger UF is not used because concentrations of ammonia that are life threatening cause severe tracheobronchial damage and pulmonary damage and these effects are not expected to be different for the elderly, asthmatics, and children and these effects would have a greater consequence than asthma. A UF of 3 should be sufficient to protect the elderly because data showed that they differ by a factor of 3 compared with younger people exposed to ammonia. Very young children may be less sensitive than adults or repair the respiratory damage more efficiently.

Modifying Factor: 1

Animal to Human Dosimetric Adjustment: 1

Time Scaling: $C^n \times t = k$ where n = 2 based upon an empirical analysis of mouse and rat lethality data in which the times of exposure ranged from 10 to 60 minutes (ten Berge et al., 1986).

Data Adequacy: No exposure estimates were available for humans who died from exposure to ammonia. Lethality data were available for two animal species, mice and rats. The AEGL-3 values were based upon two mouse studies that were in close agreement although they were conducted 12 years apart by two different laboratories using similar strains of mice.

AEGL-3 VALUES FOR AMMONIA

5 minutes	10 minutes	30 minutes	1 hour	4 hours	8 hours
3800 ppm	2700 ppm	1600 ppm	1100 ppm	550 ppm	390 ppm

Reference:
MacEwen, J.D.; Theodore, J; Vernot, E.H. 1970. Human exposure to EEL concentrations of monomethylhydrazine, AMRL-TR-70-102, paper no 23. In: Proc. 1st Ann. Conf. Environ. Toxicol., September 9-11, 1970, Wright-Patterson AFB, OH. pp-355-363. (I);

Kapeghian, J.C.; Mincer, H.H.; Hones, A.B.; et al. 1982. Acute inhalation toxicity of ammonia in mice. Bull Environ. Contam. Toxicol. 29:371-378. (II)

Test Species/Strain/Number: CF1 or ICR male mice, 10 or 12 per group

Exposure Route/Concentrations/Durations:
Inhalation: 0, 3600, 4550, or 5700 ppm for 1 hour (I)
Inhalation: 0, 1190, 1340, 2130, 3400, 3950, 4220, 4860 ppm for 1 hour (II)

Effects:
(I): Clinical signs: nasal and eye irritation, labored breathing, gasping, convulsions, and low body weight gain
Mortality: 3600 ppm (0/10), 4500 ppm (3/10), and 5720 ppm (9/10); LC_{01}: 3374 ppm
(II): Clinical signs: eye and nasal irritation, hypoactivity, labored breathing, ataxia, convulsions, and weight loss
Mortality: ≤3440 ppm (0/12), 3950 ppm (3/12), 4220 ppm (5/12), 4490 ppm (8/12), and 4860 ppm (12/12); LC_{01}: 3317 ppm

SUMMARY OF AEGL VALUES FOR AMMONIA [ppm (mg/m³)]

Classification	Exposure Duration						Endpoint (Reference)
	5 min	10 min	30 min	1 hour	4 hours	8 hours	
AEGL-1	25 (17)	25 (17)	25 (17)	25 (17)	25 (17)	25 (17)	Odor perception (Pierce, 1994)
AEGL-2	380 (266)	270 (189)	160 (112)	110 (77)	110 (77)	110 (77)	Irritation: eyes and throat; urge to cough (Verberk, 1977)
AEGL-3	3800 (2657)	2700 (1890)	1600 (1119)	1100 (769)	550 (385)	390 (273)	Lethality (Kapeghian et al., 1982; MacEwen and Vernot, 1972)

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

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

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

ACUTE EXPOSURE GUIDELINE LEVELS FOR FLUORINE
Derivation of 10-Minute Numbers

National Advisory Committee for AEGLs Meeting
April 9-11, 2002

ORNL Staff Scientist:
Sylvia S. Talmage

Chemical Manager:
Ernest Falke

Attachment 8

PROPOSED FLUORINE AEGLs

Classification	Exposure Duration				
	10-Minute	**30-Minute**	**1-Hour**	**4-Hour**	**8-Hour**
AEGL-1 (Nondisabling)	— **1.7 ppm**	2 ppm **1.7 ppm**	2 ppm **1.7 ppm**	1 ppm **1.7 ppm**	1 ppm **1.7 ppm**
AEGL-2 (Disabling)	**20 ppm**	11 ppm	5.0 ppm	2.3 ppm	1.5 ppm **2.3 ppm**
AEGL-3 (Lethal)	**36 ppm**	19 ppm	13 ppm	5.7 ppm	3.9 ppm **5.7 ppm**

Alternative Suggestion:
AEGL-2 and -3:

Considering the human experience,

experimental studies:

no respiratory difficulty:10 ppm for 3-5 min. every 15 min. for 2-3 hours

occupational exposures:

no effects at yearly average exposures of 0.3 to 1.4 ppm
(range <0.1 to 24.7 ppm) (Lyon 1962)

And, that accommodation occurs at low concentrations,

the 8-hour values can be set equal to the 4-hour values

NITRIC ACID and NITROGEN DIOXIDE

Derivation of 10-minute Values

- followed SOP (flatline or extrapolation)
- used previously accepted key studies and endpoints
- are supported by human and animal data
- time-scaled AEGL-2 and AEGL-3 10-minute values because key study exposure durations are ≤2 hours

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TIME SCALING

- $C^n \times t = k$ where n = 3.5
- n derived from NO_2 data
- Nitric acid and NO_2 have parallel dose-response curves for a 30-minute exposure
- same equation used for both chemicals

PROPOSED AEGL-1 VALUES

AEGL-1 Values for Nitric Acid (ppm)					
AEGL level	10-min	30-min	1-hr	4-hr	8-hr
AEGL-1	0.5	0.5	0.5	0.5	0.5

Key study: Sackner and Ford, 1981

Exposure: healthy humans; 1.6 ppm for 10 minutes

Effect: NOAEL

UF: 3 - intraspecies

PROPOSED AEGL-2 VALUES

AEGL-2 Values for Nitric Acid (ppm)					
AEGL level	10-min	30-min	1-hr	4-hr	8-hr
AEGL-2	6.7	4.9	4.0	2.7	2.2

Key study: Diem, L., 1907 (cited in Henschler, D., 1991)

Exposure: one human male; 11.5-12.2 ppm for 1 hour

Effect: respiratory irritation; cough; marked secretion from nose and salivary gland; burning of eyes and facial skin; lacrimation

UF: 3 - intraspecies

Time scaling: $C^n \times t = k$ where $n = 3.5$

PROPOSED AEGL-3 VALUES

AEGL-3 Values for Nitric Acid (ppm)					
AEGL level	10-min	30-min	1-hr	4-hr	8-hr
AEGL-3	37	27	22	15	12

Key study: Gray, E.LeB., et al., 1954

Exposure: rats; 244 ppm for 30 minute

Effect: LC_{50}

Modifying factor: 0.33 to estimate threshold for lethality

UF: 3 - 1: interspecies
3: intraspecies

Time scaling: $C^n \times t = k$ where n = 3.5

Summary of AEGL Values for Nitric Acid (ppm)					
Classification	Exposure Duration				
	10-Minute	30-Minute	1-Hour	4-Hour	8-Hour
AEGL-1 (Nondisabling)	0.5	0.5	0.5	0.5	0.5
AEGL-2 (Disabling)	6.7	4.9	4.0	2.7	2.2
AEGL-3 (Lethal)	37	27	22	15	12

PROPOSED AEGL-1 VALUES

AEGL-1 Values for Nitrogen Dioxide (ppm)					
AEGL level	10-min	30-min	1-hr	4-hr	8-hr
AEGL-1	0.5	0.5	0.5	0.5	0.5

Key study: Kerr, H.D. et al., 1978

Exposure: asthmatics; 0.5 ppm for 2 hours

Effect: slight burning of the eyes, slight headache, chest tightness or labored breathing with exercise in 7/13

UF: none

PROPOSED AEGL-2 VALUES

AEGL-2 Values for Nitrogen Dioxide (ppm)					
AEGL level	10-min	30-min	1-hr	4-hr	8-hr
AEGL-2	20	15	12	8.2	6.7

Key study: Henschler, D. et al., 1960

Exposure: normal humans; 30 ppm for 2 hours

Effect: burning sensation in nose and chest, cough, dyspnea, sputum production

UF: 3 - intraspecies

Time scaling: $C^n \times t = k$ where $n = 3.5$

PROPOSED AEGL-3 VALUES

AEGL-3 Values for Nitrogen Dioxide (ppm)					
AEGL level	10-min	30-min	1-hr	4-hr	8-hr
AEGL-3	34	25	20	14	11

Key study: Henry, M.C. et al., 1969

Exposure: monkeys; 50 ppm for 2 hours

Effect: marked irritation

UF: 3 - 1: interspecies
3: intraspecies

Time scaling: $C^n \times t = k$ where n = 3.5

Summary of AEGL Values for Nitrogen Dioxide (ppm)					
Classification	Exposure Duration				
	10-Minute	30-Minute	1-Hour	4-Hour	8-Hour
AEGL-1 (Nondisabling)	0.5	0.5	0.5	0.5	0.5
AEGL-2 (Disabling)	20	15	12	8.2	6.7
AEGL-3 (Lethal)	34	25	20	14	11

Attachment 10

Acute inhalation toxicity of white fuming nitric acid

Introduction

One of the key studies for red fuming and white fuming nitric acid and nitrogen dioxide is the study of Gray et al. (1954). Unfortunately he expressed all the LC50s as NO2. He observed for all three substances the LC50 to be in the same order of magnitude expressed as NO2. However , the quoted LC50s have to be corrected for the NO2 content, which is 100% in case of NO2, 8 to 17% for red fuming nitric acid and only 0.1 to 0.4 % for wet fuming nitric acid.

Acute inhalation toxicity of nitric acid

Gray et al. (1954) studied the acute inhalation toxicity of nitrogen dioxide, red fuming nitric acid and white fuming nitric acid. The vapour was generated by dripping the liquid on glass wool. A stream of air, dried over sulfuric acid and Drierite, was passed over the glass wool surface, on which the nitric acid was dispersed. In this way the liquid was completely evaporated and led to the exposure chambers. So the composition of the vapour (NO2 and HNO3) reflects the composition of the liquid red fuming nitric acid and white fuming nitric acid.

Gray et al. (1954) measured the concentration of nitrogen dioxide and not that of nitric acid. The method was specific for nitrogen dioxide. It was based on the diazotization of sulfanilic acid by NO2, which is then coupled with alfa-naphtylamine, with resultant color formation. A nearly identical method is presently used for personal sampling and specific analysis of NO2 (Palmes et al. 1976).

Gray et al. (1954) observed the following LC50s, expressed as NO2:

Chemical	NO2 (% w/w)	LC50 mg/m^3 30 minutes as NO2		LC50 mg/m^3 240 minutes as NO2	
		as NO2	total	as NO2	total
NO2	100%	333	333	169	169
red fuming nitric acid	15 %	265	1800	128	850
white fuming nitric acid	0.5 %	467	93400	[60] estimate	[12000] estimate

There is not any reason to doubt of the accuracy of the NO2 analysis. Hine et al. (1970) studied the effects of acute exposures to nitrogen dioxide and arrived at the same LC50s for NO2 as Gray et al. (1954).

Gray et al. (1954) made the following statements:
- the primary toxic constituent is NO2.
- the acid content of the vapours play a very secondary role in toxicity.
- the toxicity of wet fuming nitric acid was much less than that of red fuming nitric acid or nitrogen dioxide on the basis of evaporated total mass of the acids.
- exposure to white fuming nitric acid caused acid burns in rats, but red fuming nitric acid and NO2 did not.

The main conclusion from this study is, that white fuming nitric acid, consisting mainly of HNO3, is much less toxic than NO2. The LC50 for 240 minutes exposure to white fuming nitric acid is estimated to be 12000 mg/m^3 (4600 ppm). This is to be expected from the water solubility of nitric acid. Nitric acid is very well soluble in water, while NO2 is not. So HNO3 will be absorbed in the upper airways and cause irritation of the upper respiratory tract, without causing severe damage at levels, that are lethal in case of exposure to NO2 by severe damage to the lower respiratory tract.

Confusion in the scientific literature

Because Gray et al. (1954) reported the LC50s of NO2, red fuming nitric acid and white fuming nitric acid as NO2, people have interpreted these values as should NO2 on a molecular weight basis be converted to HNO3 (NIOSH 1976). This is a wrong interpretation, because:
- it assumes that NO2 and HNO3 have an identical mode of local toxic action. This is considered improbable because of different deposition behaviour in the respiratory tract due to different water solubility.
- due attention is not given to the experimental findings of Gray et al. (1954) on the toxicity of nitrogen dioxide, red fuming nitric acid and white fuming nitric acid.

The implication for the occupational exposure limit of HNO3

Because HNO3 is at least 50 times less toxic than NO2 on ppm basis, the occupational exposure limit and the intervention limit values in case of accidental release should at least reflect this difference in acute local toxicity.

It is advised to apply for white fuming nitric acid the occupational exposure limit and intervention limit values of HCl. HCl and HNO3 cause irritation of the upper respiratory tract by their strong acid reaction with the mucous membranes. It is expected that safe levels in ppm for hydrochloric acid are also safe for nitric acid.

In practice HNO3 will always be present together with more or less NO2. NO2 is the more hazardous agent. Control of NO2 exposure will generally control HNO3 exposure below hazardous levels.

References

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Hine C.H., Meyers F.H. and Wright R.W., 1970. Pulmonary changes in animals exposed to nitrogen dioxide, effects of acute exposures. Toxicology and Applied Pharmacology 16, 201-213.

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W.F. ten Berge,
DSM, Heerlen, NL.
17 December 1999.

ACUTE EXPOSURE GUIDELINE LEVELS FOR ETHYLENIMINE & PROPYLENIMINE

(AEGL-1 VALUES)

PRESENTED BY
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NAC/AEGL MEETING, WASHINGTON, DC
APRIL 9-11, 2002

RATIO AEGL-2 TO AEGL-1				
time	number of chemicals	geometric mean	multiplicative standard deviation	range
30-minute	40	8.85	3.70	1.50 to 1066.67
8-hour	40	3.61	3.05	1.30 to 566.67
RATIO AEGL-3 TO AEGL-2				
30-minute	72	3.97	1.94	1.67 to 36.40
8-hour	73	3.62	2.00	1.33 to 40.77
RATIO OF AEGL-1/AEGL-2 TO AEGL-3/AEGL2				
30-minute	NA	2.2	NA	NA
8-hour	NA	1.0	NA	NA

AEGL -1 VALUES Ethylenimine				
10 minutes	30 minute	1 hour	4 hour	8 hour
11 ppm	3.3 ppm	1.5 ppm	No values derived	

Key Reference: Carpenter, C.P.; Smyth, H.F., Jr.; Shaffer, C.B. 1948. The acute toxicity of ethylene imine to small animals. J. Ind. Hyg. Toxicol. 30:2-6.

Test Species/Strain/Number: Details presented in the Derivation Summary of AEGL-2 Values

Exposure Route/Concentration/Durations: See the Derivation Summary of AEGL-2 Values

Effects: See Effects for the Derivation Summary of AEGL-2 Values

Endpoint/Concentration/Rationale: AEGL-1 values were based on dividing the AEGL-2 values by a factor of 3, to adjust from a no effect level for AEGL-2 to a no effect level for AEGL-1 effects. The AEGL-2 values were based on a no-effect-level for lethality in the guinea pig, 10 ppm exposure for 4 hours; effects at 25 ppm and higher were more severe than those defined for AEGL 2. Exposure to 25 ppm for durations greater than 3 hours caused extreme respiratory difficulty.

Uncertainty Factors/Rationale:
Total uncertainty factor: The total uncertainty factor for AEGL-2 was equal to 10
Interspecies: same as described for the Derivation Summary of AEGL-2 Values
Intraspecies: same as described for the Derivation Summary of AEGL-2 Values

Modifying Factor: not applicable

Animal to Human Dosimetric Adjustment: not applicable

Time Scaling: See the rationale for AEGL-2

Data Adequacy: No specific data were not available for deriving AEGL-1 values; therefore, AEGL-2 values were scaled by a factor of 3 to derive AEGL-1 values for exposure duration of 10, 30, and 60 minutes. No values were derived for the 4- and 8-hour durations, because they would be below the published odor detection level of 0.69 1 1.9 ppm (Berzins 1967) and 2 ppm (Carpenter 1948) for ethylenimine.

AEGL -1 VALUES Propylenimine				
10 minutes	30 minute	1 hour	4 hour	8 hour
28	8.3	3.8	No values derived	

Reference: None (based on relative toxicity between ethylenimine and propylenimine and using AEGL-1 values for ethylenimine.

Test Species/Strain/Number: not applicable

Exposure Route/Concentration/Durations: not applicable

Effects: not applicable

Endpoint/Concentration/Rationale: not applicable; a relative potency factor of 5 was applied to AEGL-1 values for ethylenimine

Uncertainty Factors/Rationale: not applicable
Total uncertainty factor:
Interspecies:
Intraspecies:

Modifying Factor: 2 (limited database)

Animal to Human Dosimetric Adjustment: not applicable

Time Scaling: not applicable

Data Quality and Support for AEGL Values: No data for AEGL-1 were found in the literature. Therefore, the relative toxicity approach was used in which the toxicity of ethylenimine was compared with that of propylenimine. Moreover, experimental data also were not available to derive the AEGL-1 values for ethylenimine and the values were derived by scaling the AEGL-2 values by a factor of 3.

Summary of Proposed AEGL Values for Ethylenimine[a,b] [ppm (mg/m^3)]						
Classification	**10 min**	**30 min**	**1 hour**	**4 hour**	**8 hour**	**Endpoint (Reference)**
AEGL-1 (Nondisabling)	11 (20)	3.3 (5.9)	1.5 (2.7)	No values derived[c]		AEGL-2 values divided by a factor of 3
AEGL-2 (Disabling)	33 (59)	9.8 (18)	4.6 (8.2)	1.0 (1.8)	0.47 (0.84)	NOEL for extreme respiratory difficulty (Carpenter et al., 1948)
AEGL-3 (Lethal)	51 (91)	19 (34)	9.9 (18)	2.8 (5.0)	1.5 (2.7)	Threshold for lethality (Carpenter et al., 1948)

[a]AEGL-2 and -3 values do not take into consideration the potential cancer risk due to exposure to ethylenimine.
[b]Effects at these concentrations may be delayed until after exposure; toxic levels may be absorbed through the skin.
[c]Values would be below the odor threshold for ethylenimine.

Summary of Proposed AEGL Values for Propylenimine[a,b]						
Classification	**ppm (mg/m^3)**					**Endpoint (Reference)**
	10 minute	**30 minute**	**1 hour**	**4 hour**	**8 hour**	
AEGL-1[c]	28 (64)	8.3 (19)	3.8 (8.8)	No values derived		Relative toxicity approach
AEGL-2[c]	83 (200)	25 (58)	12 (28)	2.5 (5.8)	1.2 (2.8)	NOEL for extreme respiratory difficulty (Carpenter et al., 1948)
AEGL-3	170 (398)	50 (120)	23 (58)	5.1 (12)	2.4 (5.6)	Lethality threshold (Carpenter et al., 1948)

[a]AEGL-2 and -3 values do not take into consideration the potential cancer risk due to inhalation exposure to propylenimine.
[b]Effects including lethality, irritation to eyes, and irritation to the respiratory tract may be delayed until after exposure; propylenimine may be absorbed thorough the skin in toxic quantities.
[c]AEGL values for propylenimine = AEGL for ethylenimine × 5 (relative potency factor) ÷ 2 (modifying factor).

COMPARISON OF METHYL MERCAPTAN AND HYDROGEN SULFIDE AEGL VALUES

Methyl Mercaptan (CH_3SH)- 4-hr rat LC_{50} = 675 ppm (Tansy et al., 1981)

Hydrogen Sulfide (H_2S)- 4-hr rat LC_{50} = 444 ppm (Tansy et al., 1981)

Ratio of Methyl Mercaptan LC_{50} to Hydrogen Sulfide LC_{50} = 675 ÷ 444 = 1.5

AEGL-1

	10-min	30-min	1-hr	4-hr	8-hr
H_2S value	0.25 ppm	0.20 ppm	0.17 ppm	0.12 ppm	0.11 ppm
CH_3SH value	26 ppm	26 ppm	21 ppm	13 ppm	8.6 ppm
H_2S value ÷ CH_3SH value (ratio)	104	130	124	108	78
H_2S value x 1.5	0.38 ppm	0.30 ppm	0.26 ppm	0.18 ppm	0.17 ppm

Attachment 2

COMPARISON OF METHYL MERCAPTAN AND HYDROGEN SULFIDE AEGL VALUES

Methyl Mercaptan (CH_3SH)- 4-hr rat LC_{50} = 675 ppm (Tansy et al., 1981)

Hydrogen Sulfide (H_2S)- 4-hr rat LC_{50} = 444 ppm (Tansy et al., 1981)

Ratio of Methyl Mercaptan LC_{50} to Hydrogen Sulfide LC_{50} = 675 ÷ 444 = 1.5

AEGL-2

	10-min	30-min	1-hr	4-hr	8-hr
H_2S value	42 ppm	32 ppm	28 ppm	20 ppm	17 ppm
CH_3SH value	59 ppm	59 ppm	47 ppm	30 ppm	19 ppm
H_2S value ÷ CH_3SH value (ratio)	1.4	1.8	1.6	1.5	1.1
H_2S value x 1.5	63 ppm	48 ppm	42 ppm	30 ppm	26 ppm

COMPARISON OF METHYL MERCAPTAN AND HYDROGEN SULFIDE AEGL VALUES

Methyl Mercaptan (CH_3SH)- 4-hr rat LC_{50} = 675 ppm (Tansy et al., 1981)

Hydrogen Sulfide (H_2S)- 4-hr rat LC_{50} = 444 ppm (Tansy et al., 1981)

Ratio of Methyl Mercaptan LC_{50} to Hydrogen Sulfide LC_{50} = 675 ÷ 444 = 1.5

AEGL-3

	10-min	30-min	1-hr	4-hr	8-hr
H_2S value	76 ppm	60 ppm	50 ppm	37 ppm	31 ppm
CH_3SH value	80 ppm	80 ppm	63 ppm	40 ppm	20 ppm
H_2S value ÷ CH_3SH value (ratio)	1.1	1.3	1.3	1.1	0.65
H_2S value x 1.5	114 ppm	90 ppm	75 ppm	56 ppm	47 ppm

Odor as an Endpoint for AEGL-1 Values for Methyl Mercaptan

Odor Threshold x 12 = Level of Annoyance (LOA)

Odor Threshold	Reference	LOA
0.00000015 ppm	Williams et al., 1977	0.0000018 ppm
0.000102 ppm	ONSL0135 Japan	0.00122 ppm
0.00099 ppm	Wilby, 1969	0.0119 ppm
0.019 ppm	Nishida et al., 1979	0.228 ppm
0.021000 ppm	Patte, 1975	0.252 ppm
0.041 ppm	Katz and Talbert, 1930	0.492 ppm

AEGL-2 VALUES				
10 minute	**30 minute**	**1 hour**	**4 hour**	**8 hour**
59 ppm	**59 ppm**	**47 ppm**	**30 ppm**	**19 ppm**
Key Reference: Elf Atochem. 1996.				
Test Species: Mouse				
Concentration: 258 ppm Duration: 6 hr. Endpoint: Shallow breathing and hypoactivity: was considered to represent a threshold for potentially serious, irreversible effects that might prevent escape				

Uncertainty Factors/Rationale: Total UF = 10

Intraspecies: 3- Considered sufficient due to the steepness of the lethal response curve (600 ppm - 20% dead; 700 ppm - 100% dead; 675 ppm 4-hr rat LC_{50}; 429 ppm 4-hr rat LC_{01}) which implies limited individual variability.

Interspecies: 3. Although an interspecies uncertainty factor of 10 might normally be applied due to limited data, AEGL-2 values calculated utilizing a total UF of 30 would yield values that are inconsistent with the total data base.

AEGL-2 values for methyl mercaptan would range from 20 to 6.3 ppm, and no effects were noted in rats exposed to17 ppm methyl mercaptan 7 hours/day, 5 days/week for 3 months. It is unreasonable to expect that people exposed to this range of methyl mercaptan for 10-minutes to 8-hours would experience effects defined by AEGL-2.

The use of a total UF of 30 would yield AEGL-2 values 2- to 3-fold below the AEGL-2 values derived for hydrogen sulfide. Because a robust database exists for hydrogen sulfide and because data suggest that methyl mercaptan is less toxic than hydrogen sulfide, it would be inconsistent with the total data set to derive AEGL-2 values for methyl mercaptan that are below the AEGL-2 values for hydrogen sulfide.

Time Scaling: default 'n' values of 1 (8-hr) or 3 (30-min, 1-hr, 4-hr). The 30-minute AEGL-2 value was adopted as the 10-minute AEGL-2 value due to the added uncertainty of extrapolating from a 6-hour time point to 10-minutes

Support for Proposed Values: The proposed AEGL-2 values are considered protective because rats exposed to 57 ppm methyl mercaptan 7 hours/day, 5 days/week for 3 months experienced only decreased body weight (Tansy et al., 1981).

AEGL-3 VALUES				
10 minute	**30 minute**	**1 hour**	**4 hour**	**8 hour**
80 ppm	**80 ppm**	**63 ppm**	**40 ppm**	**20 ppm**
Key Reference: Tansy et al., 1981				
Test Species: Rat				
Concentration: 400 ppm Duration: 4 hr. Endpoint: Highest nonlethal concentration				

Uncertainty Factors/Rationale: Total UF = 10

Intraspecies: 3- Considered sufficient due to the steepness of the lethal response curve (600 ppm - 20% dead; 700 ppm - 100% dead; 675 ppm 4-hr rat LC_{50}; 429 ppm 4-hr rat LC_{01}) which implies limited individual variability.

Interspecies: 3. Although an interspecies uncertainty factor of 10 might normally be applied due to limited data, AEGL-3 values calculated utilizing a total UF of 30 would yield values that are inconsistent with the total data base.

AEGL-3 values for methyl mercaptan would range from 27 to 6.7 ppm, and no effects were noted in rats exposed to17 ppm methyl mercaptan 7 hours/day, 5 days/week for 3 months. It is unreasonable to expect that people exposed to this range of methyl mercaptan for 10-minutes to 8-hours would experience effects defined by AEGL-3.

The use of a total UF of 30 would yield AEGL-3 values 2- to 4-fold below the AEGL-2 values derived for hydrogen sulfide. Because a robust database exists for hydrogen sulfide and because data suggest that methyl mercaptan is less toxic than hydrogen sulfide, it would be inconsistent with the total data set to derive AEGL-3 values for methyl mercaptan that are below the AEGL-3 values for hydrogen sulfide.

Time Scaling: default 'n' values of 1 (8-hr) or 3 (30-min, 1-hr, 4-hr). The 30-minute AEGL-3 value was adopted as the 10-minute AEGL-3 value due to the added uncertainty of extrapolating from a 4-hour time point to 10-minutes

Support for Proposed Values: The proposed AEGL-3 values are considered protective because rats exposed to 57 ppm methyl mercaptan 7 hours/day, 5 days/week for 3 months experienced only decreased body weight (Tansy et al., 1981) and rats exposed to 100 ppm methyl mercaptan 6 hours/day for 10 days experienced occasional restlessness and bronchopneumonia at necropsy (DuPont, 1992).

Attachment 13

Phosphorus Trichloride
Revisit

NAC/AEGL-24
April 9-11, 2002

U.S. Department of Transportation
DOT Headquarters/Nassif Building. Rms 6200-6204

Hazleton Laboratories, 1983

- 15 rats/sex/group exposed to PCl_3 (0.5, 3.0, or 10. ppm [0.49, 3.37, and 10.96 analytical]) 6 hrs/day, 5 days/wk for 4 weeks
- no deaths; no treatment related adverse clinical signs
- histopathology findings (primarily nasal region) in high-dose group; no hematological or clinical chemistry alterations, no effect on body or organ weights
- 3.4 ppm NOAEL
- 11 ppm LOAEL

?? AEGL-1 Phosphorus trichloride ??

- Not recommended due to lack of available data with which to develop scientifically defensible values
- NOAEL of 3.4 ppm for rats following multiple exposures (Hazleton Labs, 1994) but no single-exposure effect data consistent with AEGL-1 effects
- Sassi (1952) - 1.8 to 3.6 ppm normal conditions in PCl_3 plant
- Proposal: use rat NOAEL of 3.4 ppm, 6 hours

AEGL-1 VALUES FOR PHOSPHORUS TRICHLORIDE					
	10-min	30-min	1-hr	4-hr	8-hr
AEGL-1	0.26 ppm	0.26 ppm	0.21 ppm	0.13 ppm	0.085 ppm

- UF intraspecies = 3; UF interspecies = ~~10~~ 3
- n =1 or 3

?? AEGL-2 Phosphorus trichloride ??

- Previously not developed
- Sassi (1952) - humans; exposure to ~14-27 ppm for 2-6 hrs (LOAEL) resulted in burning eyes and throat, photophobia, chest tightness pharyngeal irritation, mild bronchitis; reversible; 1.8-3.6 ppm "normal conditions"
- Hazleton Laboratories (1983) - rats; 11 ppm (LOAEL), 6 hrs/day, 5 days/wk for 4 weeks produced histopathologic alterations in the respiratory tract but no hematologic, biochemical, or ophthalmologic effects; 3.4 ppm was NOAEL
- Proposal: 2-hr exposure of humans to 14 ppm; upper respiratory tract irritation, bronchitis, photophobia; although a LOAEL, it can be considered a NOAEL for AEGL-2; Intraspecies UF of 10, *n* of 1 and 3

AEGL-2 VALUES FOR PHOSPHORUS TRICHLORIDE					
	10-min	30-min	1-hr	4-hr	8-hr
AEGL-2	3.2 ppm	2.2 ppm	1.8 ppm	0.7 ppm	0.35 ppm

- Justification:
  - 4-week exposure (6 hrs/day, 5 days/wk) of rats to 11 ppm produced histologic changes in respiratory tract (Hazleton Laboratories, 1983)
  - human exposure effects not necessarily AEGL-2 severity; up to 3.6 ppm "normal condition" (Sassi,1952)

AEGL-3 Phosphorus trichloride

- Previously proposed AEGL-3 not consistent with overall data set

AEGL-3 VALUES FOR PHOSPHORUS TRICHLORIDE					
	10-min	30-min	1-hr	4-hr	8-hr
AEGL-3 (currently approved)	1.1 ppm	1.1 ppm	0.88 ppm	0.56 ppm	0.28 ppm
AEGL-3 (revised)	3.3 ppm (4.8 ppm)*	3.3 ppm	2.7 ppm	1.7 ppm	0.84 ppm

* extrapolated using n=3

- Proposed AEGL-3 based upon 3-fold reduction in the 4-hr LC_{50} for guinea pigs (50.1 ppm/3 = 16.7 ppm) (Weeks et al., 1964); UF of β (interspecies) and 3 (intraspecies); n of 1 and 3

- Revised AEGL-3 justification
  - humans exposed to 14-27 ppm for 2-6 hours with only irritation (Sassi, 1953)
  - 4-week exposure (6 hrs/day, 5 days/wk) of rats to 11 ppm produced histopathologic changes in respiratory tract (Hazleton Laboratories, 1983)

Basic Acrylic Monomer Manufacturers

Comments on the NAS AEGL Committee's proposal for Acute Exposure Guidelines for Acrylic Acid

ATOFINA Chemicals, Inc
BASF Corporation
Celanese Ltd.
The Dow Chemical Company
Rohm and Haas Company

Attachment 14

AEGL Committee Proposal

July 2000, Draft

- AEGL-1
  - 1ppm (3mg/m^3)
  - All time intervals equivalent
  - Odor detection threshold in humans
- AEGL-2
  - 26 ppm (78 mg/m^3)
  - All time intervals equivalent
  - Excessive blinking and potential eye closure in rabbits (escape avoidance)
- AEGL-3
  - 470 ppm (1400 mg/m^3) - 10 minutes
    250 ppm (750 mg/m^3) - 30 minutes;
    170 ppm (510 mg/m^3) - 1 hour
    77 ppm (231 mg/m^3) - 4 hours;
    51 ppm (153 mg/m^3) - 8 hours
  - Lethality in rats

BAMM Comments
AEGL-1

- Consider basing the AEGL-1 value on mild irritancy rather than odor threshold.
  - Focal nasal lesion observed in rats and mice.
  - Mild lesions,as those occurring from low air concentrations or higher concentrations for shorter time intervals are reversible in nature
  - Severity of lesion is dose/time dependent; for instance occurring at air concentrations as low as 5 ppm in mice exposed 6-hours/day for 90-days or for 22 hours per day for 2-weeks.
  - NOEL for mice (the most sensitive species) was 5 ppm, 6 hours/day for 2 weeks and 25 ppm in rats (6-hours/day for 90-days).
- BAMM believes these data support AEGL-1 values between 5 and 10 ppm possibly time dependent.

Odor not an Appropriate End-Point to Establish an AEGL-1 Value for Acrylic Acid

- Good dose/response data currently exits for primary and sensory irritation on which to base an AEGL-1 value.
- Odor in and of itself not an "adverse effect"
  - Response to odor dependent on character and strength.
  - Occupational exposure limits well above odor threshold without overt complaints.

BAMM Comments
AEGL-2

- Consider basing AEGL-2 value on avoiding impairment of escape rather than on mild, reversible, focal lesions in the olfactory mucosa of rodents and primates.
- Blinking and involuntary eye closure noted during exposure in rabbits at 125 ppm (mild effects in one rabbit at 60 ppm).
- BAMM believes these data support AEGL-2 value(s) between 60 and 75 ppm.

BAMM Comments
AEGL-3

- BAMM is concerned that conservative values proposed for AEGL-3, based on lethality in rats, and particularly those for the longer time intervals will lack credibility.
  - Subchronic studies (exposed for 6-hours/day, 5-days/week) conducted in mice and rats at air concentrations up to 75 ppm without lethality.
  - Rabbits exposed for 6-hours/day for 10 consecutive days up to air concentrations of 250 ppm without lethality.
  - Vapor concentrations up to 2000 ppm for 60 minutes not lethal to rats as demonstrated in extensive studies by Hagan and Emmons (1988) and Nachreiner and Dodd (1988).
- BAMM believes these data support AEGL-3 value(s) in the range of 300-500 ppm (8 hours) to 1000-1500 ppm (10 minutes).

Summary

- BAMM asks the AEGL to reconsider the currently proposed AEGL values giving consideration to the following:
  - AEGL-1 values in the range of 5 to 10 ppm based on irritancy
  - AEGL-2 values in the range of 60 to 75 ppm in order to avoid impairment of escape.
  - AEGL-3 values of 1000 to 1500 ppm for shorter time intervals to 300 to 500 ppm for longer time intervals based on a wealth of lethality data from laboratory animal studies.

3AMM 120i - Acrylic Acid - reply 32.wpd

Attachment 15

Comments from The Basic Acrylic Monomer Manufacturers, Inc.

The Basic Acrylic Monomer Manufacturers, Inc. initially submitted comments on the proposed AEGL values for acrylic acid on May 31, 2001. These comments were discussed at the September 2001 Meeting of the AEGL Committee. In response to this discussion, the Basic Acrylic Monomer Manufacturers, Inc. revised and extended its comments on November 9, 2001. In addition, the histopathological results of an inhalation study in monkeys were submitted by the Basic Acrylic Monomer Manufacturers on December 31, 2001.

- ***AEGL-1 should be based on irritation as endpoint and not on odor.***

- ***The proposed AEGL-1 values are overconservative based on data in "Guidance for the Application of Odor in the Derivation of AEGL-1" by R. van Doorn, M. Ruijten and T. van Harreveld because comparison of AEGL-1 values for 7 chemicals with the odor threshold revealed that the latter was 30-4200 fold lower than the AEGL-1.***

- ***Using the above mentioned Guidance, a Level of Concern of about 40 ppm is calculated for acrylic acid.***

- ***Irritancy is a more appropriate endpoint and a value in the range of 2-10 ppm would be more in line with the AEGL definition***

Reply

- In its current form, the "Guidance for the Application of Odor in the Derivation of AEGL-1" is only a draft proposal, which has to be discussed and agreed upon in the AEGL Committee to become part of the AEGL methodology. The contents of this document are not part of the AEGL's Standing Operating Procedures.

- The proposed Guidance document (version of June 2, 2001) suggests to derive a Level of Annoyance, not a Level of Concern. When better data are lacking, this Level of Annoyance is roughly calculated by multiplying the odor detection threshold with a factor of 12 (corresponding to a default kw coefficient * of 2.33). For acrylic acid, the odor detection threshold is about 0.09 ppm (the 1 ppm recognition threshold is not the appropriate starting point here) and with a factor of 12 a Level of Annoyance of 1.1 ppm would result (which is exactly the proposed AEGL-1 level).

- The AEGL Committee decided to base the AEGL-1 value on odor as an endpoint, nevertheless, the TSD presents an alternative derivation based on histological effects on the olfactory mucosa in animals which derives at very similar concentrations (between 1.3 ppm for 8 h and 3.8 ppm for 30 min).

* The chemical-specific Weber-Fechner coefficient kw describes how the experimental odor detection threshold relates to the air concentration resulting in distinctly detectable odor under field conditions.

Comments from The Basic Acrylic Monomer Manufacturers, Inc.

- ***AEGL-2 should be based on the increase in likelihood that people might become inable to escape by irritation.***

- ***The proposed AEGL-2 values are based on olfactory epithelial cell degeneration. While focal degeneration is reversible at the LOEL, it only becomes irreversible when basal stem cell morphology is disrupted. If the derivation is based on histological effects, the latter should be the starting point.***

- ***To protect people from becoming disabled by irritation, values in the range of 50-75 ppm based on blepharospasm in rabbits are appropriate.***

Reply

- The AEGL Committee has discussed the relevance of blepharospasm in rabbits and eyelid closure in rats as a possible sign of impaired ability to escape. However, the question whether blepharospasm in rabbits is an adequate indication of impaired ability to escape in humans and the persistence and relevance of this effect for longer exposure times could not be solved. It was thus decided to base the AEGL-2 on histological effects and use the blepharospasm data as supportive evidence.

- The damage of olfactory stem stells after exposure to acrylic acid has not been definitively investigated. However, since these stem cells reside (at least part of them) in the sustentacular cell area and Frederick at al. (1998) as well as Harkema (2001)* described sustentacular cell necrosis, this is considered an adequate starting point for the derivation of AEGL-2 values. The LOEL for any histological alterations was 5 ppm for repeated exposure.

* Single Dose Inhalation Toxicity Study of Ethyl Acrylate And Acrylic Acid in Nonhuman Primates: Histopathology Report. Letter of Dr. Jack R. Harkema, Michigan State University, East Lansing to BAMM, dated November 26, 2001.

Comments from The Basic Acrylic Monomer Manufacturers, Inc.

- ***AEGL-3 values in the range of 300-500 ppm (8 hours) to 1000-1500 ppm (10 minutes) should be adopted.***

  The uncertainty factors used in the AEGL-3 derivation are too conservative because animals can be repeatedly exposed to vapor concentrations in the range of the proposed AEGL-3 values without lethality.

Reply

- It is inappropriate to directly compare an exposure concentration for humans derived by the application of uncertainty factors with an exposure level in an animal study.

- In both, the interspecies and the intraspecies uncertainty factors, the "toxicokinetic part" of the factor already has been reduced to 1, i.e., interspecies and intraspecies uncertainty factors of 3 each (total UF of 10) have been used. The rationale for reduction of the interspecies factor was based on the toxicokinetic model by Frederick et al. (1998). While the toxicokinetic model described that the rat's nasal cavity is more efficient in srubbing acrylic acid than the human nasal cavity, it should be noted that this would mean that in humans more acrylic acid can reach the lungs, the target organ of lethal effects in animals.

- The newly available histopathological results (Harkema, 2001) of the inhalation study in monkeys (Rohm and Haas Co., 1995) indicate qualitatively similar lesions after a single exposure to 75 ppm for 3 and 6 hours in rats and monkeys. If the extent (in quantitative terms) of damage in the most affected area of the olfactory mucosa was similar in rats compared to damage of 20 % and 40-60 %, respectively, of the mucosa in monkeys (Frederick et al., 1998) is unknown. Moreover, the toxicokinetic model (Frederick et al., 1998) indicated that a higher acrylic acid dose is deposited per area of olfactory mucosa in rats compared to humans. Should the deposited area dose in monkeys also be lower than in rats, this would mean that in monkeys, a similar tissue damage was caused by a lower target tissue concentration of acrylic acid. In conclusion, some uncertainty with regard to interspecies differences remains and, therefore, use of an interspecies uncertainty factor of 3 is considered adequate.

- Newer publications on the toxicokinetic model (Frederick et al., 2001*; Andersen and Jarabek, 2001**) support the conclusions drawn from the Frederick et al. (1998) publication.

* Frederick, C.B., P.R. Gentry, M.L. Bush, L.G. Lomax, K.A. Black, L. Finch, J.S. Kimbell, K.T. Morgan, R.P. Subramaniam, J.B. Morris and J.S. Ultman, 2001. A hybrid computational fluid dynamics and physiologically based pharmacokinetic model for comparison of predicted tissue concentrations of acrylic acid and other vapors in the rat and human nasal cavities following inhalation exposure. Inhalation Toxicology 13, 359-376.

** Andersen, M.E. and A.M. Jarabek, 2001. Nasal tissue dosimetry - issues and approaches for "category 1" gases: a report on a Meeting held in Research Triangle Park, NC, February 11-12, 1998. Inhalation Toxicology 13, 415-435.

Conclusion

The available data on interspecies differences, including the histopathological data (Harkema, 2001) of the monkey study (Rohm and Haas, 1995), is not considered an adequate rationale for a further reducion of the interspecies uncertainty factor to 1. It is recommended to confirm the proposed AEGL-2 and -3 values. The concentration of the odor recognition threshold is supported as a basis for the derivation of AEGL-1 values by the estimation of a Level of Annoyance according to the methodology of van Doorn et al. (which is not part of the AEGL SOP yet).

Comments from Dr. C.B. Frederick, on behalf of the Basic Acrylic Monomer Manufacturers, Inc.

Dr. Frederick presented his comments on behalf of the Basic Acrylic Monomer Manufacturers verbally at the September Meeting of the AEGL Committee.

- ***AEGL-1 should not be based on odor threshold because this is not a valid rationale for establishing an AEGL-1.***

- ***The supporting argument based on the occupational study by Renshaw (1988) ignores data from this study documenting exposure to higher concentrations without irritation.***

- ***The industrial hygiene data of BASF Corp.* documents the absence of worker complaints at 2 ppm, including exposure significantly in excess of 2 ppm.***

Reply

- The odor threshold may constitute an adequate AEGL-1 endpoint as pointed out in the Standing Operating Procedures, Section 2.2.2.1 "AEGL-1 Endpoints", which in Section 2.2.2.1.4 reads "For example, level of odor detection in humans, ... have been used as AEGL-1 endpoints".

- Since AEGL values are meant to protect sensitive individuals in the population is is considered adequate to discuss the lower bondary of concentrations that resulted in irritation and not the highest exposure at which no irritative effects were reported. In the case of the data by Renshaw (1988), no effects were reported for 2 workers exposed at 5.8-11.6 ppm, while in 9 other workers, exposed to lower or higher concentrations, irritative effects occurred.

- The industrial hygiene data do not substantiate the claim that no irritative effects occurred at 2 ppm because only 6 of a total of 259 8-hour TWA samples were 2 ppm or higher and it is questionable if irritative effects during an episode of higher exposure were reported weeks/ months later in routine check-up when workers were asked if they had "ear, nose or throat trouble".

* Letter on acrylic acid employee medical surveillance information and workplace air monitoring data for acrylic acid of BASF Corporation, Mount Olive, NJ dated May 30, 2001 submitted as an addendum to the Basic Acrylic Monomer Manufacturers' comments of May 31, 2001.

Comments from Dr. C.B. Frederick, on behalf of the Basic Acrylic Monomer Manufacturers, Inc.

- ***The proposed AEGL-2 values are not consistent with AEGL definitions.***

- ***The AEGL-2 was based on olfactory cytotoxicity, which is neither disabling nor irreversible.***

- ***A monkey study documents the lack of disabling clinical signs during a 6-hour exposure to 75 ppm***

- ***The use of uncertainty factors is inappropriate.***

Reply

- The histological effects at 75 ppm were not interpreted as irreversible effects, since otherwise a NOEL for these effects should have been used as a basis for AEGL-2 derivation. A threshold for permanent damage, caused by the destruction of olfactory stem cells, could not be defined. Instead, an effect level for histological damage was chosen and supported by effects in rabbits interpreted as clinical signs of impaired ability to escape.

- The newly available histopathological results (Harkema, 2001) of the inhalation study in monkeys (Rohm and Haas Co., 1995) indicate qualitatively similar lesions after a single exposure to 75 ppm for 3 and 6 hours in rats and monkeys. If the extent (in quantitative terms) of damage in the most affected area of the olfactory mucosa was similar in rats compared to damage of 20 % and 40-60 %, respectively, of the mucosa in monkeys (Frederick et al., 1998) is unknown. Moreover, the toxicokinetic model (Frederick et al., 1998) indicated that a higher acrylic acid dose is deposited per area of olfactory mucosa in rats compared to humans. Should the deposited area dose in monkeys also be lower than in rats, this would mean that in monkeys, a similar tissue damage was caused by a lower target tissue concentration of acrylic acid. In conclusion, some uncertainty with regard to interspecies differences remains and, therefore, use of an interspecies uncertainty factor of 3 is considered adequate.

- The fact that histopathological damage in monkeys was seen only in the olfactory, but not in the respiratory epithelium argues against an unspecific mechanism of damage. This makes a certain toxicodynamic difference in the tissue sensitivity between species likely.

- The considerable histopathological damage of the olfactory epithelium (Harkema, 2001) contrasts with the lack of any clinical signs in the animals (Rohm and Haas, 1995); some behavioral response of the animals to the irritative effect would have been expected.

- In the monkey study, the exposure concentrations were only determined in pre-exposure measurements (i.e., without animals). During the actual exposure, exhalation of humid air could have led to condensation of water in the air or on the walls of the exposure helmet, which, in turn, could have led to dissolution of acrylic acid in the water droplets and thus to a reduction of the inhaled acrylic acid vapor concentration.

Comments from Dr. C.B. Frederick, on behalf of the Basic Acrylic Monomer Manufacturers, Inc.

- ***The proposed AEGL-3 values are not consistent with AEGL definitions.***

- ***The AEGL-3 values are below the exposure value used in numerous repeat-exposure studies that have been conducted with acrylic acid vapor without an increase in mortality.***

- ***The use of uncertainty factors is inappropriate.***

Reply

- It is inappropriate to directly compare an exposure concentration for humans derived by the application of uncertainty factors with an exposure level in an animal study.

- In both, the interspecies and the intraspecies uncertainty factors, the "toxicokinetic part" of the factor already has been reduced to 1, i.e., interspecies and intraspecies uncertainty factors of 3 each (total UF of 10) have been used. The rationale for reduction of the interspecies factor was based on the toxicokinetic model by Frederick et al. (1998). While the toxicokinetic model described that the rat's nasal cavity is more efficient in srubbing acrylic acid than the human nasal cavity, it should be noted that this would mean that in humans more acrylic acid can reach the lungs, the target organ of lethal effects in animals.

- The newly available histopathological results (Harkema, 2001) of the inhalation study in monkeys (Rohm and Haas Co., 1995) indicate qualitatively similar lesions after a single exposure to 75 ppm for 3 and 6 hours in rats and monkeys. If the extent (in quantitative terms) of damage in the most affected area of the olfactory mucosa was similar in rats compared to damage of 20 % and 40-60 %, respectively, of the mucosa in monkeys (Frederick et al., 1998) is unknown. Moreover, the toxicokinetic model (Frederick et al., 1998) indicated that a higher acrylic acid dose is deposited per area of olfactory mucosa in rats compared to humans. Should the deposited area dose in monkeys also be lower than in rats, this would mean that in monkeys, a similar tissue damage was caused by a lower target tissue concentration of acrylic acid. In conclusion, some uncertainty with regard to interspecies differences remains and, therefore, use of an interspecies uncertainty factor of 3 is considered adequate.

Conclusion

The available data on interspecies differences, including the histopathological data (Harkema, 2001) of the monkey study (Rohm and Haas, 1995), is not considered an adequate rationale for a further reducion of the interspecies uncertainty factor to 1. It is recommended to confirm the proposed AEGL-2 and -3 values. The concentration of the odor recognition threshold is supported as a basis for the derivation of AEGL-1 values by the estimation of a Level of Annoyance according to the methodology of van Doorn et al. (which is not part of the AEGL SOP yet).

Inhalation exposure of monkeys to acrylic acid vapor

Single Dose Inhalation Toxicity Study of Ethyl Acrylate (EA) And Acrylic Acid (AA)

Unpublished study report, Rohm and Haas Co., September 12, 1995

Five groups of three Cynomolgus monkeys each were exposed via head-only inhalation exposure to 75 ppm acrylic acid for 3 hours, 75 ppm acrylic acid for 6 hours or air for 6 hours (control group); two additional groups were exposed to 75 ppm ethyl acrylate for 3 and 6 hours. The mean analytical exposure concentrations of acrylic acid were 80.51 and 78.06 ppm, respectively. Based upon the fluctuations in airflow through the exposure helmet, the respiration rate and tidal volume were measured for each animal. There were no abnormal clinical observations recorded for any of the animals exposed to acrylic acid or control air. From the respiration rate, tidal volume and body weights, the individual animal inhaled doses were calculated. The doses for the monkeys exposed for 3 hours were 12.7, 18.8 and 15.7 mg/kg, while doses for the 6-hour exposed animals were 26.9, 21.5 and 35.2 mg/kg. After the end of the exposure, each monkey was anesthetizsed and killed by exsanguination. At necropsy, no gross pathological treatment-related effects were observed. The nasopharyneal orifice and trachea and lungs were fixed by formalin treatment and shipped for sectioning and histopathologic evaluation; results of the histological examination were not included in this final study report.

Single Dose Inhalation Toxicity Study of Ethyl Acrylate And Acrylic Acid in Nonhuman Primates: Histopathology Report

letter of Dr. Jack R. Harkema, Michigan State University, East Lansing to BAMM, dated November 26, 2001.

These results have also been published as an one-page abstract entitled 'Olfactory Epithelial Injury in Monkeys After Acute Inhalation Exposure to Acrylic Monomers' by J.R. Harkema, J.K. Lee, K.T. Morgan and C.B. Frederick, 1997, The Toxicologist, Vol. 36, No. 1, Part 2, abstract No.576.

The nasal cavities were transversely sectioned into serial 5-10 mm-thick blocks from the nares to the posterior aspect of the soft palate. The blocks were decalcified using EDTA, embedded in paraffin and sectioned at a thickness of 4-6 microns. Sections were stained with hematoxylin and eosin. Nasal lesions were restricted to the olfactory epithelium lining the dorsal medial meatus at the level of the maxillary sinus in the proximal aspect of both nasal passages. The morphologic alterations consistently found in all acrylic acid-exposed monkeys were focal degeneration and necrosis of the olfactory epithelium with mild inflammation (influx of neutrophils and lymphocytes). No exposure-realted lesions were present in the nasal respiratory, transitional or squamous epithelium in any of the monkeys examined. The Bowman's glands and olfactory nerves in the lamina propria underlying the degenerating olfactory epithelium were also histologically normal. The extent and severity of the lesions were slightly greater in monkeys exposed for 6 hours comparred to those exposed for 3 hours. The severity of epithelial injury ranged from mild apical blebbing and cytoplasmic vacuolation of

the olfactory sustentacular cells to marked necrosis, exfoliation and attenuation of the olfactory epithelium with only a few remaining basal or sensory cells attached to the basement membrane. Approximately 20 % and 40-60 % of the olfactory epithelium in the examined sections had ethyl acrylate or acrylic acid induced damage after 3 or 6 hours, respectively. The character, severity and distribution of the morphologic alterations induced by acrylic acid and ethyl acrylate were similar. The author concluded that monkeys exposed to acrylic acid or ethyl acrylate had focal, olfactory epithelial lesions that resembled in both nature and severity those reported in rodents.

Single Dose Inhalation Toxicity Study of Ethyl Acrylate (EA) And Acrylic Acid (AA) Rohm and Haas, 1995

- groups of 3 animals exposed for 3 or 6 hours
- to air, 75 ppm acrylic acid or 75 ppm ethyl acrylate
- head-only exposure of restrained animals
- no abnormal clinical observations
- respiration rate and tidal volume were measured for each animal
- calc. body doses were for 3 hours: 12.7, 18.8 and 15.7 mg/kg, 6 hours: 26.9, 21.5 and 35.2 mg/kg.
- no gross pathological effects

Single Dose Inhalation Toxicity Study of Ethyl Acrylate And Acrylic Acid in Nonhuman Primates: Histopathology Report

letter of Dr. Jack R. Harkema, Michigan State University, East Lansing to BAMM, dated November 26, 2001.

Published as abstract: 'Olfactory Epithelial Injury in Monkeys After Acute Inhalation Exposure to Acrylic Monomers' by J.R. Harkema, J.K. Lee, K.T. Morgan and C.B. Frederick, 1997, Toxicologist, Vol. 36, No. 1, Part 2, abstract No.576.

- focal degeneration and necrosis of the olfactory epithelium with mild inflammation
- severity ranged from mild apical blebbing and cytoplasmic vacuolation of the olfactory sustentacular cells to marked necrosis, exfoliation and attenuation of the olfactory epithelium with only a few remaining basal or sensory cells attached to the basement membrane
- affected area (20 vs. 40-60 %) and severity increased with exposure time
- authors conclusion: monkeys exposed to acrylic acid and ethyl acrylate exposed focal, olfactory epithelial lesions that resemble, in both nature and severity, those reported in rodents

Does the monkey study support a further reduction of the

interspecies uncertainty factors in derivation of AEGL-2 and -3?

Current Version in proposed TSD:

AEGL-2: Interspecies UF: 3

because toxicokinetic investigations suggested a higher susceptibility of rats for local effects: deposited concentration on the olfactory epithelium about 2-3fold higher in rats vs. humans (Frederick et al. 1998).

AEGL-3: Interspecies UF: 3

because the mechanism of action of lethal effects, which involves local tissue destruction in the lung by a direct-acting toxicant with limited influences of metabolism, detoxification and elimination, is unlikely to differ between species.

Does the monkey study support a further reduction of the interspecies uncertainty factors in derivation of AEGL-2 and -3?

Critical evaluation of the monkey study:

- the considerable histopathological damage of the olfactory epithelium (Harkema, 2001) contrasts with the lack of any clinical signs (Rohm and Haas, 1995); some behavioral response of the animals to the irritative effect would have been expected.
- exposure concentrations were only determined in pre-exposure measurements (w/o animals); during exposure, exhalation of humid air could have led to condensation of water in the air or on the walls of the exposure helmet, which, in turn, could have led to dissolution of acrylic acid in the droplets and to a reduction of the inhaled vapor concentration.

Discussion:

- the fact that histopathological damage was seen only in the olfactory, but not in the respiratory epithelium argues against an unspecific mechanism of damage; this makes a certain toxicodynamic difference in the tissue sensitivity between species likely
- the toxicokinetic model by Frederick et al. (1998) indicates that the deposited area dose is about 3-fold higher in rats compared to humans
- however, the histopathological results in monkeys (Harkema, 2001) indicate qualitatively similar lesions after a single exposure to 75 ppm for 3 and 6 hours in rats and monkeys
- it is unknown if the extent (in quantitative terms) of damage in rats is similar to that in monkeys (damage of 20 % and 40-60 % of the olfactory mucosa, for 3 and 6 hours of exposure, respectively
- should the deposited area dose in monkeys also be lower than in rats, this would mean that in monkeys, a similar tissue damage was caused by a lower target tissue concentration of acrylic acid
- in conclusion, some uncertainty with regard to interspecies differences remains and, therefore, use of an interspecies uncertainty factor of 3 is considered adequate.

Does the monkey study support a further reduction of the

interspecies uncertainty factors in derivation of AEGL-2 and -3?

Conclusion:

The interspecies uncertainty factors should not be reduced, but the monkey study should be incorporated into the justification

AEGL-2: Interspecies UF: 3

because toxicokinetic and histopathologic investigations did not suggest a large difference between rats on the one side and humans and monkeys on the other side (see Section 4.5.1)

AEGL-3: Interspecies UF: 3 (unchanged)

because the mechanism of action of lethal effects, which involves local tissue destruction in the lung by a direct-acting toxicant with limited influences of metabolism, detoxification and elimination, is unlikely to differ between species.

Use of intraspecies uncertainty factors in derivation of AEGL-2 and -3

Current version in proposed TSD:

AEGL-2 and -3 Intraspecies UF: 3

because a small interindividual variability can be assumed considering that acrylic acid is a contact-site, direct-acting toxicant not requiring metabolic conversion.

Proposal is to put argument more precisely:

- intraspecies UF for both toxicokinetic and toxicodynamic differences
- toxicokinetic differences smaller for local effects occuring at the air-tissue interphase compared to systemic effects (entering of circulation, distribution and metabolic (in)activation)
- Thus, adequate to use a reduced intraspecies factor of 3 in cases of locally acting, reactive chemicals.

Conclusion:

AEGL-2 and -3 Intraspecies UF: 3

because the intraspecies uncertainty factor is used to compensate for both, toxicokinetic and toxicodynamic differences between species and for local effects occuring at the air-tissue interphase, toxicokinetic differences between species are much smaller when compared to systemic effects after inhalation exposure, where interindividual differences might exist with regard to absorption, entering of circulation, distribution through circulation and tissue distribution.

Lesions of the Olfactory Epithelium

- **loss of olfactory epithelium**, accompanied by replacement with respiratory epithelium tends to increase as a function of **age** in humans

  (Paik et al., Arch. Otolaryngol. Head Neck Surg. 118 (1992) 731-738)

- deterioration preferentially in the **anterior epithelium** suggests that environmental **insults** can accumulate or become more severe with age and overwhelm the regenerative capacity

  (Loo et al., Int. J. Devl. Neuroscience 14 (1996) 881-900)

- a capacity for **regeneration** of the olfactory epithelium has been found after methyl bromide-induced lesion

  (Yougentob et al., Physiol. Behavior 62 (1997) 1241-1252;
  Schwob et al., J. Comp. Neurol. 412 (1999) 439-457)

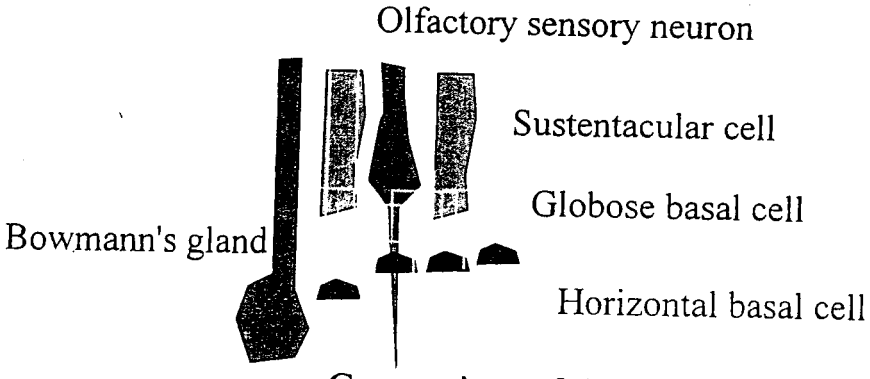
- the regeneration seems to be dependent on the **survival of pluripotent stem cells**

  Since these cannot effectively migrate laterally to reconstitute sensory epithelium, complete stem cell destruction in one area will likely lead to permanent replacement with nonfunctional epithelium

  (Talamo et al., Inhal. Toxicol. 6 suppl. (1994) 249-275)

- olfactory neurons (and sustentacular cells) arise from **globose basal cells**

  (Huard et al., J. Comp. Neurol. 400 (1998) 469-486)



Comparison of the lesions caused by

methyl bromide (MeBr) and acrylic acid (AA)

- MeBr: P450 metabolization to toxic HCHO, GSH depletion?
- AA: breakdown of mitochondrial function by induction of mitochondrial permeability transition
  (Palmeira et al., Biochem. Biophys. Res. Commun. 272 (2000) 431-435)
- Qualitatively, histology in rats seems to be comparable between
  75 ppm x 6 h acrylic acid and 330 ppm x 6 h MeBr
  (Schwob et al., J. Comp. Neurol. 359 (1995) 15-37)

Are the lesions caused by acrylic acid irreversible?

- local replacement of olfactory with respiratory epithelium after acrylic acid exposure is likely
- also after MeBr exposure reconstitution of the olfactory epithelium was incomplete and patchy replacement with respiratory epithelium was found
  (Schwob et al., J. Comp. Neurol. 359 (1995) 15-37)
- MeBr exposure hardly affected the odor threshold in trained rats
  (Youngentob et al., Physiol. Behavior 62 (1997) 1241-1252)
- since the loss of olfactory epithelium with age correlates with a reduction in olfaction, an acceleration of this development seems likely in humans
- currently, the TSD does not classify lesions as an long-lasting adverse health effect, but bases the AEGL-2 derivation on a 75 ppm x 6 h-exposure

Conclusion

Neither the damage of olfactory stem stells after exposure to acrylic acid, nor the reconstitution of the olfactory epithelium has been definitively investigated.

However, since these stem cells reside (at least part of them) in the sustentacular cell area and Frederick at al. (1998) described sustentacular cell necrosis "with only a few remaining basal or sensory cells attached to the basement membrane", exposure to 75 ppm for 6 h is considered to be a threshold for irreversible effects and, thus, constitutes an adequate starting point for the derivation of AEGL-2 values.

Trichloroethylene

- Principal author: Paul Janssen (RIVM, NL)
- Presenting author: Marcel van Raaij (RIVM,NL)

- Chemical Manager: Bill Bress
- Chemical Reviewers: George Alexeeff,Steve Barbee

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Trichloroethylene short history

- Start of the TSD preparation early 2001
- Summer-Fall 2001: contact EPA research group on recent neurotoxicity studies in rats and the associated PBPK model: request for cooperation.
- December 2001: progress report during NAC-AEGL 23, TCE discussion postponed until PBPK modelling results become available
- First modelling results available february 2002: not sufficient.
- Further modelling results available march 2002: document to CM and CR's

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Trichloroethylene - toxicological profile

- CNS is the primary target organ (additional cardiac, liver, and kidney effects)
- CNS effects may start at levels > 300 ppm; effects levels being observed at 1000 ppm.
- True narcosis occurs in humans at levels of 5000 ppm and higher.
- Initial levels to induce narcosis may reach up to 10,000 - 20,000 ppm in humans
- From a range of observations (human volunteer studies, human metabolism studies, narcosis information, rat neurobehavioral studies) it follows that Concentration is more important than Time (n may be as high as 7 for some neurobehavioral effects).

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Data relevant to AEGL-1

- Many human volunteer studies available focussed on neurobehavioral changes. Endpoints studied mostly mild in nature.
- Less human information available on airway and/or eye irritation. Results often include high level of subjectivity.
- At levels around 100-200 ppm conflicting results on subjective symptoms.
- At ≥300 ppm clinical signs are likely to occur as a consequence of exposure to TCE
- No animal data available, relevant to AEGL-1.

Human volunteer studies -1

Study	Exposure	Effects	Remark
[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]

Human volunteer studies - 2

[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]

2

AEGL-1 Selection of endpoint/study

- WEIGHT OF EVIDENCE APPROACH
- Use Vernon and Ferguson (1969) as key-study: this provides a NOAEL of 300 ppm for neurobehavioral endpoints with light effects of CNS depression (1/8 subjects with subjective symptoms)
- The value of 300 ppm is supported by several other volunteer studies (e.g. Ettema and co-workers: marginal effects at 300 ppm).
- Use PBPK modelling of EPA-research group to extrapolate over time, taking plasma [TCE] as reference.

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PBPK modelling results for AEGL-1

Calculate the blood [TCE] level reached after a 2h exposure to 300 ppm >>> 4.78 mg/l

Exposure Duration	Cblood = 4.78 ± 0.02 mg/l (2 SD)	TCE concentration (ppm) necessary to achieve Cblood 4.78 ± 0.02 mg/l
30 hr	4.78 ± 0.02	222
4 hr	4.78 ± 0.02	251
1 hr	4.78 ± 0.02	302
0.5 hr (30 min)	4.78 ± 0.02	524
0.167 hr (10 min)	4.78 ± 0.02	782

The value of 4.78 mg/l is supported by a range of human metabolism studies: at a range of 100-200 ppm for 30 min to 6h blood TCE levels will range from 1 - 3 mg/l at rest. With additional workload, levels can reach 5-6 mg/L.

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AEGL-1 Derivation

- Use PBPK modelling results for time extrapolation
- Use total assessment factor of 3 (no interspecies factor, intraspecies factor of 3 because direct CNS effects show minor inter-individual variation).
- Proposed AEGL-1 values:

TABLE 1B: Proposed AEGL-1 values for trichloroethylene [ppm]

Classification	10-minute	30-minute	1-hour	4-hour	8-hour
AEGL-1	310	175	131	84	77

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Data relevant for AEGL-2

- Various human volunteer studies on neurobehavoiral changes: mostly mild effects in terms of "impairment of the ability to escape".
- Narcosis occurs at substantially higher levels.
- Various rodent studies on neuro-behavioral changes and -toxicity (e.g. EPA research)
- Problem in using animal data: what is the relevance of observed changes for humans and impaired escape.
- Other serious effects at higher levels.

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AEGL-2 Selection of endpoint/study

- Use Vernon and Ferguson (1969) as key-study: this provides a LOAEL of 1000 ppm (2h) for neurobehavioral endpoints with some effects of CNS depression (majority of subjects show light-headiness, dizziness, lethargy).
- The effects observed at 1000 ppm are considered to be mild in terms of the "impairment of the ability to escape".
- Use PBPK modelling of EPA-research group to extrapolate over time, taking plasma [TCE] as reference.

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PBPK modelling results for AEGL-2

Calculate the blood [TCE] level reached after a 2h exposure to 300 ppm >>> 18.3 mg/l

1000

Exposure Duration	Calculated 18.3 ± 0.2 mg/l AEGL	TCE concentration (ppm) necessary to achieve C(tcl) 18.3 ± 0.2 mg/l
8 hr	18.3 - 0.2	719
4 hr	18.3 - 0.2	801
1 hr	18.3 - 0.2	1357
0.5 hr (30 min)	18.3 - 0.2	1868
0.0667 hr (10 min)	18.3 - 0.2	2989

The value of 18.3 mg/l cannot be directly supported by human metabolism studies. However, for narcosis a blood level of 100 mg/l is proposed, based on clinical experience. The proposed level of 18.3 is low compared to that level.

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AEGL-2 Derivation

- Use PBPK modelling results for time extrapolation
- Use total assessment factor of 3 (no interspecies factor, intraspecies factor of 3 because direct CNS effects show minor inter-individual variation)
- Proposed AEGL-2 values:

TABLE 11: Proposed AEGL-2 values for trichloroethylene [ppm]

Classification	10-minute	30-minute	1-hour	4-hour	8-hour
AEGL-2	903	623	452	267	240

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Data relevant to AEGL-3

- Human data on lethality lack quantitative exposure information.
- Human exposure to TCE as an anesthetic agent may range up to 20,000 ppm initially, and to 5000-7000 ppm for sustained narcosis.
- Cardiac arrhytmias probably occur only > 10,000 ppm and only few cases of arrhythmias may result in cardiac arrest.
- Animal lethality data provide a number of LC 50 values.

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Animal lethality data

Species	Exp duration	LC50	Ref.
Rat male Rat female	1h 1h	26300 25700	Vernot 1964
Rat SD (NMRI O)	4h	12500	Siegel 1964
Rat SD	6h	5918	Bonnet 1980
Mice	4h	8450	Friberg 1953
Mice OF1	6h	5807	Gradiski 1978

Adams (1951) performed a range of concentration x time experiments determining the CxT products resulting in mortality or no mortality

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AEGL-3 Selection of study

- Use Adams (1951) as the key study
- Use Probit Analysis to determine the LC05 and LC01 values and their 95% confidence limits and to extrapolate over time intervals.
- Use the 95% LCL of the LC05 (according to SOP) for each time interval as a starting point for AEGL-3 development.

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Derivation of AEGL-3

- Use Probit analysis at starting point
- Do not use an interspecies extrapolation factor
  - TCE mortality most likely results from CNS depression in which total body load determines the effect.
  - Thus, CNS depression largely follows the rules of scaling to body weight, i.e. species with higher body weight are less sensitive.
  - Indeed, the PBPK modelling approach shows that humans consistently need higher external exposures to obtain a similar internal dose (expressed as plasma [TCE]).
- Use an intraspecies factor of 3 since CNS depression shows a minor interindividual variation
- Total assessment factor is 3.

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AEGL-3 values

Time	LC_{05}	LC_{05} 95% lower confidence limit	LC_{01}	LC_{01} 95% lower confidence limit
10 minutes	19,240	11,170	29,540	18,450
30 minutes	9297	5720	14,270	9050
1 hour	5875	3576	9472	5977
4 hour	2547	1243	3603	2318
8 hour	1483	704	2277	1308

TABLE 12: Proposed AEGL-3 Values for [(ppm) (mg/m^3)]

Classification	10-minute	30-minute	1-hour	4-hour	8-hour
AEGL-3	6150	3301	1325	770	435

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AEGL-3 values in perspective.....

- Exposure levels for sustained narcosis may be as high as 5000-7000 ppm or, later on, 1000 to 2000 ppm during surgery (likely duration is up to about 4 hours ?)
- Remind: applied to non-healthy people of all ages.
- ERPG-3 value (1h) is 5000 ppm, AEGL-3 for 1h is 1325 ppm
- AEGL-3 for 8h is 435 ppm, Human volunteer studies show humans exposed to 200 up to 7h or 1000 ppm for 2h.
- So, proposed AEGL-3 values are quite conservative

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ACUTE EXPOSURE GUIDELINE LEVELS FOR TOLUENE

National Advisory Committee for AEGLs Meeting
April 9-11, 2002

ORNL Staff Scientist:
Sylvia S. Talmage

Chemical Manager:
Larry Gephart

Chemical Reviewers:
David Belluck
Robert Snyder

Attachment 19

TOLUENE

Widely used as a solvent

Human Studies

- Numerous monitoring studies
  - Chronic exposures at workplace guidelines of 100 and 200 ppm; up to 800 ppm
- 19 clinical studies
  - Concentrations of 40 to 800 ppm for up to 8 hours
  - Generally no notable effects at 100 and 200 ppm (13 studies; Table 2)
    - Some studies indicate slight eye, nose irritation (no annoyance)
    - Toluene is not a sensory irritant (mouse RD_{50} of 5300 ppm)
    - Some studies indicate subtle CNS effect in one of many tests
  - Peaks to 300 ppm with exercise (Baelum et al. 1990)
    - Similar slight effects
  - 300 ppm for 20 minutes (Gamberale and Hultengren 1972)
    - Significant difference in reaction time measured in milliseconds
  - 500, 700 ppm, each for 20 minutes (Gamberale and Hultengren 1972)
    - Subtle effects - neurobehavioral indicators
  - Exposures up to 800 ppm, 8 hours
    - (von Oettingen et al. 1942; Carpenter et al. 1944)
    - threshold for unsteadiness, gross CNS effects; poor analytical methods

TOLUENE

Animal Studies

LC_{50} values:

mouse: 1-hour = 19,018 ppm (Moser and Balster 1985)
3-hour = 8600 ppm (Bruckner and Peterson 1981a)
6-hour = 6940 ppm (Bonnet et al. 1979)

rat: 1-hour = 26,700 ppm (Pryor et al. 1978)
2-2.5 hour = 12,200 (Kojima and Kobayaski 1973)

Highest non-lethal values

mouse: 12,000 ppm for 20 minutes (Bruckner and Peterson 1981a)
6100 ppm for 24 hours (Cameron et al. 1938)

rat: 15,000 ppm for 1 hour (Hinman 1987)
6250 ppm for 2 hours (Mullin and Krivanek 1982)
5000 ppm for 2 hours (Kojima and Kobayaski 1973)

Good data base

Studies on reproduction/development, repeated/chronic exposures, neurotoxicity, genotoxicity, carcinogenicity

PROPOSED TOLUENE AEGLs (in bold)

Classification	Exposure Duration				
	10-Minute	**30-Minute**	**1-Hour**	**4-Hour**	**8-Hour**
AEGL-1 (Nondisabling)	260 ppm **200 ppm**	120 ppm **200 ppm**	82 ppm **200 ppm**	41 ppm **200 ppm**	29 ppm **200 ppm**
AEGL-2 (Disabling)	600 ppm **700 ppm**	270 ppm **700 ppm**	190 ppm **700 ppm**	94 ppm **700 ppm**	67 ppm **700 ppm**
AEGL-3 (Lethal)	1600 ppm **7200 ppm**	900 ppm **4200 ppm**	630 ppm **2900 ppm**	320 ppm **1500 ppm**	220 ppm **1000 ppm**

AEGL-1: Based on multiple studies of human exposures to 200 ppm for up to 8 hours and intermittently to 300 ppm with exercise. Additional exposures to 800 ppm for 3 and 8 hours with CNS effects. Routine metabolism studies at 200 ppm. Occupational (chronic) exposures at 100 and 200 ppm with range up to 800 ppm.
Not irritating; not highly objectionable. Intraspecies UF of 1(the thousands of subjects in working and exercising situations represent a broad spectrum of the population).
No time scaling (equilibrium reached in the blood).
Support: 700 ppm for 20 minutes = subtle CNS effect; UF of 3.

AEGL-2: Based on human exposure to 700 ppm for 20 minutes and 800 ppm for 8 hours.
Threshold for CNS depression. UF of 1 (multiple studies). No time scaling.
Support: 50-minute 2000 ppm no-adverse CNS effects in monkeys; UF of 3.

AEGL-3: Based on highest non-lethal value in rats, 6250 ppm for 2 hours. UF of 3.
Time-scaled using lethality data from mice.
Support: 1000 ppm was chronic NOAEL in rats and mice.
No deaths in human exposures to >1842 ppm for 2.5 hours, 1500 ppm for 8 hours.

Table 2. Sensory and neurobehavioral effects of toluene in controlled human studies.

Concentration (ppm)	Duration	Effects	Reference
10, 40, 100	6 hours	slight irritation of eyes and nose at 100 ppm; no effect on mood, fatigue, or sleepiness; slight increase in occurrence of headache, etc.; no effect on lung function or nasal mucous flow; no significant effect on performance of eight psychomotor tests	Andersen et al. 1983
80	4 hours	no impairment of neurobehavioral tasks	Cherry et al. 1983
80	4 hours	no subjective symptoms; no impairment in tests of simple reaction time, short-term memory, or choice reaction time; no effect on heart rate	Anshelm Olson et al. 1985
80	4.5 hours	increase in subjective symptoms; no impairment in tests of simple and choice reaction time, color-word vigilance, or memory; no effect on heart rate, EEG, or sleep latency	Iregren et al. 1986
100	3.5 hours	no behavioral deficits in psychomotor tests	Winneke 1982
100	4 hours	no serious impairment in series of neuro-behavioral tests (small impairment in one measure of a visual-vigilance test)	Dick et al. 1984
100	6 hours	no significant effect on lung function (subjects exercised for 30 minutes); slight effect on some multitask and neuropsychological tests (increased latency but not accuracy on neurobehavioral tasks)	Rahill et al. 1996
100	6.5 hours	4 groups tested: 2 exposed and 2 controls: sensory irritation (no annoyance), sleepiness, decreased performance on 4/10 tests for one or both exposure groups (manual dexterity, color discrimination, visual perception); no changes in kidney function	Baelum et al. 1985; Nielson et al. 1985
100	1, 3, or 7.5 hours, several days	No decrement in psychomotor tests on first day of exposure; slight decrement in females on one of many cognitive tests at 7.5 hours, days 3 and 5	Stewart et al. 1975
100 100 (TWA with peaks to 300)	7 hours (3 15-minute exercise periods)	sensory irritation, slight decrement in one of four psychomotor performance tests; no differences in performances between constant and varying concentrations	Baelum et al. 1990

Table 2. Sensory and neurobehavioral effects of toluene in controlled human studies.

75 150	7 hours/3 days 7 hours/3 days	mean 7% decrement in several neurobehavioral tests at 150 ppm; slight increases in headache, eye irritation, sleepiness	Echeverria et al. 1989; 1991
100, 200	30 minutes	no difference in heart rate, pulmonary ventilation, oxygen consumption or blood lactate, either at rest or during a work load of 50 W	Astrand et al. 1972
100, 200	3 hours or 7 hours with 1-hour break	decrease in pulse rate at 200 ppm for 3 hours; tendency to prolonged reaction time at 200 ppm; no clear concentration-response relationship	Ogata et al. 1970
50, 100 300, 400, 600 800	8 hours 8 hours 3 hours	moderate fatigue, sleepiness, headache; increasingly severe symptoms with increasing concentrations: incoordination, nausea, confusion, dilated pupils, and extreme fatigue; severe fatigue, nausea, confusion, incoordination, loss of self control, bone marrow suppression	von Oettingen et al. 1942
100 300 500 700	successive 20-minute exposure periods (one 5-minute break); total 85 minutes	no effect of reaction time or perceptual speed increase in simple reaction time increase in complex reaction time decrease in perceptual speed at end of exposure; no effect on heart rate during total exposure	Gamberale and Hultengren 1972
200, 400, 600, 800	7-8 hours	subjective symptoms ranged from transitory mild throat and eye irritation and slight exhilaration at 200 ppm to metallic taste, transitory headache, lassitude, inebriation, and slight nausea at 800 ppm; threshold for "steadiness" task = 800 ppm	Carpenter et al. 1944
220[a] 427[a]	not given	6/6 subjects willing to work for 8 hours 3/6 subjects willing to work for 8 hours	Carpenter et al. 1976
200	6 hours	no changes in respiration; increased heart rate	Suzuki 1973
240	three 70-minute sessions	impaired vigilance in third session; decreased fatigue during second session	Horvath et al. 1981

[a] "Toluene concentrate."

Echeverria et al. (1989; 1991) reported on the acute neurobehavioral effects of toluene in tests with 42 healthy male and female college students. The toluene concentrations tested were 0, 75, and 150 ppm over a 3-day period (7 hours each day) and were administered in random order. The odor of toluene was masked with menthol (0.078 ppm). Chamber atmospheres were measured with an infrared analyzer and confirmed by gas chromatography. A battery of 12 performance tests (verbal, visual, and psychomotor) was administered to each participant prior to exposures and again at 4 and 7 hours during the exposures. Test results were averaged over the

January 2, 2002

Sixth Interim Report of the Subcommittee on Acute Exposure Guideline Levels

BACKGROUND

In 1991, the U.S. Environmental Protection Agency (EPA) and the Agency for Toxic Substances and Disease Registry (ATSDR) asked the National Research Council (NRC) to provide technical guidance for establishing community emergency exposure levels (CEELs) for extremely hazardous substances (EHSs) pursuant to the Superfund Amendments and Reauthorization Act of 1986. In response to that request, a subcommittee of the NRC Committee on Toxicology (COT) prepared a report titled *Guidelines for Developing Community Emergency Exposure Levels for Hazardous Substances* (NRC 1993). That report provides step-by-step guidance for the derivation of CEELs for EHSs.

In 1995, EPA, several other federal and state agencies, and several private organizations convened an advisory committee—the National Advisory Committee on Acute Exposure Guideline Levels (AEGLs) for Hazardous Substances (referred to as the NAC)—to develop, review, and approve AEGLs (similar to CEELs) for up to 400 EHSs. AEGLs developed by the NAC have a broad array of potential applications for federal, state, and local governments and for the private sector. AEGLs are needed for prevention and emergency response planning for potential releases of EHSs.

THE CHARGE TO THE SUBCOMMITTEE

The NRC convened the Subcommittee on Acute Exposure Guideline Levels to review the AEGL documents approved by the NAC. The subcommittee members were selected for their expertise in toxicology, pharmacology, medicine, industrial hygiene, biostatistics, risk assessment, and risk communication.

The charge to the subcommittee is to (1) review AEGLs developed by the NAC for scientific validity, completeness, and conformance to the NRC 1993 guidelines report, (2) identify priorities for research to fill data gaps, and (3) identify guidance issues that may require modification or further development based on the chemicals reviewed.

This interim report presents the subcommittee's comments concerning the draft AEGL documents for 10 chemicals—1,1-dichlorofluoroethane, sulfur mustard, hydrogen cyanide, allyl alcohol, phosgene, toluene, hydrogen fluoride, hydrogen sulfide, furan, and tetrachloroethylene.

COMMENTS ON 1,1-DICHLOROFLUOROETHANE

At its August 29-31, 2001 meeting, the subcommittee reviewed the revised AEGL document on 1,1-dichlorofluoroethane (HCFC-141b). The document was presented by Sylvia Talmage of Oak Ridge National Laboratory. The subcommittee concluded that the revised document conforms with the *Guidelines for Developing Community Emergency Exposure Levels*

Page 2, paragraph 2: Since no exposure data are given for the Stavrakis (1971) study and there is little description of specific symptoms, perhaps this paragraph should be deleted.

Page 6: Substantial discussion is dedicated to the Polednak (1980) study; yet at the end, it is noted that evidence presented in the study was inadequate to assess the carcinogenicity of phosgene. The discussion can be substantially shortened, especially, the section on page 8 that presents all of the SMRs, or the data can be summarized in a table.

Section 2.2.2: The first two studies discussed in this section should be moved to Section 2.5.

Section 3.2: Several studies (e.g., Hatch, et al. 1986) examined exposure effects in more than one species. The experimental details of those studies should only be presented once, and in subsequent sections, the reader should be referred to this initial discussion. In addition, the section would be easier to follow if a table were developed indicating various health effects associated with different exposures in different animals species.

Section 4.4.2: The utility of this section is unclear.

Sections 6.3 and 7.3: An intraspecies UF of 3 is justified based on the assumption that the mechanism of action does not vary greatly between individuals. However, there can be great interindividual variation in response to a chemical, even when the biochemical mechanism or mode of action is the same. Thus, this justification needs to be reconsidered, although the choice of a UF of 3 may remain valid.

The Kaerkes (1992) study may be used to derive an AEGL-1 value if the concentration data are valid. Fifty ppm-min would be 0.1 ppm for 8 hr. Allowing for intraspecies variations, 0.05 ppm would seem reasonable (UF of 2, not 3).

Page 6, paragraphs 2 and 3: This section presents a great deal of data and discussion with no conclusion. Delete this section and use the Polednak and Hollis (1985) follow-up survey data instead.

COMMENTS ON TOLUENE

At its August 29-31, 2001 meeting, the subcommittee reviewed the AEGL document on toluene. The document was presented by Sylvia Talmage of Oak Ridge National Laboratory. The subcommittee recommends a number of revisions. A revised draft will be reviewed by the subcommittee at its next meeting.

General Comments

The introduction (Section 1.0) to the document should specify that the major dangers associated with uncontrolled release of toluene are explosion and fire, as in the case of automotive or aviation gasoline. The introduction should also include the flash point of toluene

and references to literature and industrial accounts of fires involving toluene, especially those that pertain to petroleum refining and shipping. The NAC should provide other properties of toluene in the table on page 9 that are relevant to chemical spills and releases (i.e., explosive limits, flash point, flammability).

The inhaled toluene concentrations and circulating toluene concentrations (e.g., Pediatrics 39:451-461, 1967) associated with human fatalities should be summarized in Section 2.1.

The AEGL recommendations on page 7 are inconsistent with the text conclusions concerning human toluene experience as listed on page 22, lines 3-7. The 30-min and 60-min AEGLs (270 ppm and 190 ppm, respectively) suggest that Astrand's bicyclists would be disabled—especially those inhaling 200 ppm and under a work load of 75 watts—but that conclusion is inconsistent with page 37, lines 17-30. Also, the 8-hr AEGL-2 value (67 ppm) is said to be disabling, but when adult female volunteers inhaled 100 ppm for 7.5 hr, not only were they not disabled (NTIS Publ. No. PB-82:154-220, 1975), but only slight reductions in their alertness could be discerned. Controlled inhalation of 100 ppm for 4 hr produced only slight reduction in visual alertness (Int. Arch. Occup. Environ. Health 54:91-109, 1984)—not an effect that could be considered disabling. In contrast to the recommended AEGL-2 values, no measurable decrements on behavioral performance were found after 3.5 to 6 hr of exposure at 80 ppm (Scand. J. Work Environ. Health 12:469-475, 1986; Br. J. Ind. Med. 42:117-122, 1985; Ergonomics 26:1081-1087, 1983) to 100 ppm (Scand. J. Work Environ. Health 9:131-139, 1972; Int. Arch. Occup. Environ. Health 54:117-122, 1985; NTIS Publ. No. PB-82:154-220, 1975; Acta Neurol. Scand. Suppl. 66(92):117-129, 1986).

The subcommittee report *Standing Operating Procedures for Developing Acute Exposure Guideline Levels for Hazardous Chemicals* (NRC 2001) recommends dividing an LC_{50} value by 3 to estimate the threshold for lethality. On that basis the 8-hr lethality threshold was estimated to be 220 ppm. However, several studies showed that no deaths occurred in humans inhaling 300-430 ppm (U.S. EPA 600/X-84/188-2, 1987), 260 ppm (Int. Arch. Arbeitsmed. 34:283-299, 1975), and 100-420 ppm (Med. Lav. 74:23-29, 1983) for similar periods of time. Therefore, the proposed 8-hr AEGL-3 is incorrect and—by extension—the AEGL-3 values for the other time points are also inaccurate. Therefore, the UF should be less than 3. For example, one-third of the mouse LC_{50}-derived AEGL-3 value (1,600 ppm) is said to predict human fatalities, but the two tile-installers exposed to greater than 1,842 ppm for 2 to 3 hr did not die (Br. J. Ind. Med. 47:417-420, 1990). It appears that the values based on human experience, presented in line 12 of page 7, are more accurate reflections of acute inhalation toxicity in humans. Although the Standing Operating Procedures document (NRC 2001) recommends dividing the LC_{50} by 3 to estimate the threshold for lethality, the resulting value must be compared with actual human-exposure data and if humans are able to tolerate exposure levels higher than those calculated from the animal data, then the LC_{50} values should be divided by a UF less than 3 so that the resulting value is consistent with human data.

The AEGL derivation section should compare and contrast the accounts of headache and dizziness in 50% of the 16 volunteers inhaling 100 ppm for 6 hr (Scand. J. Work Environ. Health 9:405-418, 1983) and the complaints of fatigue reported by 43 printers inhaling 100 ppm (99.7% toluene purity) for 6.5 hr daily (Scand. J. Work Environ. Health 11:271-280, 1985). Those accounts and the weight-of-evidence discussion can be used to either derive the AEGL-1 and AEGL-2 values directly or to verify any proposed AEGL values for once-in-a-lifetime exposure scenarios.

Regardless of the AEGL values selected, it is important to verify the nominal air concentrations in relation to the human circulating concentrations (823-1122 μg/L) and alveolar air concentrations (38-53 μg/L) associated with coma (Br. J. Ind. Med. 43:56-61, 1986), CNS degeneration (Schaumberg, 1983), and death (10-33 ppm) (Br. J. Ind. Med. 47:417-420, 1990). The calculation may assume the standard workshift ventilation rate (10 m^3) or the 24-hr ventilation rate (20 m^3), the pulmonary uptake (page 37, line 2), and a linear relation between alveolar air toluene and arterial toluene concentrations (page 36, line 34).

The justification for using an intraspecies UF of 3 is not consistent with data in the document indicating wide variability in human and animal responses (see text: page 36, line 1; page 36, lines 16-17; page 36, line 37-38). This variability is even greater if it is considered that young infants seem to be especially susceptible to toluene (page 27, lines 30-31; page 29, lines 31-32). Furthermore, the Agency for Toxic Substances and Disease Registry (ATSDR) used UFs of 10 for human variability (intraspecies variability) for all three minimal risk levels (MRLs) calculated in their toluene-toxicity profile (1999). If the NAC concludes that an intraspecies UF is appropriate in light of the citations above, a far more rigorous explanation should be included.

Many of the study descriptions in the text lack detail, especially on exposure. One such example can be found on page 14, lines 6-14 (Foo et al. 1990). Those details should be provided, or a statement should be added stating that information is unavailable.

The AEGL-3 values seem justified and appropriate for the existing database. However, the spacecraft maximum allowable concentration (SMAC) level previously recommended by COT was significantly lower for the 1-hr exposure period. The neurotoxicity data of Andersen et al. (1983) was used in establishing SMACs. Dizziness, decrements in visual perception, and psychomotor function would not be acceptable for astronauts, even for a short period of time, so the NOAEL divided by a factor equal to one-tenth of the square root of the number of subjects tested level was used in establishing the SMAC value. The SMACs subcommittee also adjusted this NOAEL to account for the relatively low number of human subjects (16) in the study as follows:

NOAEL × 1/small *n* factor
40 ppm × $\sqrt{16} \div 10 = 16$ ppm

Specific Comments

A number of studies on the reproductive and developmental toxicity of toluene exposures are not included in the AEGL document. The ATSDR toxicity profile as well as one review article (Environ. Health Perspect. 94:237-244, 1991) include additional studies that have not been considered or discussed. Many of those studies address exposure to toluene rather than to solvent mixtures. While the subcommittee understands that not all developmental and reproductive toxicity studies need to be included, the following studies should be considered:

- Zavalic et al. 1998. Quantitative assessment of color vision impairment in workers exposed to toluene. Am. J. Ind. Med. 32:297-304.
- Suzuki et al. 1983. Thinner abuse and aspermia. Med. Sci. Law 23(3):199-202.

- Svensson et al. 1992. Hormone status in occupational toluene exposure. Am. J. Ind. Med. 22:99-107.
- Svensson et al. 1992. Neuroendocrine effects in painting workers exposed to toluene. Br. J. Ind. Med. 49:402-408.

Page 6: Provide the AEGL value when discussing the results in the text. As the text reads now, all three AEGL values are included in the chart at the end of the Summary, but there is no mention of the values in the text where AEGL-1 and AEGL-2 value are discussed. The AEGL-3 value is already included in the text.

Page 6, line 7: Although inhalation is the primary route of exposure, the text should note that toluene can also be absorbed through the skin and alimentary tract.

Page 6, line 9: Add the ambient air concentration that causes eye irritation.

Page 6, lines 20, 25-26: Define "mild sensory irritation."

Page 6, line 10: Insert to read: "...humans after accidental or intentional inhalation of very high concentrations (>1,000 to 10,000 ppm) (Wiseman et al. 1987; Press et al. 1967)..."; insert a reference to Pediatrics 39:451-461, 1967, on page 61, line 23.

Table 1. The table notes that the odor threshold was 2-40 ppm, but page 10 states that the odor threshold is 100 ppm. Which is correct? Because odor is not a physical property of a material, odor threshold does not belong in Table 1.

Table 10: Superscripts e, f, g, h, and i are not correct. There is no ACGIH STEL for toluene. On page 47, line 37, the NIOSH reference is incomplete.

Page 7, lines 9-11: It should be noted that both of these men were overcome and collapsed after inhaling toluene at the indicated concentration for 2-3 hr. Also state that these victims experienced amnesia, paresis, sinus bradycardia, drowsiness, headache, mucosal irritation, and slurred speech.

Page 7, line 11: Define "this exposure."

Page 7, line 19: The rationale for using "eye irritation" to derive even a 10-min (let alone 8-hr) AEGL-1 of 29 ppm is not supported by the available human data. While mild throat irritation occurs at 1,100 ppm (Toxicol. Ind. Health 4:49-75, 1988), even very high exposure concentrations (>10,000 ppm) are without marked ocular irritation. Transient, mild irritation has been a common complaint from exposures to toluene at a concentration of approximately 400 ppm. Based on the results of controlled human chamber studies and published industrial experience, it is not possible that exposure at a concentration of 29 ppm for 8 hr could present an increased risk for ocular irritation.

Page 8, lines 26-27: It would be better to cite the most recent (i.e., 2000) ATSDR Toxicological Profile here.

Page 9, line 14: Odor threshold is not a chemical or physical property of toluene. Describe the odor parameters on page 7, line 30.

Page10, line 21: The text should include the studies of Andersen et al. (1983) and Baekum et al. (1985), both of whom demonstrated that exposure to 100 ppm caused complaints of "slight" and "moderate" eye irritation (define "slight" and "moderate"), headaches, and fatigue. Consider including a discussion of the results from the Anderson et al. (1983) study, which showed that the NOAEL for irritation and CNS depression was 40 ppm.

Page 10, Section 2.2.1, Case Report: Of the three cases reported, two involved occupational exposure (the other was a case of toluene abuse). Those two should be included in Section 2.2.2—Occupational Exposures.

Page 10, lines 25-26: What is meant by "... a significant six fold shift..."?

Pages 10-14, Section 2.2.2: A great deal of discussion is devoted to occupational exposure studies. In most of those cases, the exposure concentrations are only estimates, and usually, the exposures involved other compounds. This section should be significantly reduced in size, because these data were not used in establishing AEGLs.

Page 10, Section 2.2: In the section titled Nonlethal Toxicity, the exposure durations are not clear. For example, how many 3-day exposure sessions were carried out?

Page 10, line 40: "...would have sunk to the bottom of the pool...": Were not the men actually working at the bottom of the pool from the outset?

Section 2.1: Does the NAC believe that these case reports contribute significantly to the database on toluene toxicity even though they all involve exposure to a mixture of solvents rather than toluene alone? Explain.

Page 11, line 2: Define the phrase "an excessive anion gap"? Include a brief statement on its clinical relevance.

Page 11, line 9: On what basis is it known that there were no permanent or persistent effects? Was another study or evaluation available that lead to this conclusion? Or was this the conclusion of the study authors?

Page 11, line 20: Change "possible" to "taken."

Page 11, line 21-22: The percentages listed add to more than 100%; toluene alone is 100%. Is this correct?

Page 11, line 35 et seq: Are exposure concentrations available for any of these studies? If such data are not available, then the text should indicate that gap.

Sections 2.2.1 and 2.2.2: Both sections contain case studies, so the separation seems arbitrary. Furthermore, since many of the studies described in Section 2.2.2 do not indicate exposure levels, those descriptions should be condensed.

Page 12, lines 1-2: Ron (1986) has a review on neurological and psychiatric sequelae as a consequence of toluene abuse. This review should be considered and the results cited here.

Page 12, line 10: Delete "attempt to."

Page 12, lines 14-20: The text summarizes signs of intoxication observed in workers exposed to a mixture of solvents; the exposure to mixtures of similar substances needs to be addressed in the document.

Page 12, lines 14-20: When did White et al. (1995) test their subjects? (That is, were these impairments associated with acute exposures, or were they long-term sequelae?)

Page 12, lines 22-42: What was the estimated exposure concentration in these cases?

Page 12, lines 22-27: Is there any information on exposure levels? If not, the document should say so.

Page 12, lines 30-40: Did the authors conduct the same test protocols in the 3-year follow-up study as they did in the initial investigation immediately following toluene exposure?

Page 13, line 6: Expand on the description of exposure. The text says, "...for periods of one to three weeks...." Was this a continuous exposure? Expand if this information is available; if no information is available to address exposure frequency and duration, make a note of that in the text.

Page 13, lines 4-10: The discussion concerning the exposure of the workers is unclear. Which or how many employees were grouped according to toluene-exposure concentration?

Page 13, line 15, "These subjects...": How many?

Page 13, lines 20-21: Are there more details on the exposure of these workers? (That is, how many workers were exposed? What was the duration and frequency of exposure and at what concentrations?)

Page 13, lines 31-38. Provide greater detail on exposure for the Ukai et al. (1993) study. If no details are available, that should be indicated.

Page 14, lines 1-4: From the findings of Lee et al. (1998), what was the exposure threshold for symptoms of toluene intoxication?

Page 14, line 11: It is stated that the average concentration was 88 ppm. What was the concentration range?

Page 14, lines 29-34: The study by Astrand et al. (1972) is not listed in Table 2. Although the protocol did not involve neurological parameters, that study is of interest, because it reported no adverse effects at 200 ppm (30 min), even with exercise.

Page 16, lines 21-22: The text states, "This indicates that short-term exposures to toluene below 300 ppm are not associated with psychomotor dysfunction." This is incorrect. The data indicate that exposure to 100 ppm was considered a NOAEL for impaired reaction time. From this study, one cannot know if, for example, 200 or 250 ppm caused effects or not, only that at 100 ppm, there was no effect.

Page 16, lines 30-31: What does it mean to be exposed for an "8-hr session over the course of an 8-wk period"? Were the subjects exposed only once? Also, the effects of exposure to 50 and 200 ppm are not included in Table 2. The subjects exposed to 800 ppm were exposed for 3 hr and then to an additional 2 hr after a 2-hr break. Table 2 only indicates a 3-hr exposure.

Page 16, lines 29-32: The description of exposure parameters is not clear. How often during the 8-week period did the 8-hr exposure occur? Were the subjects exposed only once each week or 5 days/week? Expand the text description if information is available; if not, note.

Page 17, line 4, "...in all groups...": What does this phrase refer to? Both male and female groups? Or were the males and females divided into additional exposure groups?

Page 17, line 33 and page 18, lines 1-8: The text is inconsistent; a number of adverse effects are described in this section. A concentration of 100 ppm was unacceptable because of an increase in irritation of eyes and nose, increases in headaches, dizziness, and feeling of intoxication. However, Table 2 states that in the Andersen et al. (1983) study there were "no effects."

Page 17, line 41: What is meant by the term "unacceptable"?

Page 18, line 42: The Carpenter et al. study involved exposure to a mixture of solvents; therefore, it is not clear how an odor threshold for toluene could be obtained. Because a mixture was involved, the utility of this study in terms of toluene levels with respect to response is also unclear. Explain.

Page 19, Section 2.3: The developmental and reproductive toxicity study by McDonald et al. (1987) examined 301 women, who had recently given birth to children with congenital defects. In only those women who were exposed to aromatic solvents (primarily toluene) was there "suspicious excess in number of cases of birth defects." See the toluene documents prepared by the Subcommittee on Spacecraft Maximum Allowable Levels and the ACGIH TLV documentation concerning the developmental toxicity of toluene.

Page 19, line 17: Revise to read: "...fetal effects clearly associated with gross toluene...."

Page 20, lines 38-42: List the benzene content of the toluene to which these workers were exposed. Note the total numbers of workers examined, their ages, and the toluene concentrations in workplace air and whether or not smoking and ethanol consumption were taken into account. Define any other occupational materials to which these workers were exposed. Explain the nature of the operations (e.g., painting, printing) in which they were engaged. Is there any information on toluene exposure levels? If so, add; if not, note the lack of information.

Page 21, lines 15-19: State the benzene concentrations to which the cohort was exposed.

Page 21, lines 15-19: This study does not contribute to information on carcinogenicity of toluene because it involved multiple-solvent exposures and, therefore, the possibility that some of the cancers (or all of them) were due to chemicals other than toluene.

Page 21, lines 31-32: Did the IARC document conclude that the carcinogenicity of toluene was not "classifiable," or was that conclusion attributable to EPA?

Page 21, lines 39-40: This sentence is repetitive; delete.

Page 22, Carpenter et al. (1976) study: Table 3 should include the following: 12,000 ppm produced 100% mortality.

Table 3: Pryor et al. (1978) was not discussed in the text. The study reported that the LC_{50} for a 60-min toluene exposure was 40,000 ppm. Table 3 should show that a 6-hr exposure of mice to 24,400 ppm resulted in 100% mortality (Cameron et al. 1938).

Page 22, lines 4-7: The information in the second sentence in this paragraph seems to have been taken from Wilson (1943) or von Oettingen et al. (1942), but it appears that the information is attributable to Gamberale and Hultengren (1972). The latter found 300 ppm to be the threshold for increased reaction time in their subjects. Reaction times increased with increasing level of exposure. No effect on perceptual speed was observed until the exposure level reached 700 ppm.

Page 22, lines 13-14: Is the lack of evidence for adverse health effects in women due to a lack of exposure studies, or is there a real indication that effects differ between genders?

Page 22, line 22 et seq.: This study involved a mixture of various chemicals, and therefore, the LD_{50} noted here and in the table may not be due solely to toluene. Thus, the study should not be included in Table 3.

Table 3: In the Cameron et al. (1938) study, exposure to 24,000 ppm for 1.5 hr produced 60% mortality in rats and 10% in mice, but exposure to 12,200 ppm for 6.5 hr produced 50% mortality in rats and 100% in mice. Thus, in one case, the mice were apparently more sensitive, and in the other, the rats were more sensitive. These numbers should be verified.

Page 22, line 39: What are "head tremors"?

Page 23, line 16: What is meant by "Lt-50"?

Page 24: In the discussion of rabbit, cat, and dog studies, no details are provided to explain how the animals were exposed other than by inhalation. Is there more information that can be added here to clarify the presentation?

Page 24: The section on cats and dogs should not be included in Section 3.1 (Acute Lethality). They were not mortality studies.

Page 24, line 10: Define "changes in respiration."

Page 25, Line 1: Were these adult monkeys?

Page 25, lines 24-35: The study protocol description is not clear. Were rats exposed to the stated individual nominal concentration for 4 hr, or was there some type of progressive increase in chamber toluene concentrations from 125 to 4,000 ppm over the 4-hr interval?

Pages 25-30: All the studies on these pages describe neurobehavioral effects. Why not include a new section titled "Neurobehavioral Effects."

Page 26, line 1: The percentage of escape responses should be "decreased" rather than "increased."

Page 26, line 3: Add a period at the end of the sentence.

Page 26, line 9, Table 4: Delete "during 2 hours" in the 3rd column.

Page 27, line 12, "... increased during the 30-120 period...": Does this sentence refer to minutes? Also, in the text above, the recovery periods are defined as 0, 30, 60, or 90 min. There is no mention of a 120-min period.

Page 28, line 1-2: How long were the rats exposed to 1,500 ppm?

Page 28, line 33: Add the dates for the Tegeris and Balster studies.

Page 28, lines 39-42: Add the concentration and exposure duration for the Glowa et al. (1981) study.

Page 30, lines 5-6: What were the dose levels of toluene and pentobarbital that produced "mild narcosis"?

Page 30, lines 5-7: Findings of "flattened" mice (prostrate?) and animals lying on their sides are indicative of a response considered more than "mild narcosis."

Page 30, line 22: Define "RD."

Page 30, line 29: Is "2.5 ppm" the correct exposure level?

Page 30, lines 34-41: Define the purity of the toluene used in the study. State the benzene concentration, if any. If no purity data are available, that should be stated in the text.

Page 31, Table 5: Move table to the first full page following its introduction in the text (page 28).

Page 31, line 19: What was the duration of the exposure in the rabbit study?

Page 31, line 29 et seq.: Many of the effects described here are not related to developmental toxicity and should be moved to an appropriate section of the document.

Page 31, lines 29-36: Define maternal body-weight changes in control and toluene-treated groups. State on page 32 whether the toluene exposures associated with developmental toxicity were also associated with maternal toxicity. State whether gross pathology and histology studies (e.g., kidney) were conducted on dams and, if so, what were the findings?

Page 33, line 9: Define "LDH."

Page 33, line 13: What is a "pregnancy guidance value"? What is the pregnancy guidance value (20 ppm) for rabbits? How does a "pregnancy guidance value" fit in, if at all, with the AEGL values? Does this value imply the danger of human congenital malformations after inhaling 20 ppm of toluene for some unspecified period of time? How does this "guidance" compare to the Hemminki (Int. Arch. Occup. Environ. Health 47:191-207, 1980) evaluation?

Page 34, lines 27-29: The text should note that all CNS depressants and anesthetics produce an initial excitatory stage, followed by narcosis.

Page 34, line 36: Does the NAC consider low birth weight a teratogenic effect, fetotoxic effect, or another form of developmental toxicity? Refer to the published literature to support any conclusions in this regard.

Page 35: It would be helpful to add a figure from ACGIH to illustrate the toluene biotransformation pathways. A discussion should be added to address the concentrations at which saturation of human toluene metabolism occurs and whether or not the biotransformation rates, intermediates, and pathways differ as a function of dose (e.g., see current ACGIH BEI documentation for toluene).

Page 35: Delete the sentence that begins on line 26.

Page 35, line 5: Change "doubled or tripled" to "increased."

Page 35, paragraph 2: Provide a reference for the information provided in this paragraph.

Page 35, line 10: Provide the reference for this sentence.

Page 35, lines 12-13: Instead of using the Bruckner and Peterson (1981) data, the data of Lof et al. (1990) and Hjelm et al. (1988) should be used to derive AEAGL values. The text should note that the ratio of toluene concentration in brain versus blood is constant after the first 20-30 min of inhalation exposure.

Page 35, line 15: The sentence seems to be missing an ending.

Page 35, lines 17-18: Cite ATSDR (2000) report rather than NTP (1990) report as a source of toluene kinetic information.

Page 35, lines 17-18: This sentence implies that a fraction of inhaled toluene (much of which is not absorbed and is exhaled unchanged) undergoes metabolic biotransformation in the liver following absorption. If that is what the text intends to convey, then it should be clarified. Also, the material in the next paragraph is unclear, and there is some confusion as to the extent of inhaled toluene exhalation and the fraction of toluene absorbed into the systemic circulation.

Page 35, line 18: It should be pointed out here that the metabolism of the absorbed dose is dose-dependent. The higher the absorbed dose, the lower the percentage metabolized and the higher the percentage that is exhaled as the parent compound. Data should be discussed and summarized here to illustrate the dose-dependent disposition of toluene and how those parameters relate to the toxicity of this material in humans.

Page 35, lines 26-30: The half-life ($t_{½}$) found by Benoit et al. (1985) is likely to be applicable to the secondary elimination phase of the volatile organic chemicals (VOCs). This phase is more relevant to a person's time to recovery from the CNS depression associated with gross toluene exposures.

Page 35, lines 31-34: This sentence is awkward and needs to be rewritten. The discussion implies that the metabolic capability to handle toluene varies widely among humans. If that is correct, does not it contradict the general reasoning used to support the use of a UF of only 3 for intraspecies variations? Provide references to the published data to support the extent of "wide variability," the magnitude of that "wide variability," and how it relates to AEGL derivation.

Page 35, lines 41-42: Why is the information given here of "limited relevance"? If the information presented has little relevance, then it should not be included in the document. Which group of investigators determined that humans metabolize toluene at 1.3 times the rate of rats? Does this conclusion include considerations of toluene's dose-dependent rates of elimination (page 35, line 18)?

Page 35, last line: This statement as written is probably incorrect. Does the NAC refer here to in vitro rates?

Page 36, line 5: The number "0.5" seems to be missing a word or phrase—perhaps "0.5-fold"?

Page 36, line 5: Does the statement refer to acute or chronic ethanol consumption (Int. Arch. Occup. Environ. Health 59:475-483, 1987; Ibid 60:31-35, 1988)?

Page 36, lines 5-6: This sentence is unclear.

Page 36, line 9: Should it be "3.3-fold"?

Page 36, lines 20-21: This sentence should be reworded.

Page 36, line 31: Were there 18 rats? Provide the number of humans in the Tardif et al. (1995) study.

Page 37, line 1: The parenthetical information "(1 mg of toluene = 11 μmol)" seems to be out of place. Where does it belong?

Page 37, line 6: "Read" should be "reach."

Page 37, lines 1-8: Were blood concentrations expressed in milligrams per kilogram?

Page 38, lines 5-11: These tissue concentrations should be related to exposure levels.

Page 38, lines 10-11: What is the basis for the statement that humans and rodents experience similar CNS effects at similar toluene levels? Does "similar toluene levels" refer to nominal air concentrations, circulatory concentrations, or brain concentrations of this material? Does this statement refer to parent compound or its metabolite(s)?

Page 38, lines 41-42: A discussion of the frank clinical kidney disease associated with high-dose toluene exposure should be provided here (Ann. Intern. Med. 94:758-762, 1981; West. J. Med. 4:192-196, 1963; Calif. Med. 100:19-22, 1964; N. Engl. J. Med. 269:1340-1344, 1963; Br. Med. J. 2:29-30, 1971; N. Engl. J. Med. 290:765-768, 1974; Arch. Neurol. 37:673, 1980; J. Urology 123:89-91, 1980; JAMA 241:1,713-1,715, 1979; Ann. Intern. Med. 92:69-70, 1980; Med. J. Aust. 2:121-122, 1981; Clin. Toxicol. 24:213-223, 1986; Nephron 49:210-218, 1988), particularly in contrast to the in vitro turtle-bladder discussion listed in the draft.

Page 39, Section 4.4.2, Susceptible Populations: This discussion is not consistent with the text, where several examples are provided of variations in response, metabolism, and toxicity among humans and animals. Also, the discussion concerns generic reactions to volatile chemical mixtures, not to toluene per se. Elsewhere in the document, the consequences of exposure to volatile mixtures seem to be intentionally avoided. The NAC should include data on toluene in this section and then draw appropriate conclusions on the material of interest.

Page 39, lines 14-19: It is stated here that there is "little difference" in the sensitivity of mice and rats to toluene lethality. However, line 18 of page 44 states that the mouse is the most sensitive species. The results cited in lines 14-19 of page 39 demonstrate that the mouse is more sensitive to toluene CNS depression than is the rat. This species difference is anticipated because of species-dependent differences in VOC kinetics (pertinent comments on AEGL-3 determination).

Page 39, lines 23-38: This paragraph begins by noting that children and infants are more resistant to effects of volatile anesthetics than adults. However, on line 32, it notes that newborns are very susceptible. Some modification of the text needs to be made to clarify this discrepancy.

Page 39, line 38: The main point here appears to be that healthy, older infants are less likely to be susceptible to inhaled toluene-induced anesthesia than are healthy adults? Thus, a "child modifying factor" for toluene AEGL derivation would not be necessary or appropriate here. What is the intended message of this paragraph in relation to toluene AEGLs?

Page 39, line 40: Insert to read: "...who complained that they were...."

Pages 39, lines 40-42 and page 40, lines 1-6: Was the odor of toluene masked in the study of Little et al. (1999). Were those who scored the test results aware of the identity of the subjects and their exposures?

Page 39, Section 4.4: It states that "comparison of LC_{50} for rat and mouse shows little differences in sensitivity between these species." However, on page 44, in the establishment of the AEGL-3 values (line 18), the authors state that "mouse is the most sensitive species based on LC_{50}." Both statements cannot be correct.

Page 39 and Page 41: It states that there appears to be a 2- to 3-fold difference among humans in susceptibility to volatile anesthetics, and that could provide the basis for an intraspecies UF of 3 for toluene. However, the justification provided is that the mechanism of action is not expected to vary greatly between individuals. Due to pharamcogenetic and other factors (e.g., body weight), there can be great interindividual variation in response to chemical exposures, even if the mechanism or mode of action is the same for all humans. Thus, this justification needs to be reconsidered, although the choice of an intraspecies UF of 3 may be valid.

Page 40, lines 1-6: Because substantial bias can occur when studies are not conducted using a double-blind protocol (e.g., Occup. Med. 44:95-98, 1994), describe whether or not patients and/or investigators were blinded to the toluene exposure. As written, it appears that the concentration studied was less than the odor threshold (AIHA 1989)?

Page 40, line 3: How does this response—impaired cognitive function produced by 20-min exposure to 15 ppm—compare with the AEGL values? Is it consistent? Why was this study not considered?

Page 40, line 13: The statement about sensitivity differences contradicts the previous statement made on page 39, line 14. Description of interspecies sensitivity differences must be consistent.

Page 40, Section 6.1: If available, use a study other than the Wilson (1943) study?

Page 40, line 41: The document states here that in the Andersen et al. (1983) study, exposure at 100 ppm resulted in mild sensory irritation. That finding is not stated in Table 2. The information in the table must be consistent with the material in the main text. Also, define the nature of this "mild sensory irritation."

Page 43, lines 10-35: The toluene exposure level that would significantly "impair one's ability to escape" would be considerably higher than 200 ppm. As described in pages 14-19, approximately 100 ppm is close to a threshold for minimal decrements in a limited number of the most sensitive objective measures of psychophysiological performance. Echeverria et al. (1989, 1991) only observed small decreases from optimal performance in subjects inhaling 150 ppm for 4 to 7 hr. Such effects are quite different from impaired ability to escape. In the Taylor and Evans (1985) study, monkeys exposed to concentrations greater than or equal to 2,000 ppm for 50 min exhibited significantly impaired reaction times. However, inhaled concentrations less than or equal to 1,000 ppm did not significantly influence the animals' cognitive functions, including attention and visual-motor abilities.

In general, the AEGL-2 values are inconsistent with the published human-experience data. Toluene is a CNS depressant with little residual effect. There also appears to be a less than 3-fold difference in onset of effects among individuals. Toluene does not produce carcinogenic effects, and teratogenic effects occur only in chronic abusers. Section 8.2 states that the AEGL values are consistent with other standards. To the contrary, the AEGL-2 values are considerably lower.

As for the AEGL-1 calculations, the subcommittee recommends that a toluene PBPK model rather than the ten Berge approach be used to extrapolate across time. Once the near steady-state level is achieved, the blood/brain toluene levels and CNS effects will not be affected by duration of exposure.

Page 42, line 22: The 200-ppm exposure level for the von Oettingen et al. (1942) study is not shown in Table 2.

Page 42, line 34: Is this referring to the same CNS threshold as reported in the von Oettingen et al. (1942) study? Clarify.

Page 43, lines 33-35, "Scaling to the 30 minutes, 1, 4 and 8-hour time points...": Is that correct? Was the study used to calculate the 10-min exposure? The actual exposure was for 50 min.

Page 44, lines 27-28: It is not clear why 19,018 ppm was divided by 3 to "estimate the lowest concentration for lethality." Also, explain why the 1-hr LC_{50} for mice was divided by 3. No explanation or justification is given.

Page 45, Table 9: AEGL-2 values for 4 hr and 8 hr should read "90 and 70 ppm," respectively. The AEGL-3 value for 10 min should be 2,000 ppm (7,520 mg/m^3).

Page 47, line 27: Incomplete sentence.

Page 47-48: OSHA references are incomplete. (Cite the appropriate year.)

Page 57, line 10: "Kathol" should read "Katoh" (see page 39, line 24).

Page 74, line 34: Change "rat" to "mouse."

Page 75, line 24: Should be "mouse," not "rat" lethality data.

The references on pharmacokinetic modeling of toluene in humans are:

Tardif, R., S. Lapare, C. Charest-Tardif, J. Brodeur, and K. Krishnan. 1995. Physiologically-based modeling of a mixture of toluene and xylene in humans. Risk Anal. 15:335-342.

Pelekis, M., D. Krewski, and K. Krishnan. 1997. Physiologically-based algebraic expressions for predicting steady-state toxicokinetics of inhaled vapors. Toxicol. Methods 7:205-225.

Derivation of AEGL-1 Values

The use of Haber's rule is inappropriate for the derivation of AEGL-1, because sensory irritation is taken as the critical end point (see pages 41, 43, 69). The use of Haber's rule is justified for acute toxicity (AEGL-3) or systemic CNS effects (AEGL-2) but not for irritant effects.

Page 41, lines 18-36: Is it appropriate to use the threshold of 100 ppm as a basis for the derivation of AEGL-1 values? It is important to recognize that inhalation of 100 ppm of toluene for several hours produced minimal changes in a few psychophysiological indices in some exposed individuals. Anderson et al. (1983), for example, found borderline changes in just three of eight such tasks. Three of 16 subjects inhaling 100 ppm found this concentration unacceptable, but nasal mucus flow and pulmonary function were unaffected. The AEGL-1 is defined as the concentration above which persons could experience notable discomfort, irritation, or non-sensory effects. Nevertheless, 100 ppm could potentially be used as a starting point, because persons who are exercising can receive 3 to 4 times as great a dose as a person at rest (Astrand 1975), but a weight-of-evidence discussion, including all of the human data cited in the document, should be brought to bear in the AEGL-1 derivation for toluene.

The ten Berge equation $C^n \times t = k$ cannot be used to scale accurately across time for toluene. That process can result in overestimation of the 10-min value and substantial underestimation of the 1-, 4-, and 8-hr values. Toluene, like most other VOCs, is very rapidly absorbed from the lungs and reaches near steady-state, or equilibrium, in the blood and brain within 1-2 hr (Lof et al. 1990; Hjelm et al. 1988). Thereafter, the brain toluene concentration and level of CNS depression remain quite constant, irrespective of the duration of exposure. A physiologically based pharmacokinetic (PBPK) model (e.g., Pierce et al. 1999) should be utilized here to predict the blood/brain toluene concentrations for 10-min, 1-, 4-, and 8-hr inhalation exposures. These concentrations should then be compared with the data of Astrand et al. (1972), who measured blood toluene concentrations in persons inhaling 100 and 200 ppm.

Derivation of AEGL-2 Values

Page 42, lines 13-31. The studies by von Oettingen et al. (1942) and Wilson (1943) are unreliable and outdated. Neither study should be used for the derivation of the AEGL-2 values.

The results reported by von Oettingen et al. (1942) are questionable. Their analytical methodology (i.e., interferometrics) is no longer acceptable. Only three human subjects were used. No objective measures of CNS dysfunction were evaluated. Based on the results of other laboratories, the severity of the complaints both during and post-exposure substantially exceeds what would be anticipated at 200 ppm.

The basis of the AEGL-2 values (Wilson 1943) is weak because of the highly questionable concentrations. These concentrations were measured using a combustible gas indicator (CGI). With an LEL of 1.2% vol/vol, 200 ppm is only 1.7% LEL. That is typically much lower than the reliable range of the CGI (generally greater than 5%), and this is with today's technology. There is also no indication of confounding exposures. The Wilson (1943) article states that the test material was commercial toluene. A CGI measures all combustibles. Furthermore, there is no indication that the CGI was calibrated to toluene. In fact, it is unlikely, because most CGIs are calibrated to a combustible gas (methane, propane, etc.).

Derivation of AEGL-3 Values

Page 34, lines 27-40: The mouse is the most sensitive species to toluene exposure because it shows the highest internal doses upon inhalation of toluene. That is due to its relatively high respiratory rate, cardiac output, and blood-to-air partition coefficient. An interspecies uncertainty factor is not necessary under these circumstances—it is already built in. Because there is such an extensive data set for toluene, it might be better to use the published mouse LC_{50} values for 10, 30, and 60 min and 3 and 7 hr to calculate the corresponding AEGL-3 values. Their use will very likely result in more accurate values.

As with the AEGL-1 and AEGL-2 values, use of the ten Berge equation in the derivation of AEGL-3 values results in longer-term values (4-8 hr) that are "unduly conservative" and

concentrations that cannot be supported by the published human experience. The proposed 8-hr AEGL is about the same as the current OSHA 8-hr TWA of 200 ppm. Either use the LC_{50}s for different exposure durations or identify an applicable LC_{50} value for a single time-point and incorporate the results of appropriate PBPK modeling.

Page 45, lines 1-10: As mentioned previously, these individuals were likely exposed to toluene concentrations substantially higher than 1,842 ppm.

Page 45, line 2: As described previously, the proposed AEGLs are not in close agreement with existing occupational exposure standards.

COMMENTS ON HYDROGEN FLUORIDE

At its August 29-31, 2001 meeting, the subcommittee reviewed the revised AEGL document on hydrogen fluoride. The presentation was made by Sylvia Talmage of Oak Ridge National Laboratory. The subcommittee suggested the following minor revisions. The subcommittee also recommended that the hydrogen fluoride document not be published until the hydrogen chloride AEGL document is finalized, because the conclusions in the two documents must be consistent with the known acute toxicities of these two congeners.

General Comment

For AEGL-1: What is the justification for dividing the 1-hr value by 2 to obtain the 4- and 8-hr values? The subcommittee recommends the use of the same AEGL-1 value for all time periods, unless clear compound-specific justification for dividing the 1-hr value by 2 to derive the 4- and 8-hr values can be provided.

When rat data were used for the derivation of the 10-min AEGL-2 and 10-min AEGL-3 values, an interspecies UF of 3 was used, even though the rat was considered 2-4 times less sensitive than the mouse. Is an interspecies UF of 3 sufficient when data from the most sensitive species (i.e., mouse) are not used?

The discussion of the structure-activity relationships (SARs) for HF and HCl states the following: "The NAC understands that based on lethality data, HF is more toxic than HCl." However, the 8-hr AEGL-3 for HF listed on page vii (line 35) is essentially equivalent (15 ppm) to that previously proposed AEGL for HCl (13 ppm). The 4-hr AEGL-3 for HF is only slightly different (22 ppm) than that proposed for HCl (26 ppm). Although the 8-hr AEGL-2 for HCl is 2.7 ppm, the corresponding value for HF is 8.6 ppm, nearly 4 times the HCl value. This apparent inconsistency is carried through the 4- and 1-hr AEGL-2 relationships as well. Whether the problem is due to the use of additional modifying factors, time-scaling discrepancies, or other difficulties, it should be resolved prior to the joint publication of the HCl and HF documents.

ALLYL ALCOHOL

[as brought to COT August, 2001]

SUMMARY OF AEGL VALUES FOR ALLYL ALCOHOL (ppm)						
Level	**10-m**	**30-m**	**1-hr**	**4-hr**	**8-hr**	**Endpoint (Reference)**
AEGL-1	1.8	1.8	1.8	1.8	1.8	Mean odor detection threshold
AEGL-2	9.6	9.6	7.7	4.8	3.5	Reversible irritation in rats exposed to 40 ppm for 7 h for 60 exp. (increased lung wt observed at necropsy)
AEGL-3	36	25	20	10	7.1	Highest conc. causing no mortality in mice, rabbits, and rats: 200 ppm for 1 h

Comment: Limited Database

- AEGL-2 based on study where 10 rats/group exposed to 1, 2, 5, 20, 40, 60, 100, or 150 ppm allyl alcohol for 7 h/d, 5 d/wk, for a total of 60 exposures.
- AEGL-3: The data used for the AEGL derivation were obtained from a 1-page summary provided by Union Carbide (1951). No information given about controls, method of exposure, strain or sex of rats, analytical verification of concentration, or period of observation following exposure.

TOTAL UF of 10:

- **Interspecies: 3** - Not much variation between species (highest conc. causing no mortality in mice, rats, rabbits)
- **Intraspecies: 3** - Traditional approach would call for UF of 10, but this would result in composite factor of 30. This would drive the AEGL-2 and -3 values to level that would be inconsistent with available data (see executive summary for details). Therefore, composite value of 10 was used.

SCALING ACROSS TIME:

- **AEGL-2:** Default of n = 1,3. 10-min value set equal to 30-min value because extrapolating from 7-h exposure duration.
- **AEGL-3:** If go with default of n=1,3, the 4-h AEGL-3 value approaches 4-h AEGL-2 (5.0 vs. 4.8 ppm) and the 8-h AEGL-3 is below the 8-h AEGL-2 (2.5 vs. 3.5 ppm). Therefore, an n=3 was used to extrapolate from longer to shorter durations, and an n=2 was selected for shorter to longer duration extrapolations

CHANGES PROPOSED BY COT:

Because available data do not clearly indicate the extent to which the AEGL-3 value should exceed the AEGL-2 value, the subcommittee recommends that the AEGL-3 and AEGL-2 values be identical.

Support for the suggestion of setting AEGL-3 values equal to the AEGL-2 values:

- Study used for AEGL-3 is very weak - database does not provide good background for assessing acute lethal concentrations. Really is no clear indication of how much AEGL-3 value should exceed AEGL-2 value. Conversely, decent support for the AEGL-2 value, which is the level for "action."
- Would eliminate the inconsistency observed during the time scaling of the AEGL-2 and AEGL-3 values.

SUMMARY OF PROPOSED AEGL VALUES FOR ALLYL ALCOHOL (ppm)					
Level	**10-m**	**30-m**	**1-hr**	**4-hr**	**8-hr**
AEGL-1	1.8	1.8	1.8	1.8	1.8
AEGL-2	9.6	9.6	7.7	4.8	3.5
AEGL-3	9.6	9.6	7.7	4.8	3.5

FURAN
[as brought to the COT August, 2001]

Only one acceptable study in database:

Terrill et al., (1989. Am. Ind. Hyg. Assoc.): 5 male or female Sprague Dawley rats/group, exposed to 1014, 2851, or 4049 ppm for 1 h; sacrificed 14 days after exposure

Toxicity signs: respiratory distress, increased secretory response (degree at each concentration not provided)

Body weights ↓ in mid- and high-conc. groups

No treatment-related gross lesions

Mortality Rate of Furan in SD Rats		
Concentration (ppm)	Mortality rate	
	Male	Female
1014 ± 36.6	0/5	0/5
2851 ± 246.7	0/5	0/5
4049 ± 227.8	5/5	4/5

1-hour LC_{50} = 3464 ppm

Concentration/Time Selection Rationale:

AEGL-2 Lowest exposure conc. of 1014 ppm for 1 h. Although severity of clinical signs (respiratory distress, increased secretory response) not reported, this group did not exhibit decrease in b.w. like rats exposed to 2851 or 4049 ppm for 1 h.

AEGL-3 Highest nonlethal exposure conc. for 1 h = 2851 ppm

Summary of Proposed AEGL Values for Furan (ppm)*					
Level	**10-m**	**30-m**	**1-h**	**4-h**	**8-h**
AEGL-1	NR	NR	NR	NR	NR
AEGL-2	18	13	10	2.5	1.3
AEGL-3	52	46	29	7.1	3.6

*Note: these numbers will change no matter what because [uncertainty factor of 30] x [modifying factor of 3] = 90, not 100!

1-hour SMAC value: 4 ppm

AEGL-1

- Not recommended; insufficient data

AEGL-2 and -3

- **Reference:** Terrill et al. (1989)
- **Value of n:** default of n = 1 or 3
- **Total UF/Modifying Factor = 100**
  Interspecies UF : 10
  Following simulated exposure to 10 ppm for 4 h, predicted absorbed dose of furan (mg/kg) in humans, and consequently liver dose of reactive metabolite, was 10-fold less than in mice and 3.5-fold lower than in rats. However, differences between humans and rodents in sensitivity to reactive metabolite are not known.

  Intraspecies UF : 3
  Because blood flow predicted to be limiting factor in bioactivation of furan, levels of reactive intermediate will not be influenced by interindividual variations in the levels of cytochrome P450 2E1
- **Modifying Factor (MF): 3:** only one data set

CHANGES PROPOSED BY COT:

The NAC should consider using larger MF to account for paucity of data. Currently, AEGL-2 and AEGL-3 values include MF of 3 because "only one data set addressing furan toxicity following inhalation exposure was available." It is suggested that a MF of 5 or 10 be considered, and basis for any database MF should be clearly presented in the text.

Note: Terrill et al. study was from reliable lab (Hazelton Labs and QO Chemical, Inc.), but not peer reviewed. A greater MF would not be inconsistent with database limitations.

Furan AEGL Values (ppm): UF=30; MF of 3, 5, or 10					
Level	**10-m**	**30-m**	**1-h**	**4-h**	**8-h**
AEGL-1	NR	NR	NR	NR	NR
Currently proposed: MF=3; total UF/MF=90					
AEGL-2	20	14	11	2.8	1.4
AEGL-3	58	40	32	7.9	4.0
MF=5; total UF/MF=150					
AEGL-2	12	8.5	6.8	1.7	0.85
AEGL-3	35	24	19	4.8	2.4
MF=10; total UF/MF=300					
AEGL-2	6.1	4.3	3.4	0.85	0.43
AEGL-3	17	12	9.5	2.4	1.2

Hydrogen Cyanide Chronology

NAC/AEGL-3: September 17-19, 1996
- AEGL-1 not recommended
- AEGL-2 based on Wexler (1947) i.v. study with humans
- AEGL-3 based on multiplying AEGL-2 by 2

NAC/AEGL-6: June 9-11, 1997
- Values reviewed again

NAC/AEGL-8: December 8-10, 1997
- AEGL-2 and AEGL-3 values redone based on monkey, mouse data
- no AEGL-1 values determined

HCN TSD submitted to Federal Register

NAC/AEGL-17: April 26-28, 2000
- AEGL-2 and AEGL-3 moved to Interim status
- 10-minute time-scaled AEGL-2 and AEGL-3 values derived
- Discussion of derivation of AEGL-1; no values passed

NAC/AEGL-18: July 26-28, 2000
- Peter Griem supplies Leeser et al. (1990) study
- Passed AEGL-1 values based on Leeser et al. (1990), other studies
- John Morawetz - questions interpretation of Leeser et al. study
  - → El Ghawabi used as key study; Leeser used as support

NAC/AEGL-20: January 8-10, 2001
- AEGL-1 revisited (George Rodgers)
- NAC re-approves values by show of hands; additional detail
- AEGL doses converted to oral intakes; shows no effect on infants
  - based on U.S. EPA chronic NOAEL

March 2001

Presented HCN to COT

John Morawetz expresses his concern with studies used to derive AEGL-1 by telephone

COT suggests more clarification on uncertainty factors (June 2001, 5th Interim Report)

NAC/AEGL-21: June 11-13, 2001

AEGL-1 revisited

Three options for approval of AEGL-1: "The Committee agreed the Leeser study generally supported the approved AEGLs.... used as supporting evidence."

August 2001

Revised TSD reviewed by COT

January 2, 2002

HCN approved as **FINAL** by COT (6th Interim Report)

Summary of Studies Used for HCN AEGL-1

(Preponderance of the Evidence)

El Ghawabi et al. (1975)

three electroplating factories in Egypt
average atmospheric concentrations of 6, 8, 10 ppm (range 4.2-12.4 ppm)
symptoms of headache, weakness, changes in taste and smell
half of the workers had enlarged thyroids associated with chronic cyanide exposure
National Research Council says 8 ppm causes no more than mild headache (NRC 2000)

Leeser et al. (1990)

63 cyanide salt production workers in the U.K.
geometric mean concentration of ≤1 ppm with range of 0.1-3.6 ppm (personal samplers)
concentrations up to 6 ppm measured with area samplers
increased subjective symptoms (lack of energy), but no work-related health problems

Grabois (1954)

New York State health survey of 5 apricot kernel processing plants
exposures of <1 to 17 ppm depending on specific operation (air sampling)
10 ppm was workplace standard at the time; therefore, controls instituted "where needed"
no medical examinations
NIOSH (1976) stated that 5 ppm was a no-effect concentration in an occupational setting

Hardy et al. (1950)

medical doctor at Massachusetts General Hospital
cites two cases presenting with symptoms
    presumably due to chronic exposure or overexposure
    employees involved in "case hardening," which employs a liquid cyanide bath
    symptoms of weakness, dizziness; one had enlarged thyroid
review of literature; cites 10 ppm as safe because body able to metabolize, excrete
cites Mass. Division of Occupational Hygiene occupational survey
    in which 4-6 ppm HCN routinely encountered

Maehly and Swensson (1970)

not a medical survey
workers routinely exposed to 1-10 ppm (work area samples)
exposure appeared to have no influence on blood concentration of cyanide
    i.e., smoking and diet (as well as air exposure) influenced blood cyanide content

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

National Institute for Occupational
Safety and Health
Robert A. Taft Laboratories
4676 Columbia Parkway
Cincinnati OH 45226-1998

August 3, 2001

Attachment 21

Mr. John S. Morawetz
Director
ICWU Center for Worker Health & Safety Training
329 Race Street
Cincinnati, OH 45202-3534

Dear Mr. Morawetz:

In your letter of July 11, 2001, you inquired about the basis for the National Institute for Occupational Safety and Health (NIOSH) recommended exposure limit (REL) for hydrogen cyanide (HCN) including clarification of how the study results from the Gabois [1954] study were used in the derivation of the REL.

In 1976, NIOSH published the document *Criteria for a Recommended Standard....Occupational Exposure to Hydrogen Cyanide and Cyanide Salts* in which recommendations for an occupational standard were proposed. NIOSH concluded from the available health data that high concentrations to cyanide can inhibit cytochrome oxidase and result in histotoxic anoxia and death. NIOSH also concluded that the Occupational Safety and Health Administration (OSHA) permissible exposure limit (PEL) of 5 mg/m^3 (4.7 ppm) as a 8-hr. time-weighted average was not sufficiently protective to prevent acute effects from cyanide salts. This conclusion was based on the study by El Ghawabi et al. [1975] in which an increase in subjective systems (e.g., irritation of the throat, abdominal colic, nervous instability) was noted in workers exposed to cyanide at concentrations ranging from 4.2 to 12.4 ppm. Results from studies reported by Sato et al. [1955], Heymans and Masoin [1900], Chaumont [1960], Colle [1972], Radojicic [1973], and Saia et al. [1970] were also cited in support of a short-term exposure limit. Based on these data, NIOSH proposed a REL of 5 mg/m^3 (as CN) as a ceiling concentration determined from a 10-minute sampling period. This recommendation was restated again by NIOSH in 1988 testimony to OSHA's proposed rule on air contaminants [53 FR 20960].

The study reported by Gabois [1954] was cited in the 1976 NIOSH criteria document as an assessment of worker exposure to HCN during the processing of apricot kernels. The Gabois [1954] study was not used by NIOSH in the derivation of the REL since it did not evaluate any health outcomes in exposed workers.

Please give Ralph Zumwalde (513-533-8320) or me a call if you have any questions. I can be contacted at (513) 533-8481.

Sincerely yours,

Paul A. Schulte, Ph.D.
Director
Education and Information Division

cc:
R. Niemeier
M. Sweeney
R. Zumwalde

Hydrogen Cyanide AEGL-1 Chronology

- Originally not recommended
- July, 2000 – Set AEGL-1 based on Leeser summary (area sample data)
- October, 2000 – Committee agreed to look at Leeser personal sampling data
- November, 2000 – NAS Discussion deferred

AEGL-1 Chronology (cont)

- January, 2001 – Need to accurately summarize Leeser, Grabois and El Ghawabi presented to AEGL meeting
  Agreed to revise justification
- June, 2001 –Agreed to revise justification
- Final TSD approved for NAS/COT publication Jan. 2002

Primary Human Studies – AEGL-1

- **Leeser, 1990**
  - Personal sampling of 8 job titles
  - Medical interviews collected at two times
  - 63 workers in April/May
  - 50 workers in August/September
- **Grabois, 1954**
  - Air sampling: No medical evaluation
- **El Ghawabi, 1975**
  - 15 minute air samples: Health findings above AEGL-1

Reported Symptoms

Table 9 Leeser, 1990

Symptom	Cyanide (n=63)	Controls DPO (n=100)
	Yes % (n)	Yes % (n)
Short of breath	14 (9)	7 (7)
Headaches	6 (4)	3 (3)
Sleep problem	13 (8)	8 (8)
Lacking Energy	14 (9)	5 (5)
Dizzy Spells	8 (5)	2 (2)
Nausea	3 (2)	0

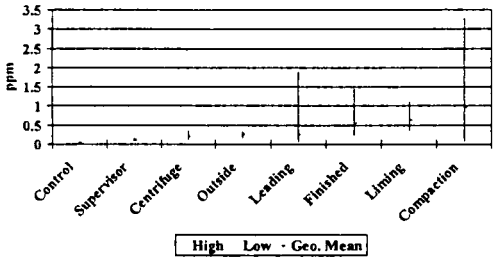
Author's statements

- "The number of symptoms noted by cyanide workers was significantly higher than that of diphenyl workers"
- "Overall, the cyanide workers complained of more symptoms than the DPO workers"
- "More cyanide workers than DPO workers complained of symptoms but these were not reflected in the numbers of pre-existing conditions reported"

Leeser, 1990 Personal samples (ppm)

Job Title	Geo. mean	Low	High	N
Supervisor	.11	.09	.15	2
Leading Hand	.25	.07	1.89	5
Control Rm Op	.027	.009	.064	4
Outside Oper.	.24	.15	.33	3
Treatment Op. Liming	.19	.11	.34	4
Treatment Op. Centrifuge	.63	.36	1.1	4
Compaction Oper.	.96	.08	3.3	8
Finished Product	.54	.23	1.5	4

Hydrogen Cyanide
Exposures by Job Title
Leeser, 1990



Study Findings

- Leeser, 1990 –Slight elevation of some symptoms. Exposures "could" be between .5 and 1 ppm
- Grabois, 1954 - Air sampling only
  - Can not be used for AEGL-1 derivation
- Conclusions: These two studies should not be used as primary studies to set AEGL-1

Other Human Studies

- **Hardy, 1950:**
  Serious symptoms in 2 workers
- **Maehly, 1970: blood and urinary cyanide and thiocyanate levels**

Other Human Studies – AEGL-1

- **Maehly, 1970**
  - Sampling "in the working area" of 13 exposed workers; average of 5 ppm (1-10 ppm)
  - Short term Draeger tube samples
  - No symptom investigation
  - Blood and urinary cyanide and thiocyanate
  - Results stratified by smoking status
  - No symptom investigation

Other Human Studies – AEGL-1

- **Hardy, 1950**
  - 2 cases of serious symptoms
  - No exposure information
  - Occupational recommendation - 10 ppm
  - Past studies by the Mass. Division of Occupational Hygiene; 1937-1950
  - "with adequate engineering devices, the HCN in the workers' breathing zone is not over 4 to 6 ppm"

AEGL values are "threshold exposure values for the general public" for once in a lifetime exposures. In some contexts, the question has been asked regarding the applicability of AEGL values in a chemical emergency to an occupational setting.

A. The AEGL values are "threshold exposure values for the general public". As described in the recent publication of four chemicals by the National Research Council (Acute Exposure Guideline Levels for Selected Airborne Chemicals, 2000), these are intended for "only once in a lifetime" exposures.

B. Other nationally recognized organizations (OSHA, NIOSH and ACGIH) currently recommend or set short term occupational exposure values; however, exposures to these values may be repeated during a single work-shift or work-week and are not considered once-in-a-lifetime exposures.

A number of issues arise when attempting to apply the AEGL values to an occupational setting.

1. The vast majority of the studies that the AEGL committee utilizes are single dose studies. The committee usually disregards animal and human studies that are from repeated doses. The occupational population is usually exposed to a number of chemicals at variable levels for different time periods during a single working day, week and year. This can result in variable chronic exposures both before and after a chemical release which are not considered in the AEGL process or the determination of Uncertainty Factors.

2. With regular chronic exposures and possible peak exposures, there is the possibility of sensitization. This is not considered in the AEGL process by definition since exposures are thought to be the first and only exposures.

3. The occupational population is typically a healthier population than the general population with no members at the younger and few at the older ages. People with various illnesses typically are found at much lower percentages within working populations compared to the general population. This is often noted as the "healthy worker effect" in occupational studies where disease rates to unexposed working sectors are lower than the general population.

4. Typically occupational values apply to the normal workday. Some individuals are unaware, however, that occupational values also apply in chemical spills and emergency response. Often occupational values are set due to the risk of serious or fatal diseases from chronic exposures; however, they can be set based upon acute symptoms. The OSHA act is designed so that "no employee will suffer diminished health" which has been interpreted to be protective of a wide range of symptoms.

5. Nationally recognized organizations (OSHA, NIOSH and ACGIH) may recommend or set short-term occupational exposure values, such as STELs, Ceilings or IDLH values. These organizations/committees are comprised of people with a range of expertises specifically needed to evaluate occupational studies and their application in occupational settings.

6. Occupational values determined by OSHA or recommended by NIOSH must adhere to the Occupational Safety and Health Act's mandates which require these agencies to consider feasibility (economic and/or technical).

AEGL values should be used with caution and caveats for any purpose other than those which they were specifically designed (the Technical Support Document and supporting documents can be obtained from the EPA). Since the AEGL values are intended for a single dose, they can often be higher than short term limits recommended for working populations, with repeated exposures. However, since AEGLs are set for susceptible populations not in the workforce, they can also be lower than a short term value for the workforce. Therefore the AEGL values can not easily be directly applied to the occupational setting. The NRC publication (Acute Exposure Guideline..) noted this difficulty in stating that "these limits (*OSHA and ACGIH*) are not easily or directly translated" for short, high and rare exposures to susceptible populations .

Where these organizations have set an occupational value(s) for a chemical, two possible scenarios may arise when attempting to compare the occupational value to the AEGL.

First, the AEGL value may be lower than the occupational recommendation. This may be due to the nature of the AEGL value in being protective of newborns, the elderly or sub-populations with impaired health and may therefore be overly protective relative to the occupational population.

Second, the AEGL value may be higher than the occupational value(s). In this situation, the occupational values may be taking into account that workers are rarely exposed only for a single instance. It is likely that these organizations have considered workplace studies of chronic exposure where the AEGL committee did not.

Therefore, when there is a distinct difference between the AEGL values and those set by OSHA, NIOSH and/or ACGIH, clear guidance in the SOP needs to be offered so as not to diminish the value of OSHA, NIOSH or ACGIH's values.

RECOMMENDATIONS

I. The AEGL committee should consider recommending that when these organizations have NOT set an occupational exposure recommendation, the AEGL values and the associated TSD can be used as a first step. Lacking these other chemical specific, inhalation risk based values, risk assessors use the AEGL values as a starting point, however, the TSD document and their supporting data needs to be examined to determine the rational for each level and whether it needs to be modified for a working population and occupational context.

II. The AEGL committee should consider language in the SOP which states that when these organizations have a short term exposure recommendation, applications of the AEGL values in an occupational setting should first reference the OSHA (the legally enforceable standard), NIOSH and ACGIH values. This would allow open comparison of values to the AEGL values with full knowledge of the legal, historical and proper context.

SECOND AEGL CHEMICAL PRIORITY LIST

First AEGL Priority List of 85 Chemicals has been Updated to 100 Chemicals

Second AEGL Priority List of 373 Chemicals (*137 High Priority):
*ATSDR Medical Management List
*ATSDR Top 20 Chemicals at Superfund Sites
DOE Remaining Initial Priority List
DOE Laboratory List
DOE SCAPA TEEL-3 and VP Lists
DOT ERG Isolation and Protective Action List
*Listed on 150 Hazardous Materials Transported by Rail
*EPA CAAA 112r (RMP) Including New Proposed
*EPA CAAA 112b List High Priority
EPA Superfund List
EPA SARA 302 List of Extremely Hazardous Substances
*EPA Office of Pesticides Nomination
OSHA Priority List
*Dutch Priority List
*French Priority List
*German Priority List
*Korean Priority List
*Russian Priority List
*DOJ Counter Terrorism High and Medium Chemicals List

Additional Notations on AEGL Priority List of 373 Chemicals
ATSDR Toxicology Profile Chemicals
Chemical Weapons Convention Schedules 1, 2, 3
DOD SERDP List
Air Force Installation Restoration Program List
Army Toxicity Summary Chemicals List
DOD Non-Stockpile Chemical Warfare List
DOE Other TEEL Master List
DOT Emergency Response Guidebook Chemical
Other Top 150 Hazardous Materials Transported by Rail
OSHA Chemical Process Safety List
Chemical Market Reporter (High Production)
Top RQ Chemical
Toxic Release Inventory List
Production Volume
ERPG
IDLH

Second List of 137(* chemical name) High Priority and 236 Low Priority Chemicals for Acute Exposure Guideline Level (AEGL) Development*

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Underlined lists were used to identify 139 Priority Chemicals and numbers in parentheses refer to total chemicals captured per listing (includes overlap)

ORGANIZATION LISTS USED FOR THE SELECTION OF PRIORITY CHEMICALS

ATSDR — **Agency for Toxic Substances and Disease Registry (36)**

A = ATSDR "Top 20" Toxicology Profile Chemicals (6)
B = Medical Management Guide Chemical (7)
C = Chemicals with an ATSDR Toxicology Profile (33)

DOD — **Department of Defense (18)**

A = Chemical Weapons Convention Schedule 1, 2, or 3 (2)
B = Strategic Environmental Research and Development Program (SERDP) Chemical (7)
C = Air Force Installation Restoration Program Chemical (10)
D = Army Toxicity Summary Chemical (9)
E = Non-Stockpile Chemical Warfare Substance (4)

DOE SCAPA — **Department of Energy Subcommittee for Consequence Assessment and Protective Action (80)**

A = TEEL chemical with vapor pressure >3.2 mm (35)
B = TEEL chemical with TEEL-3 <25 ppm (9)
C = Lab List (9)
E = Other TEEL chemicals (39)

DOJ — **Department of Justice Office of Justice Programs (23)**

A = "High" concern Toxic Industrial Material (TIM) (3)
B = "Medium" concern TIM (19)
C = "Low" concern TIM (10)

DOT ERP — **Department of Transportation Emergency Response Guidebook (106)**

A = Department of Transportation Emergency Response Guidebook Isolation Table (46)
B = Other ERG (50)
C = Top 150 Hazardous Material transported by rail (31)

EPA — **Environmental Protection Agency (95)**

A = Evironmental Protection Agency Clean Air Act 112r (Risk Management Program) (10)
B = CAAA 112b Chemical (Hazardous Air Pollutant) (40)
B* = April 1, 1994 list submitted by OAQPS (HAP with current acute toxicity interest) (9)
C = Environmental Protection Agency Superfund Chemical (24)
D = EPA Extremely Hazardous Substance List (* = EHS solid with RTECS LC data) (8)
E = CAAA 112r Proposed Update Chemical (16)
F = Office of Pesticides Nomination (28)

OSHA	**Occupational Safety and Health Administration (43)** A = OSHA Process Safety Management Chemical (38) B = OSHA nomination for current acute toxicity interest (6)
OTHER	C = Chemical Market Reporter list D = Dutch chemical list (36) F = French chemical list (8) G = German chemical list H = High Production Volume chemical challenge list I = Illinois chemical list J = New Jersey chemical list K = Korean chemical list (6) N = New York chemical list P = Active U. S. Pesticide ingredient chemical R = Russian chemical list (5) S = Seveso Annex III International Seveso Convention List
Release 10^3 lb	Total Reportable Quantity (RQ) lbs released to air reported to National Response Center (1995-9)
1999 TRI	Total Air Emissions reported in 1999 EPA Toxic Release Inventory (527 chemicals) (lbs; K=1,000 lbs or M=1,000,000 lbs)
Prod Est	Toxic Substance Control Act Inventory 1998 reported production volume estimate; or >1,000,000 lbs for HPV (High Production Volume) chemical; or P for pesticide ingredient (active or inactive); K=1000; M=10^6
Production_est (lbs)	Toxic Substances Control Act (TSCA) Inventory Production Range (P = Pesticide chemical, thus not in TSCA Inventory; NA = Not Applicable, such as for a byproduct; X = not reported in TSCA Inventory update; (-) = listed in TRI, but no reports by companies; note: when only TRI release data is available, highest release amount to any media is used as a base for minimal production)
ERPG	American Industrial Hygiene Association Emergency Response Planning Guideline

(* = Already initiated for review)

CAS NO	CHEMICAL (PHYSICAL STATE/Liquid Boiling Point °C)	DOJ	ATSDR	DOD	DOE SCAPA	DOT ERG	EPA	OSHA PSM	OTHER	Release 10^3 lb	1999 TRI (lbs)	Production (lbs)	ERPG
50-00-0	*Formaldehyde (g)	A	BC		A	C	ABD	A	SCI	83[1]	12.4M	>12.4M	X
50-29-3	4,4'-DDT (s)		C	BCD	E	B	C					NA	
50-32-8	*Benzo(a)pyrene (s)		AC	D	E		C					NA	
54-11-5	Nicotine (l/247)					B	D					X	
56-38-2	*Parathion (l/375)	C	BC		E	A	BDF		P		0	P	
56-55-3	Benzo(a)anthracene (s)		C	D	E		C					NA	
56-72-4	Coumaphos (s)						D*		P			P	
57-24-9	*Strychnine (s)				E		DF		P		5	P, >180	
57-57-8	beta-Propiolactone (l/162)				E		BD					X	
57-74-9	*Chlordane (l/400)		BC	BCD	E		ABCD				45	P	
58-89-9	Lindane (s) (hexachlorocyclohexane)			CD			D*		P		30	10-500K	
60-29-7	Ethyl ether (l/35)		C		E	B				9			
60-51-5	Dimethoate (s)						D*		P		51	P	
60-57-1	Dieldrin (s)		C	D	E	B	C					P	
62-38-4	*Phenylmercuric acetate						F						
62-73-7	Dichlorvos (l/400)				E	B	BCD		H		258	P	
62-74-8	*Sodium fluoroacetate						F						
62-75-9	Nitrosodimethylamine (l/151)		C	C	E		BD				5	>5	
64-18-6	Formic acid (l/101)				A	B			PH		766K	>12M	
64-19-7	Acetic acid (l/118)				A	B			HI	150	>1M	>1M	
67-64-1	*Acetone (l/56)		C	CD	E	BC			CGI	67		>1M	
74-82-8	Methane (g)		C		E	B	C	A	HI			>1M	
74-83-9	*Methyl bromide (g)	B	BC		A	A	B*CF	A	HS	9	1.4 M	>1.4M	X
74-87-3	*Methyl chloride (g)		C		A	BC	AB*C	A	CHI	79	2.8 M	>3M	X

CAS NO	CHEMICAL (PHYSICAL STATE/Liquid Boiling Point °C)	DOJ	ATSDR	DOD	DOE SCAPA	DOT ERG	EPA	OSHA PSM	OTHER	Release 10^3 lb	1999 TRI (lbs)	Production (lbs)	ERPG
74-88-4	Methyl iodide (l/43)				A	A	B	A		<1	68 K	20-200K	X
74-89-5	*Methyl amine (l/48)				A	B		A	DFH	1		5M-5B	X
74-98-6	*Propane (g)				CE	BC			H			>1M	
75-00-3	Chloroethane(g)		C	C	E	B	BC		H	18	2.1 M	>2.1M	
75-01-4	*Vinyl chloride (g)		AC	BCDE	A	BC	B*C		CFGHI	79	849 K	>1M	
75-02-5	Vinyl fluoride (g)				A	B			H			>1M	
75-04-7	*Ethyl amine (l/17)					B		A	FH			10M	
75-05-8	Acetonitrile (l/82)				AC	B	B		H	6	883K	>1M	X
75-07-0	*Acetaldehyde (l/21)				A	BC	B*	A	H	6	12 M	>13M	X
75-08-1	*Ethyl mercaptan								D				
75-12-7	Formamide (l/71)				A				H			>1M	
75-15-0	*Carbon disulfide (l/47)	A	C		A	BC	AB*CD	B	CGHKS	728	36M	>36M	X
75-18-3	Dimethyl sulfide(l/38)				A	B		A				X	X
75-25-2	Bromoform (l/150)			BD	E	B	B				7	10-500K	
75-34-3	1,1-Dichloroethane (l)		C	BCD	E	B	BC		H		22 K	>1M	
75-36-5	*Acetyl chloride (l/151)				E	A			DH			1M	
75-50-3	*Trimethylamine (g)				A	B			D*H	1		>1M	X
75-54-7	*Methyl dichlorosilane						E						
75-65-0	t-Butyl alcohol (l/82)			E					H			>1M	
75-93-4	Methyl sulfate (l)					A						X	
76-02-8	*Trichloroacetyl chloride (l/118)	B				A	D	A			1	>1, X	
76-06-2	*Chloropicrin (l/112)			AE	A	A	F	A	D*		7 K	P	X
76-44-8	Heptachlor (s)		C	D	E		BC				5	P	
77-47-4	Hexachlorocyclopentadiene (l/239)	C	C		B	A	BD				1.1 K	P, >2K	

CAS NO	CHEMICAL (PHYSICAL STATE/Liquid Boiling Point °C)	DOJ	ATSDR	DOD	DOE SCAPA	DOT ERG	EPA	OSHA PSM	OTHER	Release 10^3 lb	1999 TRI (lbs)	Production (lbs)	ERPG
77-78-1	*Dimethyl sulfate (l/189)	C			E	A	ABD	B	GH		10 K	>1M	
78-00-2	Tetraethyl lead (l/110)	C		C	E	B	D		H			NA	
78-71-7	Oxetane, 3,3-bis(chloromethyl)- (l)												
78-85-3	*Methacrylaldehyde						E	A	D				
78-87-5	1,2-Dichloropropane (l/97)		C	C	E	B	BC		HI		250 K	>1M	
78-94-4	*Methyl vinyl ketone (l/81)				B	A	D	A	D			X	
78-95-5	*Chloroacetone (stabilized) (l/119)	B			E	A			H			>1M	
78-97-7	Lactonitrile						D		H			>1M	
79-04-9	*Chloroacetyl chloride (l/108)	C			A	A	E					2M-2B	X
79-06-1	Acrylamide (s)				E	B	BD*		H	2	25 K	100M	
79-09-4	Propionic acid (l/141)				A	B			H			>1M	
79-14-1	Glycolic acid (s)				B				H			10M	
79-19-6	Thiosemicarbazide (s)				B		D				3	>100	
79-38-9	Trifluorochloroethylene (g)				E	A		A	H		10.8K	>1M	X
79-41-4	*Methacrylic acid (l/163)					B			GH			>1M	
79-57-2	*Terramycin								R			?	
80-15-9	Cumene hydroperoxide (l/153)				E	B		A		<1	63 K	>430K	
80-56-8	alpha-Pinene (l/155)				A	B			H			>1M	
80-62-6	*Methyl methacrylate (l/101)		C		E	BC	B		G	2	4.4 M	>5M	
80-63-7	Methyl 2-chloroacrylate (l/140)				A		D					X	
81-81-2	Warfarin (s)						D		P		10	P, >300	
82-66-6	Diphacinone (s)						D*		P			P	
84-66-2	Diethyl phthalate (l/302)		C	BCD	A				H			>1M	
84-74-2	di-n-butyl phthalate (s)		C	CD	E		BCD		H		34 K	>1M	

CAS NO	CHEMICAL (PHYSICAL STATE/Liquid Boiling Point °C)	DOJ	ATSDR	DOD	DOE SCAPA	DOT ERG	EPA	OSHA PSM	OTHER	Release 10^3 lb	1999 TRI (lbs)	Production (lbs)	ERPG
85-68-7	Butyl benzyl phthalate (s)		C	C			C		H			>1M	
86-50-0	*Azinphos-methyl (s)						DF		P			P	
86-74-8	Carbazole (s)		C		A							10-500K	
87-86-5	Pentachlorophenol (s)		C	CD	B	B	BD			<1	1.3 K	>100K, X	
92-52-4	Biphenyl (s)		C		E		B		HI	1	680	>1M	
94-75-7	2,4-Dichlorophenyoxy acetic acid (s)		C	C	E	B			H	2	0	>1M	
95-48-7	o-Cresol (s)		C		E	B	BD*		H		1.4 M	10M	
95-63-6	Trimethyl benzene (l/176)		C	B	E	B	CD		H		7.7M	>1M	
96-29-7	2-Butanone oxime								H			10M	
97-02-9	*2,4-Dinitroaniline(s)				E	B		A	D*H			>1M	
98-05-5	Phenyl arsonic acid (s)				B		D					X	
98-07-7	Benzyl trichloride (l/220)				B		BD		H		2 K	10M	
98-09-9	Benzenesulfonyl chloride					B	D		H			>1M	
98-13-5	Trichlorophenyl silane (l/202)						D		H			>1M	
98-16-8	3-(Trifluoromethyl) Aniline (l/188)					B			H			>1M	
98-82-8	Cumene (l/152)				E	B	B		H	5	1.4M	>1.4M	
98-87-3	Benzal chloride (l/205)				E		D		H		410	>1M	
98-88-4	Benzoyl chloride					A			H		10 K	10M	
98-95-3	Nitrobenzene (l/211)			DE	E	B	BD		H			>1M	
100-14-1	Benzene, 1-(chloromethyl)-4-nitro- (s)						D*						
100-41-4	Ethyl benzene (l/136)		C	CD	E	B	BC		CH	12	8.7 M	>10M	
100-42-5	*Styrene (l/145)		C		A	BC	B*C	B	CGHI	46	55 M	>8M	X
100-44-7	Benzyl chloride (l/179)				E	B	BD		H		26 K	>1M	X
100-51-6	Benzyl alcohol (l/205)				E		C		H			>1M	

CAS NO	CHEMICAL (PHYSICAL STATE/Liquid Boiling Point °C)	DOJ	ATSDR	DOD	DOE SCAPA	DOT ERG	EPA	OSHA PSM	OTHER	Release 10^3 lb	1999 TRI (lbs)	Production (lbs)	ERPG
101-68-8	*4,4-methylenediphenyl diisocyanate	C				BC	B		FH			>1M	X
103-71-9	Phenyl isocyanate (I/165)					A						10-500K	
105-60-2	Caprolactam (I/267)				B		B		H			1 B	
106-44-5	p-Cresol(s)		C		E	B	B		H		1.4 M	50 M	
106-50-3	p-Phenylenediamine (I/267)				B	B	B		H		1,500	10 M	
106-88-7	1,2-Butylene oxide (I/63)				E	B	B		H	9	12 K	>1M	
106-93-4	*Dibromoethane (I/131)	B	C	C	E	A	B				9 K	>1M	
106-96-7	Propargyl bromide (I/88)						D	X				X	
106-97-8	*Butane (g)				E	BC			H			1 B	
106-99-0	*Butadiene (g)		C		A	BC	BD		CHI	204	1.9M	1 B	X
107-05-1	Allyl chloride (I/45)				A	B	B	X	H	1767	79 K	>1M	X
107-06-2	*1,2-Dichloroethane (I/83)		C	CD	E	BC	BC		HI	100	550 K	>1M	
107-07-3	Chloroethanol (I/130)				A	A	D					10-100K	
107-13-1	*Acrylonitrile (I/77)	B	BC		A	BC	ABCD		CFGHKS	20	980K	>1M	X
107-14-2	*Chloroacetonitrile (I/125)	B				A						X	
107-16-4	Formaldehyde cyanohydrin (I/183)						D		H			>1M	
107-19-7	Propargyl alcohol (I/115)				A	B			H		10 K	>1M	
107-20-0	*Chloroacetaldehyde (I/85)	C			A	A	D		D*			10-500K	
107-21-1	Ethylene glycol (I/197)		C	BC	E	B	B		HN	274	6 M	>6M	
107-37-9	Allyl trichlorosilane					A						X	
107-72-2	Amyltrichlorosilane						B					10-500K	
108-05-4	*Vinyl acetate monomer (I/73)		C		A	BC	BCD	B	H	32	3.4M	1B	X
108-10-1	4-Methyl-2-pentanone (I/117)		C	D	E	B	BC		H	2	15 M	>1M	
108-24-7	*Acetic anhydride (I/140)				A	BC			H			>1M	

CAS NO	CHEMICAL (PHYSICAL STATE/Liquid Boiling Point °C)	DOJ	ATSDR	DOD	DOE SCAPA	DOT ERG	EPA	OSHA PSM	OTHER	Release 10^3 lb	1999 TRI (lbs)	Production (lbs)	ERPG
108-31-6	*Maleic anhydride (l/200)				B	BC	B		H		380 K	500M	
108-39-4	m-Cresol				E	B	B		H		1.4 M	>1.4M	
108-65-6	Propylene Glycol Monomethyl Ether Acetate								H			50M	
108-67-8	Mesitylene (l/165)		C	B	E		CD		H			>1M	
108-90-7	*Chlorobenzene (l/130)		C	C		BC	BC		CH	1	680 K	>1M	
108-98-5	*Phenylmercaptan (l/169)					A	D		D*FH			>1M	
109-73-9	n-Butylamine					A			H			1M	
109-77-3	*Malononitrile						D*		D*		17	10-500K	
109-89-7	Diethyl amine (l/56)				A	B			H	4		>1M	
109-90-0	Ethyl isocyanate (l/60)					A						X	
109-99-9	*Tetrahydrofuran (l/65)		C		E	BC		AB	H	65		>1M	
110-54-3	*Hexane (l/69)		C		E	BC	B*		HI	64	68 M	100M	
110-57-6	Trans- 1,4-dichlorobutene (l/156)					B	D		H		936	>1M	
110-78-1	n-Propyl isocyanate (l/83)					A						X	
110-82-7	*Cyclohexane (l/81)		C		E	BC	BC		CH	20	4.8 M	1B	
110-86-1	Pyridine (l/116)		C		A	B			H	1	70 K	>1M	
111-34-2	Butyl vinyl ether (l)											10-500K	
111-36-4	*n-Butyl isocyanate (l/115)	C			A	A	E		D*H			>1M	X
111-42-2	Diethanolamine (l/270)				E		B	A	H	3	374 K	>1M	
111-44-4	Dichloroethyl ether (l/178)		C	C	E	B	BD	A	H			>1M	
111-48-8	Thiodiglycol (l-165/14mm)			AE									
111-69-3	Adiponitrile (l/295)					B	D		H			>1M	
111-77-3	Diethylene glycol monomethyl ether (l/193)				B				H			50M	

CAS NO	CHEMICAL (PHYSICAL STATE/Liquid Boiling Point °C)	DOJ	ATSDR	DOD	DOE SCAPA	DOT ERG	EPA	OSHA PSM	OTHER	Release 10^3 lb	1999 TRI (lbs)	Production (lbs)	ERPG
111-88-6	*n-Octylmercaptan	B											
115-21-9	Trichloroethyl silane (l/98)						D		H			>1M	
116-06-3	*Aldicarb (s)				B		D*F		P		177	P	
116-14-3	Tetrafluoroethylene (g)				A				H			>1M	X
116-15-4	Hexafluoropropylene (g)				A				H			>1M	X
117-84-0	Dioctyl phthalate (l/220)		C		E		D		H			>1M	
118-52-5	1,3-Dichloro-5,5-dimethylhydantoin (l/100)			E									
120-82-1	1,2,4-Trichlorobenzene (l/214)		C	C	E	B	BC		H	<1	170 K	>180K	
121-75-5	Malathion (l/156-0.7mm)		C	C	E		C				5000	P, >5000	
122-14-5	Fenitrothion (l/370)						D		P			P	
123-31-9	Hydroquinone (l/285)				E	B	BD*		H		59K	10M	
123-38-6	*Propionaldehyde (l/48)				E	B	B		D*H	1	426 K	>540K	
123-86-4	*n-Butyl acetate						E						
124-40-3	*Dimethyl amine (g)				A	BC		A	DH	4		>1M	X
124-63-0	*Methanesulfonyl chloride (l/161)	B				A			H			>1M	
124-65-2	Sodium cacodylate (s)						D		P			P	
129-00-0	Pyrene (s)			D	B		D*		P			10-500K	
131-11-3	Dimethyl phthalate				E		D		H		432	>1M	
140-88-5	*Ethyl acrylate (l/100)				A	BC	B		HI	<1	131 K	>180K	X
141-32-2	*Butylacrylate (l/48)				E	AC					245K	290K	X
141-43-5	Monoethanolamine (l/171)			E	E	C			H			>1M	
141-59-3	t-Octyl mercaptan (l/200)					A						X	
141-66-2	Dicrotophos (l/400)						D		P			P	
141-78-6	*Ethyl acetate (l/77)				E	BC			CH	17		>1M	

CAS NO	CHEMICAL (PHYSICAL STATE/Liquid Boiling Point °C)	DOJ	ATSDR	DOD	DOE SCAPA	DOT ERG	EPA	OSHA PSM	OTHER	Release 10^3 lb	1999 TRI (lbs)	Production (lbs)	ERPG
143-33-9	*Sodium cyanide						F						
144-62-7	Oxalic acid (s)				E				H			>1M	
149-74-6	Dichloromethylphenyl silane (l/205)						D		H			>1M	
150-76-5	p-Methoxyphenol (l/243)								H			>1M	
151-38-2	*Methoxyethyl mercury						F						
207-08-9	Benzo(k)fluoranthene (s)		C	BD			C					NA	
218-01-9	Chrysene (s)		C	BD	E		C					NA	
287-92-3	Cyclopentane (l/49)					B			H			>1M	
297-78-9	Isobenzan (s)						D		H			>1M	
298-00-0	*Methyl parathion (s)		C		B	B	D*F		P		15	P	
298-02-2	*Phorate (l/290)						DF		P			P	
298-04-4	*Disulfoton (l/400)		C				DF		P			P	
300-62-9	Amphetamine (l/200)						D		P			P	
333-41-5	Diazinon (l/206)		C	C		B	C				27 K	P	
334-88-3	*Diazomethane (g)				A		BE	A			4	X	
353-50-4	*Carbonyl fluoride (l/306)				A	A		A	D*			X	
354-32-5	Trifluoroacetyl chloride (g)					A	D					1M-1B	
371-62-0	Ethylene fluorohydrin (l/104)						D	A				X	
382-21-8	Perfluoroisobutylenene (g)			A	A							X	X
453-18-9	*Methyl fluoroacetate						E						
460-19-5	*Cyanogen (g)				A	A		A	D*			X	
463-51-4	*Ketene (g)				A		E	A	D			X	
463-58-1	*Carbonyl sulfide (l/50)				E	A	BC		D		21 M	21M	
463-71-8	Thiophosgene (l/73)					A						X	

CAS NO.	CHEMICAL (PHYSICAL STATE/Liquid Boiling Point °C)	DOJ	ATSDR	DOD	DOE SCAPA	DOT ERG	EPA	OSHA PSM	OTHER	Release 10^3 lb	1999 TRI (lbs)	Production (lbs)	ERPG
503-38-8	Diphosgene (l/128)			E		A						X	
506-68-3	*Cyanogen bromide (s)						D		D*				
506-78-5	Cyanogen iodide (s)				B		D						
506-96-7	Acetyl bromide (l/77)					A						10-500K	
534-52-1	4,6-Dinitro-o-cresol (s)		C		B	B	D*					1M	
538-07-8	Bis(2-chloroethyl)ethylamine (l/200)			A		A	D					X	
541-25-3	Lewisite (l/190)			AE		A	D					NA	
541-41-3	*Ethyl chloroformate (l/93)	C				A			DH		2200	>1M	
542-88-1	*bis-Chloromethyl ether (l/104)		C		B	B	ABCD	A	DKS		1.3 K	100K-1M	X
543-27-1	i-Butyl chloroformate (l/129)	C				A						200K-2M	
555-77-1	Tris(2-chloroethyl)amine (N-Mustard) (l/256)			A	E	A	D					NA	
556-61-6	Methyl isothiocyanate (l/117)					A	D*		H		1.1 K	500K-1M	
556-64-9	*Methyl thiocyanate (l/130)				E		ACD		K			X	
563-12-2	Ethion (l/150)					B	D		P			P	
578-94-9	Adamsite (s)			E		A						P, X	
592-34-7	n-Butyl chloroformate (l/142)	C				A						X	
593-53-3	Methyl fluoride (g)											X	
593-89-5	Methyl dichloroarsine					A						X	
598-14-1	Ethyl dichloroarsine					A						X	
598-31-2	Bromoacetone (g)				A	A						X	
622-44-6	Phenyl carbylamine chloride					B						X	
624-92-0	*Dimethyl disulfide (l/110)				A	B	DE		H			>1M	X
625-55-8	Isopropyl formate (l/68)						D		H			>1M	
627-44-1	Diethyl mercury (l)				B							X	

CAS NO	CHEMICAL (PHYSICAL STATE/Liquid Boiling Point °C)	DOJ	ATSDR	DOD	DOE SCAPA	DOT ERG	EPA	OSHA PSM	OTHER	Release 10^3 lb	1999 TRI (lbs)	Production (lbs)	ERPG
640-19-7	Fluoroacetamide (s)						D*						
646-06-0	Diulane (l/75)						D		H			>1M	
674-82-8	*Diketene (l/127)	B			A	A			H			>1M	X
675-14-9	Cyanuric fluoride (l)						D	A					
676-83-5	Methyl phosphonous dichloride					A						X	
676-97-1	Methyl phosphonic dichloride (s)			A	E	A	D*		R			X	
681-84-5	Tetamethoxysilane (l/121)				E	A			H			10-500K	X
684-16-2	*Hexafluoroacetone (g)				A	A		A	D*			10-500K	X
696-28-6	Phenyl dichloroarsine (l/254)					B	D					X	
732-11-6	Phosmet (s)						D*		P			P	
757-58-4	Hexaethyl tetraphosphate					A						X	
813-78-5	Dimethyl phosphate								R			10-500K	
919-86-8	Demeton S-methyl (l/305)						D		P			P	
920-46-7	Methacryloyl chloride (l/96)						D	A				X	
944-22-9	*Fonofos (l/380)						DF		P			P	
950-37-8	*Methidathion (s)						DF		P			P	
993-00-0	*Methyl chlorosilane	B				A						X	
993-13-5	Methylphosphonic acid			A									
993-43-1	Ethylphosphonodithioic dichloride (l/132)	C				A			H			>1M	
999-81-5	Clormequat chloride (s)						D		P			P	
1024-57-3	Heptachlor epoxide (s)		C	D	B							P?	
1120-71-4	1,3-Propane sultone (s)				B		B				5	X	
1303-28-2	Arsenic pentoxide (s)				E		D*		P			P	
1306-02-1	Lewisite oxide			E									

CAS NO	CHEMICAL (PHYSICAL STATE/Liquid Boiling Point °C)	DOJ	ATSDR	DOD	DOE SCAPA	DOT ERG	EPA	OSHA PSM	OTHER	Release 10^3 lb	1999 TRI (lbs)	Production (lbs)	ERPG
1314-84-7	Zinc phosphide (s)						D*		P			P	
1319-77-3	*Cresol (l/88)		C		E	B	B		HI	55	1.4M	>1M	
1327-53-3	*Arsenic trioxide (s)		C		B	B	BD*F			<1		X	
1336-36-3	Polychlorinated biphenyl (s)		C	BCD	E	B				24	500	NA	
1341-24-8	*Chloroacetophenone (l/225) (nominated by Robert Snyder, NAC/AEGL)			E	E	B						X	
1341-49-7	Ammonium bifluoride (s)				B	B						10K	
1397-94-0	Antimycin A (s)						D		P			P	
1498-40-4	Ethylphosphonous dichloride					A						X	
1498-51-7	Ethylphosphorodichloridate (l/60-10mm)				E	A			H			>1M	
1558-25-4	Chloromethyl (trichloro) silane (l/118)				E		D	A				X	
1563-66-2	*Carbofuran (l/200)					B	DF		PH		14K	>1M	
1582-09-8	Trifluralin (s)		C		E		BC				5.2K	>20K	
1609-86-5	t-Butyl isocyanate (l/85)	C				A						X	X
1634-04-4	*Methyl t-butyl ether (l/55)		C			BC	B*		H	1	4 M	1B	
1675-54-3	Bisphenol A diglycidyl ether (s)				B				H			1M	
1737-93-5	3,5-Dichloro-2,4,5-trifluoropyridine					A							
1746-01-6	*2,3,7,8-Tetrachlorodibenzo-p-Dioxin (s)		C	C	CE		BC		R			NA	
1832-54-8	Isopropyl methyl phosphonic acid			E									
1873-29-6	Isobutyl isocyanate (l)					A						X	
1910-42-5	*Paraquat dichloride (s)				B		D*F		D*		-	X	
2032-65-7	Methiocarb (s)						D		P			P	
2231-57-4	Thiocarbazide (s)						D*		H		-	>1M	

CAS NO	CHEMICAL (PHYSICAL STATE/Liquid Boiling Point °C)	DOJ	ATSDR	DOD	DOE SCAPA	DOT ERG	EPA	OSHA PSM	OTHER	Release 10^3 lb	1999 TRI (lbs)	Production (lbs)	ERPG
2487-90-3	Trimethoxysilane (l/84)				E	A		A	H			>1M	X
2524-03-0	Dimethyl phosphorochloridothioate (l/180)					B	D		H			>1M	
2696-92-6	*Nitrosyl chloride (g)				A	A			D*			X	
2698-41-1	*o-Chlorobenzylidene malononitrile (l/310)					B			R			X	
2699-79-8	*Sulfuryl fluoride (g)	B				A	F		D*		506K	>506K	
2937-50-0	Allylchloroformate (l/110)					A						10-500K	
2941-64-2	Ethyl chlorothioformate (l/132)					A			H			>1M	
3048-64-4	Vinyl norbornene (l/141)						D		H			>1M	
3173-53-3	*Cyclohexyl isocyanate (l/169)					A			D*H			>1M	
3282-30-2	Trimethylacetyl chloride (l/105)					A			H			>1M	
3689-24-5	*Tetraethyl dithiopyrophosphate (Sulfotep) (l/310)					A	DF		P			P	
3691-35-8	Chlorophacinone (S)						D		P			P	
4098-71-9	Isophorone diisocyanate (s)						D*		H			>1M	
4109-96-0	Dichlorosilane (g)					A		A				X	
4300-97-4	Chloropivaloyl chloride					A			H			>1M	
4418-66-0	Phenol, 2,2'-thiobis(4-chloro-6-methyl-)												
5332-73-0	3-Methoxypropyl amine (l/116)				A				H			>1M	
5798-79-8	Bromobenzyl cyanide (s)			E									
6427-21-0	Methoxymethyl isocyanate (l/85-60mm)					A						X	
6581-06-2	3-Quinuclidinyl benzilate (s)			AE									
6923-22-4	*Monocrotophos						F						

CAS NO	CHEMICAL (PHYSICAL STATE/Liquid Boiling Point °C)	DOJ	ATSDR	DOD	DOE SCAPA	DOT ERG	EPA	OSHA PSM	OTHER	Release 10^3 lb	1999 TRI (lbs)	Production (lbs)	ERPG
7439-92-1	*Lead & compounds (s) including lead phosphate		AC	BD	E	B	C				1.2 M	>350M	
7439-96-5	Manganese & compounds (s)		C	D	E	B	BC	B			2.5M	>500M	
7439-97-6	*Mercury & compounds (l/357) including methyl mercury		AC	BD	CE	B	BC	B		<1	5.8K	>3.2M	
7440-02-0	*Nickel and compounds (s)			D	E	B	B*				1.2M	>69M	
7440-38-2	*Arsenic & compounds (s)		AC	BDE	E	B	BC		F	<1	290 K	>570M	
7440-39-3	Barium & compounds (s)		C	D	E	B	C				2.9 M	>300M	
7440-41-7	*Beryllium & compounds (s)		C	D	BC	B	B*C	B			8K	>900K	X
7440-43-9	*Cadmium & compounds (s)		AC	D	CE	B	BC			<1	50 K	>12M	
7440-48-4	Cobalt & compounds (s)				B		D				80K	>16M	
7440-50-8	Copper & compounds (s)		C	D	E	B	C				2.2 M	>1.8M	
7440-62-2	Vanadium & compounds (s)		C	D	E	B	C	B			18 K	>720K	
7440-66-6	Zinc & compounds (s)		C	D	E	B	C		I		8M	>1B	
7446-18-6	*Thallium sulfate						F						
7446-70-0	Aluminum chloride (s)				E	A							
7521-80-4	Butyltrichlorosilane					A							
7550-45-0	*Titanium tetrachloride (l/136)	B	C		A	A	ABD		K	7	27 K	>288K	X
7580-67-8	Lithium hydride (s)				B		D*						X
7616-94-6	Perchloryl fluoride (g)					A		A					
7631-89-2	Sodium arsenate (s)				E		D		P			P	X
7647-19-0	*Phosphorus pentafluoride (g)	B			E	A							
7664-38-2	*Phosphoric acid (l/260)				E	ABC			N	330	1.2 M	>1M	
7705-07-9	Titanium chloride (l/136)				A						27 K	>288 K	
7719-09-7	*Thionyl chloride (l/80)			A	AC	A		A	D*				

CAS NO	CHEMICAL (PHYSICAL STATE/Liquid Boiling Point °C)	DOJ	ATSDR	DOD	DOE SCAPA	DOT ERG	EPA	OSHA PSM	OTHER	Release 10^3 lb	1999 TRI (lbs)	Production (lbs)	ERPG
7722-84-1	*Hydrogen peroxide (concn>52%) (l/152)		B		E	BC	D	A				10-500K	X
7723-14-0	Phosphorus (s)						BD*				88 K	>3 M	
7727-15-3	Aluminum bromide (s)					A							
7738-94-5	Chromic acid (s)				E	B				11			
7782-65-2	Germane (g)					A							
7782-68-5	Iodic acid (s)				B								
7783-07-5	*Hydrogen selenide (g)	B			A	A	ABD	A	D*KS				
7783-41-7	*Oxygen difluoride (g)					A	E	A					
7783-54-2	*Nitrogen trifluoride (g)				CE	B		A	F				
7783-61-1	*Silicon tetrafluoride (g)	B				A							
7783-70-2	Antimony pentafluoride (l/141)				E	A	D						
7783-71-3	Tantalum V fluoride (s)				A								
7783-79-1	*Selenium hexafluoride (g)	B			CE	A		A					
7783-80-4	*Tellurium hexafluoride (g)	B			A	A	D	A					
7783-82-6	Tungsten hexafluoride (g)	C			E	A							
7784-46-5	*Sodium arsenite						F						
7786-34-7	*Mevinphos						F						
7787-71-5	*Bromine trifluoride (g)				E	A	E	A	I				
7789-21-1	Fluorosulfonic acid					A							
7789-30-2	*Bromine pentafluoride (g)	C				A	E	A					
7789-59-5	Phosphorus oxybromide (l/193)					A							
7789-69-7	Phosphorus pentabromide (s)					A							
7789-75-5	Calcium fluoride (s)				E								
7790-94-5	*Chlorosulfonic acid (l/158)	B			E	A							X

CAS NO	CHEMICAL (PHYSICAL STATE/Liquid Boiling Point °C)	DOJ	ATSDR	DOD	DOE SCAPA	DOT ERG	EPA	OSHA PSM	OTHER	Release 10^3 lb	1999 TRI (lbs)	Production (lbs)	ERPG
7791-23-3	Selenium oxychloride (l/180)					B	D						
7791-25-5	*Sulfuryl chloride (l/69)					A			D*				
7803-49-8	*Hydroxylamine (l/110)				A			A				X	
7803-52-3	*Stibine (Antimony Hydride) (g)	B			A	A	B	A	D*				X
7803-62-5	*Silane (g)				CE	B			D*F				
8001-35-2	Camphechlor (s)						BD						
8006-61-9	*Gasoline (l/32-225)		BC	BC	E	B						>1M	
10025-67-9	Disulfur dichloride (l/138)			A	A					1			
10025-73-7	Chromic chloride (s)				B		D*					10-100K	
10026-13-8	Phosphorus pentachloride (s)			A	E	A	D*						X
10028-15-6	*Ozone (g)						D	A	D*			610K	>610
10034-85-2	*Hydrogen iodide (g)	C			A	A			D*				
10035-10-6	*Hydrogen bromide (g)	A			A	A		A	F				
10265-92-6	*Methamidophos (s)						D*F		P			P	
10294-33-4	*Boron tribromide (l/91)	B			A	A							
10544-72-6	Nitrogen tetroxide (g)					A		A					
10544-73-7	Nitrogen trioxide (g)					A		A					
10545-99-0	*Sulfur dichloride						E						
11099-02-8	*Nickel oxide (s)								F				
12002-03-8	*Copper Acetoarsenite						F						
12108-13-3	Manganese, tricarbonyl methylcyclopentadienyl (l/232)						BD		H			>1M	
13071-79-9	*Terbufos (l/315)						DF		P			P	
13194-48-4	Ethoprophos (l/300)						D		P			P	
13470-08-1	Titanium III fluoride (s)				B								

CAS NO	CHEMICAL (PHYSICAL STATE/Liquid Boiling Point °C)	DOJ	ATSDR	DOD	DOE SCAPA	DOT ERG	EPA	OSHA PSM	OTHER	Release 10^3 lb	1999 TRI (lbs)	Production (lbs)	ERPG
13637-63-3	*Chlorine pentafluoride (g)					A	E	A					
13863-41-7	*Bromine chloride (g)	C				A	E	A				P	
16752-77-5	*Methomyl (s)						D*F		P			P	
17462-58-7	iso-Butyl chloroformate	C				A						1M-1B	
19624-22-7	*Pentaborane (l/58)					A	DE	A	D*				
20816-12-0	*Osmium tetroxide (s)				A	B	D	A	D*		-		
20859-73-8	*Aluminum phosphide (s)					A	D*F		PD*		4	P, >160	
22224-92-6	Fenamiphos (s)						D*		P			P	
22967-92-6	Methyl mercury		C	D	B								
23135-22-0	Oxamyl (s)						D*		P			P	
23422-53-9	Formetanate hydrochloride (s)						D*		P			P	
25321-14-6	Dinitrotoluene (s)		C	D	E	B	B		H	<1	11K	1B	
25321-22-6	Dichlorobenzene (l/180)		C	BCD	E	B	BC		C	2	14 K	>14K	
26419-73-8	Tirpate (s)						D		P			P	
27137-85-5	Trichloro (dichlorophenyl)silane (l/260)					B	D	A				X	
28772-56-7	Bromodiolone (s)						D		P			P	
30674-80-7	Methacryloyloxyethyl isocyanate						D	A				X	X
32315-10-9	Triphosgene (l/203)												

[1] Solution

Second AEGL Chemical Priority List Rationale

The organizations listed below contributed chemical nominations for the development of the Second AEGL Chemical Priority List of 400 substances.

Agency for Toxic Substance and Disease Registry
Department of Defense
Department of Energy
Department of Transportation
Environmental Protection Agency
Occupational Safety and Health Administration
International (Dutch, French, German, Korean, Russian) Lists
Department of Justice Counter-Terrorism List

Several lists were selected as a base and other lists were cross-checked against this to insure equitable distribution of chemicals from the stakeholder organization lists. Each organization was asked for its priority list of chemicals - some organizations provided comprehensive lists and also a subset of chemicals of highest priority for AEGL development. The numbers of chemicals below indicate total coverage of chemicals on AEGL Priority Lists 1 and 2.

BASE ORGANIZATION CHEMICAL LISTS USED FOR THE SECOND AEGL CHEMICAL PRIORITY LIST (number of chemicals on AEGL Priority Lists 1 and 2)

1. ATSDR Medical Management List (31/33 chemicals)
2. Department of Defense Chemical Warfare Agents (5/5 chemicals)
3. Department of Energy priority list of March 11, 1997 (10/14 chemicals)
4. Department of Energy Laboratory list (solicited AEGL nominations) (30/44 chemicals)
5. DOE SCAPA TEEL Master List with Vapor Pressure >3.2 mm Hg (71/71 chemicals)
6. DOE SCAPA TEEL Master List with TEEL-3 <25 ppm (60/91 chemicals)
7. Department of Transportation ERG Isolation and Protective Action (149/149 chemicals)
8. EPA CAAA 112r (77/77 chemicals)
9. EPA CAAA 112b April 1, 1994 priority list (25/25 chemicals)
10. EPA Superfund priority chemicals (62/62 chemicals)
11. EPA Extremely Hazardous Substances not occurring on other organization lists - including active pesticide ingredients (205/366 chemicals)
12. OSHA March 3, 2000 priority list (10/10 chemicals)
13. Dutch priority list (11/11 chemicals)
14. French priority list (11/11 chemicals)
15. German priority list (15/15 chemicals)
16. Korean priority list (6/6 chemicals)
17. Russian priority list (6/6 chemicals)
18. DOJ Counter Terrorism List of Toxic Industrial Materials (High and Medium concern)

In addition to these base chemicals, a summary of each organization's chemicals from other than the its base list (occurring due to overlap with other organization chemicals) was prepared.

2nd PRIORITY LIST OF 400 CHEMICALS: RATIONALE BY ORGANIZATION

1. **Agency for Toxic Substances and Disease Registry**
   A. 32 Medical Management List of 32 Chemicals
      23 chemicals on list 1 and 8 on list 2 (99%)
   B. Top 20 Chemicals Found at Superfund Sites
      3 chemicals on list 1 and 6 on list 2 (45%)
   C. 275 ATSDR Toxicology Profile Chemicals
      15 chemicals on list 1 and 84 on list 2 (32%)

2. **Department of Defense**
   A. 22/47 Chemical Weapons Convention Schedules 1, 2, or 3 (47%)
   B. 28/64 SERDP chemicals (44%)
   C. 52/79 (14 on priority list 1 and 38 on list 2) Air Force Installation Restoration Program chemicals (66%)
   D. 52/94 (13 on priority list 1 and 39 on list 2) Army Toxicity Summary chemicals (55%)
   E, 29/38 (5 on priority list 1 and 24 on list 2) Non-Stockpile Chemical Warfare substances (76%)

3. **Department of Energy**
   A. List of 14 chemicals was submitted by DOE on March 11, 1997
   10 of these chemicals were already included, however, on the First Chemical Priority List (benzene, chloroform, methylene chloride, dimethyl formamide, nitric acid, nitrogen oxides, perchloroethylene, trichloroethylene, uranium hexafluoride, and 1,1,1-trichloroethane). Beryllium and hydrogen peroxide were added to the second list. (86%)
   B. 44 DOE Lab chemicals
   29 chemicals on priority list 1 and 10 chemicals on list 2 (89%)
   C. 71 DOE/SCAPA TEEL Master List chemicals with Vapor Pressure > 3.2 mm Hg
   6 chemicals on priority list 1 and 65 chemicals on list 2 (100%)
   D. 91 DOE/SCAPA TEEL Master List chemicals with TEEL-3 <25 ppm
   4 chemicals on priority list 1 and 56 chemicals on list 2 (66%)
   E. 1436 DOE/SCAPA complete TEEL Master List chemicals
   35 chemicals on priority list 1and 210 chemicals on list 2 (17%)

4. **Department of Transportation**
   A. Approximately 149 Emergency Response Guidebook (ERG) Isolation and Protective Action" Chemicals
      35 chemicals on priority list 1 and 114 on list 2 (100%)
   B. Approximately 2,000 Other ERG chemicals (including many not otherwise specified,"nos," listings)
      5 chemicals on list 1 and 112 on list 2 (about 6%)
   C. Top 150 Hazardous Materials Transported by Rail
      23 chemicals on list 1 and 37 on list 2 (40 %)

Approximately 130 chemicals make up DOT's Emergency Response Guidebook "Initial .

114 of these chemicals were selected for the Second Chemical Priority List and, when combined with 35 chemicals on First Chemical Priority list, complete this DOT nominated list, except for some more specialty and low production chemicals or chemical mixtures. The rationale for including so many DOT chemicals on the two lists was to identify a list of known hazardous chemicals of concern in chemical accident spills and to later narrow the list based upon a consideration of production volume.

5. **Environmental Protection Agency**

A. 77 CAAA 112r Risk Management Program Chemicals
65 chemicals on priority list 1 and 12 chemicals on list 2 (100%)
B. 189 CAAA 112b Hazardous Air Pollutants
15 chemicals on list 1 and 10 chemicals on list 2 (100%)
17 additional HAP chemicals on list 1 and 70 on list 2 (60% HAPs total)
B*. 25 Highest Priority CAAA 112b Hazardous Air Pollutant chemicals (from a list submitted by Dr. Dan Guth April 1, 1994)
C. 62 Superfund chemicals - Risk Assessment completed in FY93-95 for airborne exposure concerns
14 on list 1 and 48 on list 2 (100%)
(See also ATSDR Toxicology Profiles for additional chemicals of interest to Superfund)
D. 366 SARA Title III Extremely Hazardous Substances
66 chemicals on priority list 1 and 139 chemicals on list 2 (56%)

6. **Occupational Safety and Health Administration**

A. 135 OSHA Chemical Process Safety Chemicals
50 on priority list 1 and 51 on list 2 (75%)
B. List of 10 OSHA Chemicals
OSHA submitted on March 3, 2000 a list of 10 chemicals for AEGL development and these were already included on the Second Chemical Priority List from other organization nominations. (100%).

7. **Other**

C Chemical Market Reporter
Chemicals that have this chemical profile are considered to be "high production." This list was used as a further check on production of listed chemicals
D Dutch First Priority Chemical List
11/11 Top Priority chemicals on list 2 (100%)
D* Dutch Second Priority Chemical List
34/51 chemicals (5 chemicals on list 1 and 29 on list 2); 67%
F France Chemical List
11/11 chemicals on list 2; Nitrogen fluoride is unique to the France Chemical List; 100%
G German Chemical List
15 chemicals on the Second Chemical Priority List appear on the German FOBIG submitted list of chemicals. Methacrylic acid and methyl methacrylate are uniquely

FOBIG chemicals; 100%
H High Production Volume Chemical
About 2,800 High Production Volume Challenge Chemicals
31 chemicals on list 1 and 137 on list 2 (6%)
I Illinois Chemical List
K Korean Chemical List
6/6 chemicals on list 2 = 100%
J New Jersey Chemical List (No unique additions, although ethylene, carbon dioxide, ethyl alcohol, coke oven gas, naphtha, ethyl acrylate, asbestos, n-heptane and biphenyl, wood creosite, gasoline, benzoyl peroxide, chlorpyrifos, propane, ethylene and o-cresol could be considered - gasoline has been mentioned in the past)
NY New York Chemical List
New York Chemical List (No unique additions, although sodium hypochlorite could be considered)
P Active Pesticide Ingredient Chemical List
R Russian Chemical List
6/6 chemicals; 100%
S Seveso Chemical List

8. **Top 25 Reportable Quantity (RQ) Releases (10^{3} lbs)**
Top 25 RQ air releases by number of notifications or pounds released to air (1999-1995). 4 chemicals were added separately based on presence on this list (all others were already accounted for by other organization lists): butadiene, ethylene glycol, hexane and phosphoric acid.(100%)

9. **1998 Toxic Release Inventory (lbs)**
Amounts of chemicals released to air.

10. **Production volume (lbs)**

11. **ERPG**
Emergency Response Planning Guide availability.

12. **National Institutes for Occupational Safety and Health**
A. 387 NIOSH Immediately Dangerous to Life or Health chemicals
43 on list 1 and 61 on list 2 (27%)
B. NIOSH Top 200 Worker Exposure Chemical
16 chemicals on list 2

Value of Chemical Classes Approach

1. Utilize "universal" pharmacokinetic and pharmacodynamic information from chemical class chemicals

2. Identify chemicals for which AEGLs may be developed together (including chemicals from differing classes, such as chemicals that release HCl upon hydrolysis).

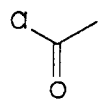
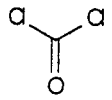
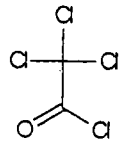
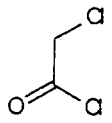
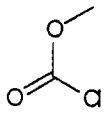
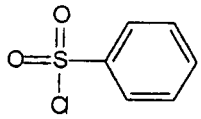
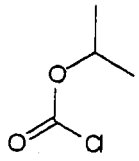
3. Provide a range of AEGL levels for purposes of developing chemical class personal monitors.

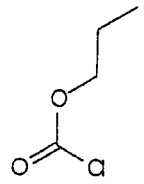
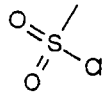
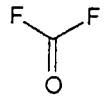
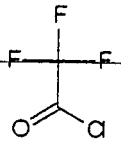
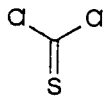
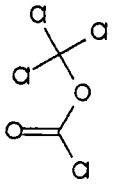
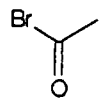
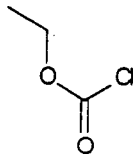
4. Provide a chemical class approach to protective equipment, decontamination and other counter-terrorism activities related to toxic chemical release (DOJ approach).

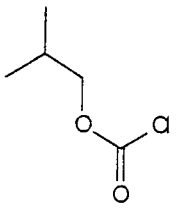
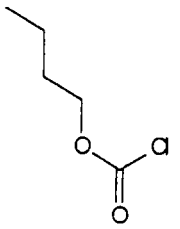
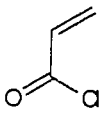
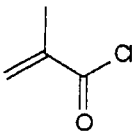
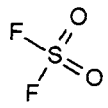
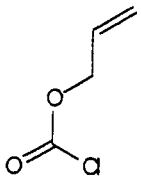
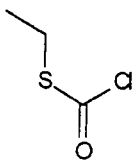
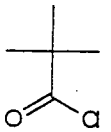
5. Present for local use a systematic concept of acute toxicity of chemical classes. Illustrate the universe of acutely toxic chemicals.

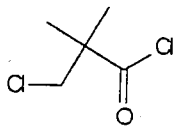
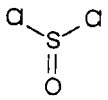
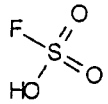
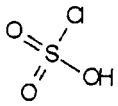
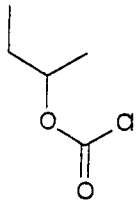
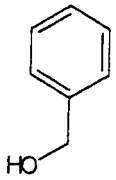
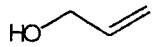
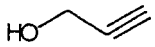
6. Allow for inherently safer chemistry suggestions, based on substitution or modification of current practices.

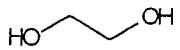
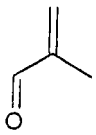
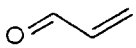
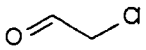
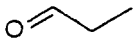
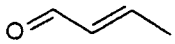
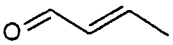
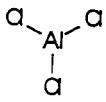
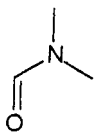
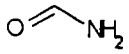
7. Provide Suggestions for Revision of Existing Regulatory Chemical Lists

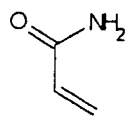
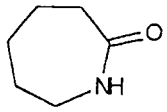
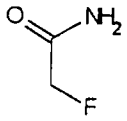
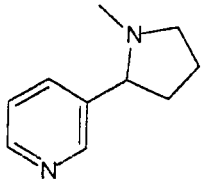
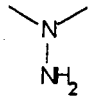
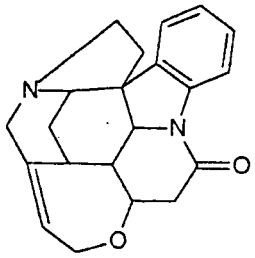
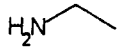
CHEMISTRY	CASNo	ChemName	List	AEGL-3 1 Hr	AEGL-2 1 Hr	AEGL-1 1 Hr
Acid Halides						
 O=C(Cl)C	75-36-5	acetyl chloride	2			
 O=C(Cl)Cl	75-44-5	phosgene	1	0.75	0.30	NR
 O=C(C(Cl)(Cl)Cl)Cl	76-02-8	trichloroacetyl chloride	2			
 O=C(CCl)Cl	79-04-9	chloroacetyl chloride	2			
 O=C(OC)Cl	79-22-1	methyl chloroformate	1			
 O=S(=O)(c(cccc1)c1)Cl	98-09-9	benzene sulfonyl chloride	x			
 O=C(c(cccc1)c1)Cl	98-88-4	benzoyl chloride	x			
 O=C(OC(C)C)Cl	108-23-6	isopropyl chloroformate	1			

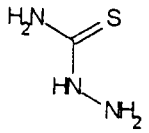
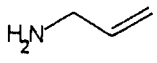
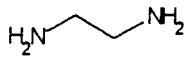
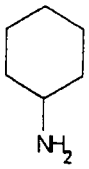
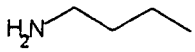
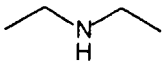
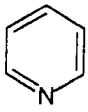
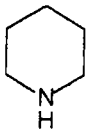
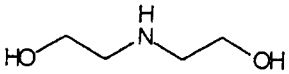
 O=C(OCCC)Cl	109-61-5	propyl chloroformate	1			
 O=S(=O)(C)Cl	124-63-0	methanesulfonyl chloride	2			
 O=C(F)F	353-50-4	carbonyl fluoride	2			
 O=C(C(F)(F)F)Cl	354-32-5	trifluoroacetyl chloride	x			
 S=C(Cl)Cl	463-71-8	thiophosgene	x			
 ClC(=O)OC(Cl)(Cl)Cl	503-38-8	diphosgene	x			
 O=C(Br)C	506-96-7	acetyl bromide	x			
 O=C(OCC)Cl	541-41-3	ethyl chloroformate	2			

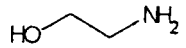
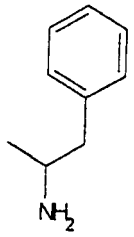
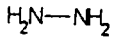
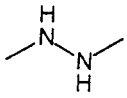
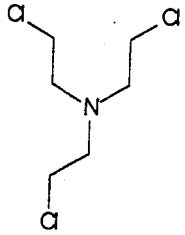
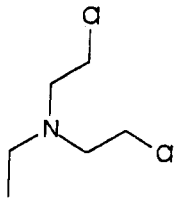
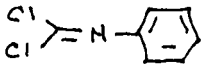
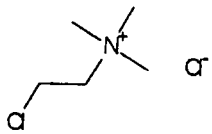
 O=C(OCC(C)C)Cl	543-27-1	i-butyl chloroformate	x			
 O=C(OCCCC)Cl	592-34-7	n-butyl chloroformate	x			
 O=C(C=C)Cl	814-68-6	acrylyl chloride	1			
 O=C(C(=C)C)Cl	920-46-7	methyacryloyl chloride	x			
 FS(F)(=O)=O	2699-79-8	sulfuryl fluoride	2			
 O=C(OCC=C)Cl	2937-50-0	allyl chloroformate	x			
 O=C(SCC)Cl	2941-64-2	ethylchlorothioformate	x			
 O=C(C(C)(C)C)Cl	3282-30-2	trimethylacetyl chloride	x			

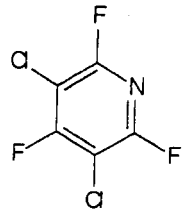
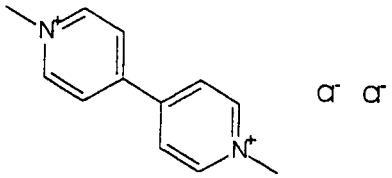
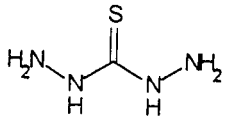
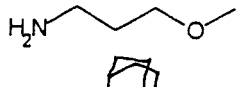
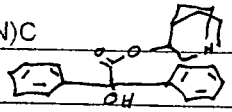
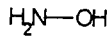
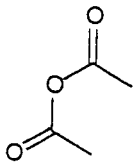
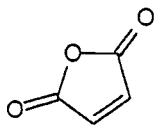
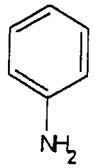
 O=C(C(CCl)(C)C)Cl	4300-97-4	chloropivaloyl chloride	x			
 O=S(Cl)Cl	7719-09-7	thionyl chloride	2			
 OS(F)(=O)=O	7789-21-1	fluorosulfonic acid	x			
 S(=O)(=O)(Cl)O	7790-94-5	chlorosulfonic acid	2			
	17462-58-7	iso-butyl chloroformate	x			
Alcohols						
 OC	67-56-1	methanol	1	7900	2100	530
 OC(C)(C)C	75-65-0	t-butyl alcohol	x			
 OCc(cccc1)c1	100-51-6	benzyl alcohol	x			
 OCC=C	107-18-6	allyl alcohol	1	20	7.7	1.8
 OCC#C	107-19-7	propargyl alcohol	x			

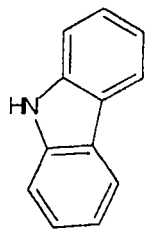
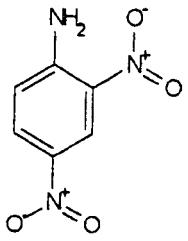
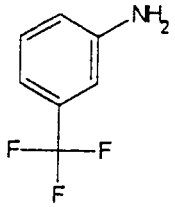
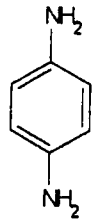
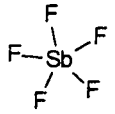
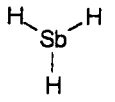
 OCCO	107-21-1	ethylene glycol	x			
Aldehydes						
 O=C	50-00-0	formaldehyde	2			
 O=CC	75-07-0	acetaldehyde	2			
 O=CC(=C)C	78-85-3	methacryladehyde	2			
 O=CC=C	107-02-8	acrolein	1	1.4	0.10	0.030
 O=CCCl	107-20-0	chloroacetaldehyde	2			
 O=CCC	123-38-6	propionaldehyde	2			
 O=CC=CC	123-73-9	(E-) crotonaldehyde	1	14	4.4	0.19
 O=CC=CC	4170-30-3	crotonaldehyde	1	14	4.4	0.19
Aluminum Compounds (not otherwise classified)						
 Cl[Al](Cl)Cl	7446-70-0	aluminum chloride	x			
Amides						
 O=CN(C)C	68-12-2	dimethylformamide	1	180	90	NR
 O=CN	75-12-7	formamide	x			

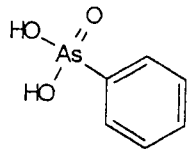
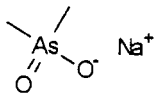
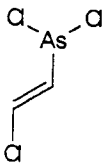
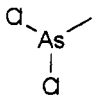
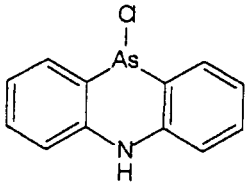
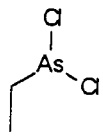
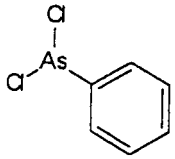
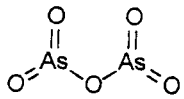
 O=C(N)C=C	79-06-1	acrylamide	x			
 O=C(NCCCC1)C1	105-60-2	caprolactam	x			
 O=C(N)CF	640-19-7	fluoroacetamide	x			
	1397-94-0	Antimycin A	x			
Amines						
 n(cccc1C(N(CC2)C)C2)c1	54-11-5	nicotine	x			
 N(N)(C)C	57-14-7	1,1-dimethyl hydrazine	1	11	3.0	NR
 O=C(N(c(c(C1(C(N(C2)CC(C3C4C5OC6)=C6)(	57-24-9	strychnine	2			
 N(N)C	60-34-4	methyl hydrazine	1	3.0	1.0	NR
 NC	74-89-5	methyl amine	2			
 NCC	75-04-7	ethyl amine	2			

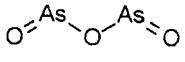
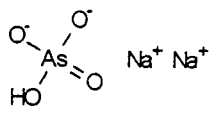
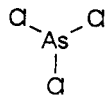
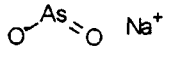
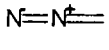
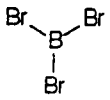
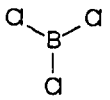
 N(C)(C)C	75-50-3	trimethyl amine	2			
 NC(=S)NN	79-19-6	thiosemicarbazide	x			
 NCC=C	107-11-9	allyl amine	1	18	2.8	0.20
 NCCN	107-15-3	ethylene diamine	1	20	9.7	NR'
 NC(CCCC1)C1	108-91-8	cyclohexylamine	1	30	8.6	1.8
 NCCCC	109-73-9	n-butyl amine	x			
 N(CC)CC	109-89-7	diethyl amine	x			
 n(cccc1)c1	110-86-1	pyridine	x			
 N(CCCC1)C1	110-89-4	piperidine	1	38	NA	NA
 OCCNCCO	111-42-2	diethanolamine	x			
 N(C)C	124-40-3	dimethyl amine	2			

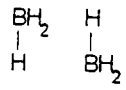
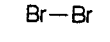
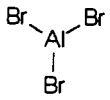
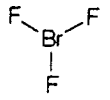
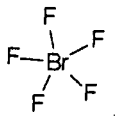
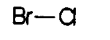
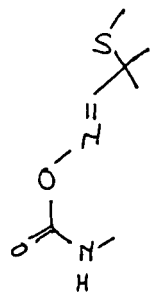
 OCCN	141-43-5	monoethanolamine	x			
 NC(C)Cc(cccc1)c1	300-62-9	amphetamine	x			
 NN	302-01-2	hydrazine	1	35	13	0.10
 CNNC	540-73-8	1,2-dimethylhydrazine	1	11	3.0	NR
 ClCCN(CCCl)CCCl	555-77-1	N-Mustard	x			
 CCN(CCCl)CCCl	538-07-8	bis(2-chloroethyl) ethylamine	x			
	622-44-6	phenylcarbylamine chloride	x			
 ClCC[N+](C)(C)C.[Cl-]	999-81-5	chlormequat chloride	x			

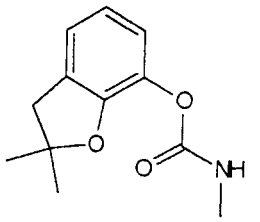
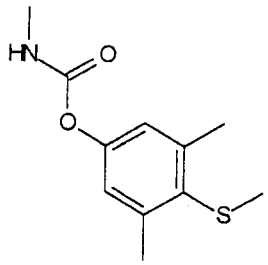
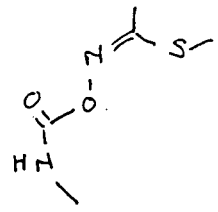
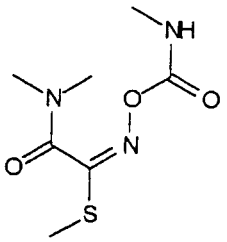
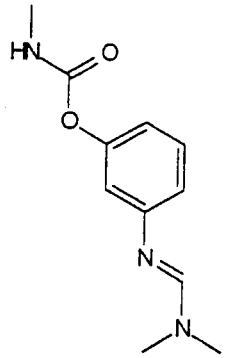
 Clc(c(F)nc1F)c(F)c1Cl	1737-93-5	3,5-dichloro-2,4,5-trifluoropyridine	x			
 C[n+]1ccc(cc1)c2cc[n+](C)cc2.[Cl-].[Cl-]	1910-42-5	paraquat dichloride	2			
 N(N)C(=S)NN	2231-57-4	thiocarbazide	x			
 O(CCCN)C	5332-73-0	3-Methoxypropylamine	x			
	6581-06-2	BZ	x			
 NO	7803-49-8	hydroxyl amine	2			
Anhydrides						
 O=C(OC(=O)C)C	108-24-7	acetic anhydride	2			
 O=C1OC(=O)C=C1	108-31-6	maleic anhydride	2			
Anilines						
 Nc(cccc1)c1	62-53-3	aniline	1	20	12	8

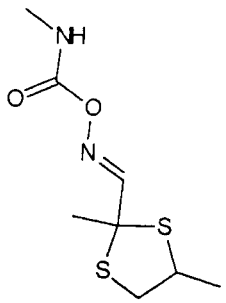
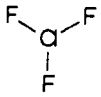
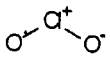
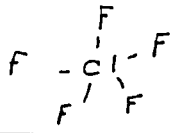
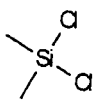
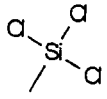
	86-74-8	carbazole	x			
 O=[N+]([O-])c(ccc(N)c1[N+]([O-])=O)c1	97-02-9	2,4-dinitro aniline	2			
 FC(F)(F)c(cccc1N)c1	98-16-8	3-Trifluoromethylanili ne	x			
 Nc(ccc(N)c1)c1	106-50-3	p-phenyl diamine	x			
Antimony Compounds (not otherwise classified)						
 F[Sb](F)(F)(F)F	7783-70-2	anitmony pentafluoride	x			
 [H][Sb]([H])[H]	7803-52-3	stibine	2			
Arsenic Compounds (not otherwise classified)						

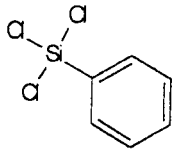
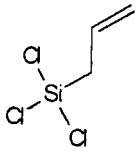
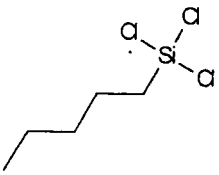
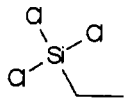
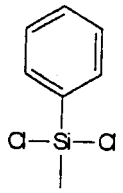
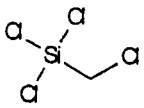
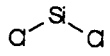
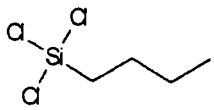
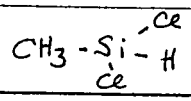
 O[As](O)(=O)c1ccccc1	98-05-5	phenyl arsonic acid	x			
 [As](=O)(C)(C)[O-].[Na+]	124-65-2	sodium cacodylate	x			
 ClC=C[As](Cl)Cl	541-25-3	lewisite	x			
 Cl[As](Cl)C	593-89-5	methyldichloroarsine	x			
 Chemistry 2	578-94-9	adamsite	x			
 CC[As](Cl)Cl	598-14-1	ethyl dichloroarsine	x			
 Cl[As](Cl)c1ccccc1	696-28-6	phenyl dichloroarsine	x			
 O=[As](=O)O[As](=O)=O	1303-28-2	arsenic pentoxide	x			
	1306-02-1	lewisite oxide	x			

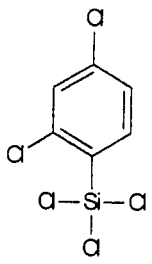
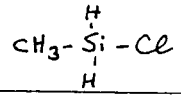
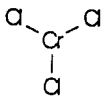
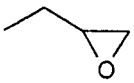
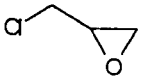
 O=[As]O[As]=O	1327-53-3	arsenic trioxide	2			
As [As]	7440-38-2	arsenic and compounds	2			
 O[As]([O-])([O-])=O.[Na+].[Na+]	7631-89-2	sodium arsenate	x			
 [As](Cl)(Cl)Cl	7784-34-1	arsenous trichloride	1			
As [As]	7784-42-1	arsine	1	0.50	0.17	NR
 [O-][As]=O.[Na+]	7784-46-5	sodium arsenite	2			
Cu (AsO2)(AsO2)	12002-03-8	copper acetoarsenite	2			
Azo						
 N#N=C	334-88-3	Diazomethane	2			
Barium Comounds (not otherwise classified)						
Ba	7440-39-3	barium and compounds	x			
Beryllium Comounds (not otherwise classified)						
Be [Be]	7440-41-7	beryllium and compounds	2			
Boron Comounds (not otherwise classified)						
BF3 (CH3OCH3)	353-42-4	boron trifluoride methyl etherate	1	39	16	0.60
 BrB(Br)Br	10294-33-4	boron tribromide	2			
 ClB(Cl)Cl	10294-34-5	boron trichloride	1	28	7.3	0.60

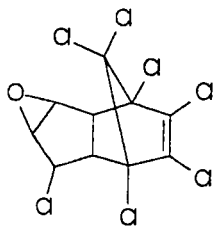
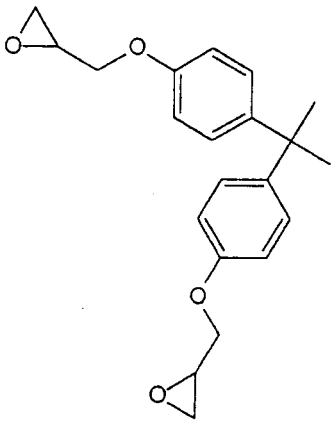
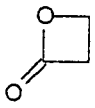
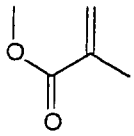
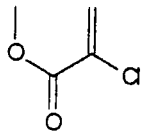
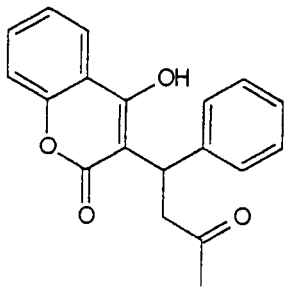
B5H9 bridged	19624-22-7	pentaborane	2			
 H3B-BH3	19287-45-7	diborane	1	3.7	1.0	NR
Bromine Compounds (not otherwise classied)						
 BrBr	7726-95-6	bromine	1	8.5	0.24	0.024
 Br[Al](Br)Br	7727-15-3	aluminum bromide	x			
 Br(F)(F)F	7787-71-5	bromine trifluoride	2			
 FBr(F)(F)(F)F	7789-30-2	bromine pentafluoride	2			
 BrCl	13863-41-7	bromine chloride	2			
Cadmium Compounds (not otherwise classified)						
 [Cd]	7440-43-9	cadmium and compounds	2			
Carbamate						
 O=C(ON=CC(SC)(C)C)NC	116-06-3	aldicarb	2			

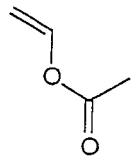
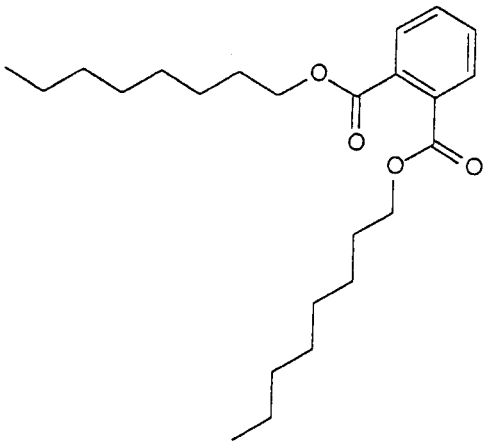
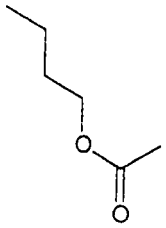
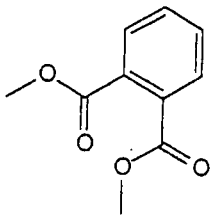
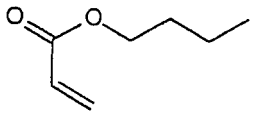
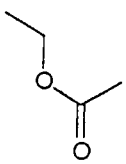
 O=C(Oc(c(OC(C1)(C)C)c1cc2)c2)NC	1563-66-2	carbofuran	2			
 CNC(=O)Oc1cc(C)c(SC)c(C)c1	2032-65-7	methiocarb	x			
 CNC(=O)ON=C(C)SC	16752-77-5	methomyl	x			
 CNC(=O)ON=C(SC)C(=O)N(C)C	23135-22-0	oxamyl	x			
 CNC(=O)Oc1cccc(N=CN(C)C)c1	23422-53-9	formetanate hydrochloride	x			

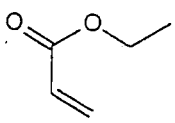
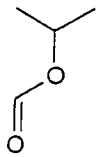
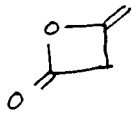
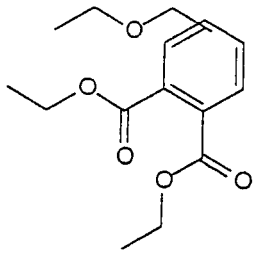
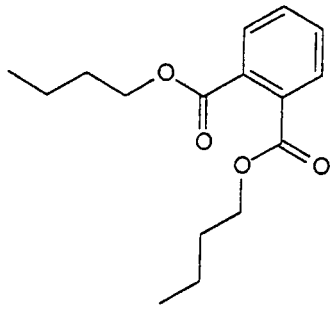
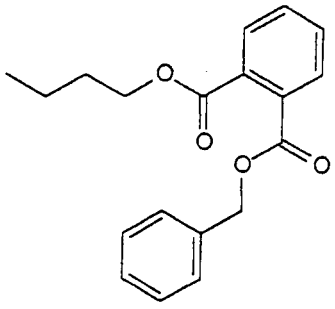
 S1C(C=NOC(=O)NC)(C)SC(C)C1	26419-73-8	tirpate	x			
Carbonate						
Cl3COCOOCCl3	32315-10-9	triphosgene	x			
Chlorine Compounds (Inorganic, not otherwise classified)						
 ClCl	7782-50-5	chlorine	1	20	2.0	0.50
 Cl(F)(F)F	7790-91-2	chlorine trifluoride	1	14	3.1	0.35
 [O.][Cl+][O-]	10049-04-4	chlorine dioxide	1	2.4	1.1	0.15
 ClF5	13637-63-3	chlorine pentafluoride	2			
Chlorosilanes						
 Cl[Si](C)(C)C	75-77-4	trimethyl chlorosilane	1			
 C[Si](C)(Cl)Cl	75-78-5	dimethyl dichlorosilane	1	53	13	0.90
 C[Si](Cl)(Cl)Cl	75-79-6	methyl trichlorosilane	1	28	6.2	0.60

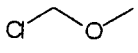
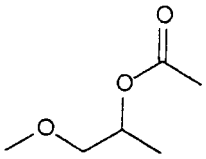
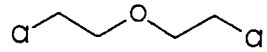
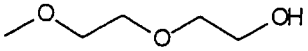
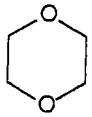
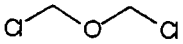
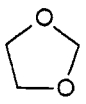
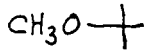
 Cl[Si](Cl)(Cl)c1ccccc1	98-13-5	trichlorophenyl silane	x			
 ClSi(Cl)(Cl)CC=C	107-37-9	allyl trichlorosilane	x			
 CCCCC[Si](Cl)(Cl)Cl	107-72-2	amyltrichlorosilane	x			
 CC[Si](Cl)(Cl)Cl	115-21-9	trichloroethyl silane	x			
 Cl[Si](c1ccccc1)(Cl)C	149-74-6	dichloromethyl phenyl silane	x			
 Cl[Si](Cl)(Cl)CCl	1558-25-4	chloromethyl trichloro silane	x			
 Cl[Si]Cl	4109-96-0	dichlorosilane	x			
 Cl[Si](Cl)(Cl)CCCC	7521-80-4	butyl trichlorosilane	x			
CH3SiCl2H 	75-54-7	methyl dichlorosilane	2			

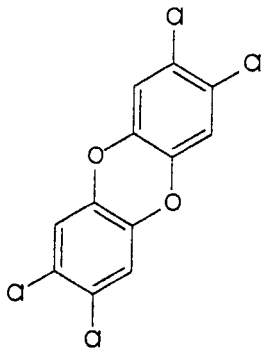
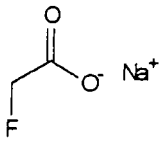
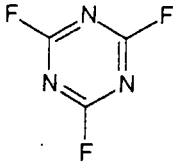
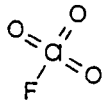
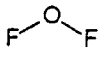
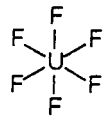
 Cl[Si](c1c(cc(cc1)Cl)Cl)(Cl)Cl	27137-85-5	trichloro(dichlorophenyl) silane	x			
 CH3SiClH2	993-00-0	methyl chlorosilane	2			
Chromium Compounds (not otherwise classified)						
 Cl[Cr](Cl)Cl	10025-73-7	chromic chloride	x			
Cobalt Compounds (not otherwise classified)						
[Co]	7440-48-4	cobalt and compounds	x			
Copper Compounds (not otherwise classified)						
[Cu]	7440-50-8	copper and compounds	x			
Epoxides						
 O(C1)C1	75-21-8	ethylene oxide	1	200	45	NR
 O(C1C)C1	75-56-9	propylene oxide	1	610	290	60
 O(C1CC)C1	106-88-7	1,2-butylene oxide	x			
 O(C1CCl)C1	106-89-8	epichlorohydrin	1	72	24	5.0

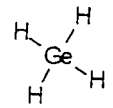
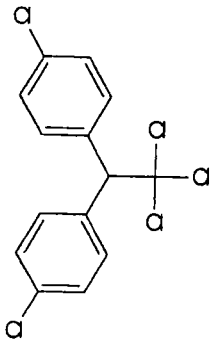
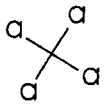
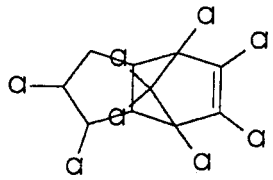
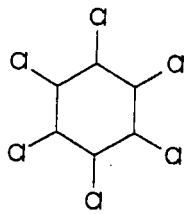
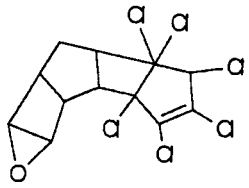
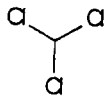
 ClC2C1OC1C3C2C4(Cl)C(=C(Cl)C3(Cl)C4(Cl)	1024-57-3	heptachlor epoxide	x			
 O(C1COc(ccc(c2)C(c(ccc(OCC(O3)C3)c4)c4)(	1675-54-3	bisphenol A diglycidyl ether	x			
Esters						
 O=C(OC1)C1	57-57-8	beta-propiolactone	x			
 O=C(OC)C(=C)C	80-62-6	methyl methacrylate	2			
 O=C(OC)C(=C)Cl	80-63-7	methyl 2-chloroacrylate	x			
 c1ccc2C(O)=C(C(c3ccccc3)CC(=O)C)C(=O)Oc	81-81-2	warfarin	x			

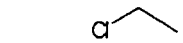
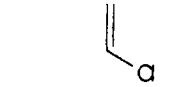
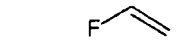
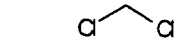
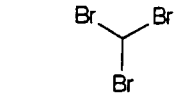
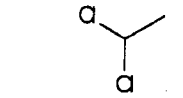
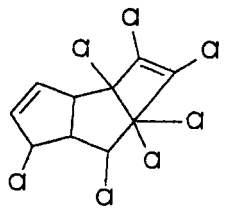
 O=C(OC=C)C	108-05-4	vinyl acetate monomer	2			
 O=C(OCCCCCCCC)c(c(ccc1)C(=O)OCCCCC(	117-84-0	dioctyl phthalate	x			
 O=C(OCCCC)C	123-86-4	n-butyl acetate	2			
 O=C(OC)c(c(ccc1)C(=O)OC)c1	131-11-3	dimethyl phthalate	x			
 O=C(OCCCC)C=C	141-32-2	butyl acrylate	2			
 O=C(OCC)C	141-78-6	ethyl acetate	2			

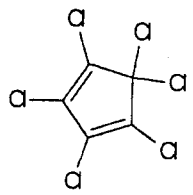
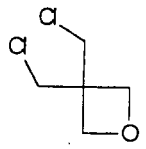
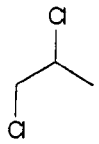
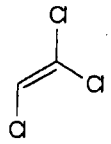
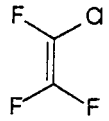
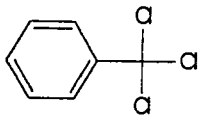
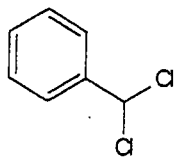
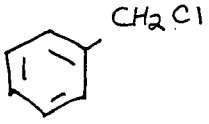
 O=C(OCC)C=C	140-88-5	ethyl acrylate	2			
 O=COC(C)C	625-55-8	isopropyl formate	x			
 O=C(OC1=C)C1	674-82-8	diketene	2			
 O=C(OCC)c(c(ccc1)C(=O)OCC)c1	84-66-2	diethyl phthalate	x			
 O=C(OCCCC)c(c(ccc1)C(=O)OCCCC)c1	84-74-2	di n-butyl phthalate	x			
 O=C(OCc(cccc1)c1)c(c(ccc2)C(=O)OCCCC)c2	85-68-7	butyl benzyl phthalate	x			
Ethers						
O(CC)CC	60-29-7	ethyl ether	x			

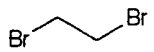
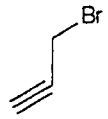
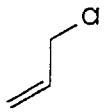
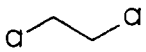
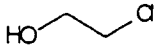
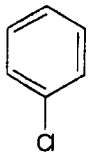
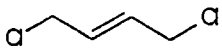
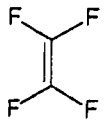
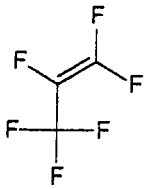
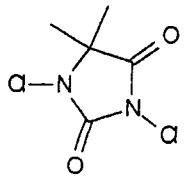
 O(CCl)C	107-30-2	chloromethyl methyl ether	1	0.94	0.061	NA
 COCC(OC(=O)C)C	108-65-6	propylene glycol monomethyl ether acetate	x			
 O(CCC1)C1	109-99-9	tetrahydrofuran	2			
 O1C=CC=C1	110-00-9	furan	1	29	10	NA
 O(C=C)CCCC	111-34-2	butyl vinyl ether	x			
 O(CCCl)CCCl	111-44-4	dichloroethyl ether	x			
 O(CCOC)CCO	111-77-3	diethylene glycol monomethyl ether	x			
 O(CCOC1)C1	123-91-1	1,4-dioxane	2			
 O(CCl)CCl	542-88-1	bis-chloromethyl ether	2			
 O(CCO1)C1	646-06-0	1,3-dioxolane (diulane)	x			
 O(C(C)(C)C)C	1634-04-4	methyl t-butyl ether	2			

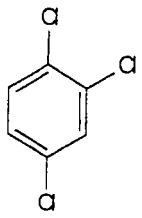
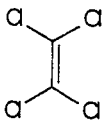
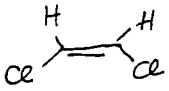
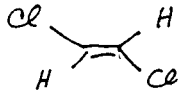
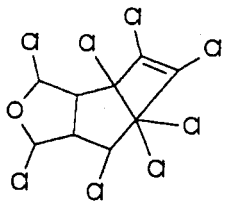
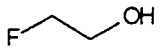
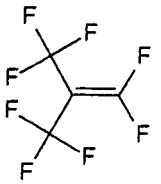
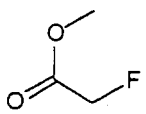
 Clc3cc2Oc1cc(Cl)c(Cl)cc1Oc2cc3Cl	1746-01-6	dioxin	2			
Fluorine Compounds (not otherwise classified)						
 FCC(=O)[O-].[Na+]	62-74-8	sodium fluoroacetate	2			
 Fc(nc(F)nc1F)n1	675-14-9	cyanuric fluoride	x			
 ClF(=O)(=O)=O	7616-94-6	perchloryl fluoride	x			
 FF	7782-41-4	fluorine	1	13	5.0	2.0
 FOF	7783-41-7	oxygen difluoride	2			
 F[U](F)(F)(F)(F)F	7783-81-5	uranium hexafluoride	1	36	9.6	3.6
 [Ca](F)F	7789-75-5	calcium fluoride	x			
Germanium Compounds (not otherwise classified)						

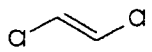
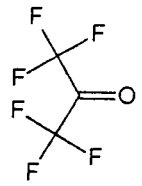
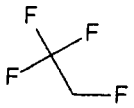
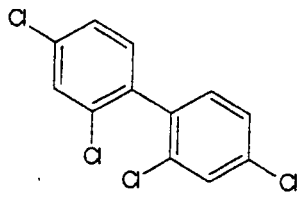
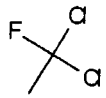
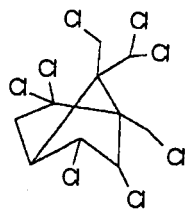
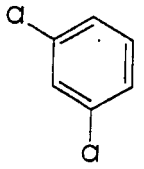
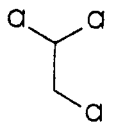
 [H][Ge]([H])([H])[H]	7782-65-2	germane	x			
Halogens						
 c(ccc(c1)Cl)(c1)C(c(ccc(c2)Cl)c2)C(Cl)(Cl)Cl	50-29-3	4,4'-DDT	x			
 C(Cl)(Cl)(Cl)Cl	56-23-5	carbon tetrachloride	1	170	68	12
 ClC1CC2C(C1Cl)C3(Cl)C(=C(Cl)C2(Cl)C3(Cl)C	57-74-9	chlordane	2			
 C(C(C(C(C1Cl)Cl)Cl)Cl)(C1Cl)Cl	58-89-9	lindane (hexachlorocyclohexane)	x			
 ClC4=C(Cl)C5(Cl)C3C1CC(C2OC12)C3C4(Cl)	60-57-1	dieldrin	x			
 C(Cl)(Cl)Cl	67-66-3	chloroform	1	650	88	NA

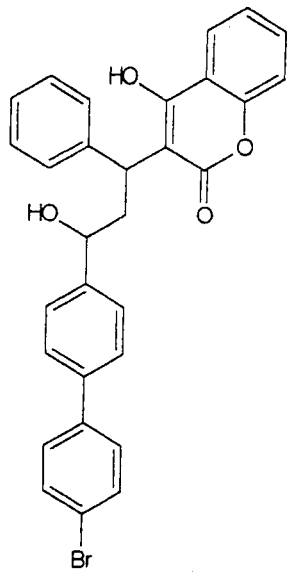
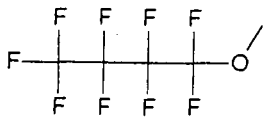
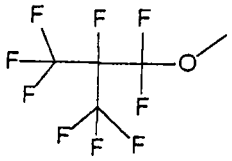
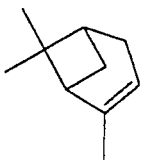
See CAS # 25323-89-1	71-55-6	1,1,1-trichloroethane				
 BrC	74-83-9	methyl bromide	2			
 ClC	74-87-3	methyl chloride	2			
 CI	74-88-4	methyl iodide	x			
 ClCC	75-00-3	chloroethane	x			
 C(=C)Cl	75-01-4	vinyl chloride	2			
 FC=C	75-02-5	vinyl fluoride	x			
 ClCCl	75-09-2	methylene chloride	1			
 BrC(Br)Br	75-25-2	bromoform	x			
 C(Cl)(Cl)C	75-34-3	1,1-dichloroethane	x			
 ClC1C=CC2C1C3(Cl)C(=C(Cl)C2(Cl)C3(Cl)Cl)	76-44-8	heptachlor	x			

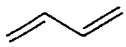
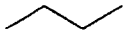
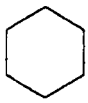
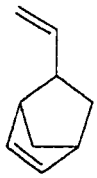
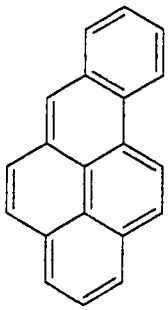
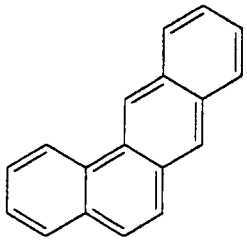
 C(=C(C(=C1Cl)Cl)Cl)(C1(Cl)Cl)Cl	77-47-4	hexachlorocyclopentadiene	x			
 ClCC1(CCl)COC1	78-71-7	oxetane, 3-3bis(chloromethyl)	x			
 ClCC(Cl)C	78-87-5	1,2-dichloropropane	x			
 C(=CCl)(Cl)Cl	79-01-6	trichloroethylene	1			
 FC(F)=C(F)Cl	79-38-9	trifluorochloroethylene	x			
 c(cccc1)(c1)C(Cl)(Cl)Cl	98-07-7	benzyl trichloride	x			
 c(cccc1)(c1)C(Cl)Cl	98-87-3	benzal chloride	x			
 c(cccc1)(c1)CCl	100-44-7	benzyl chloride	x			

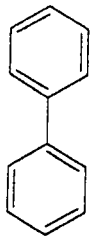
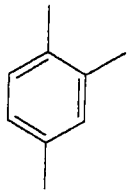
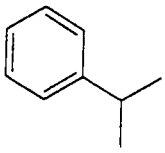
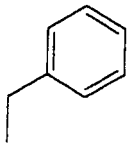
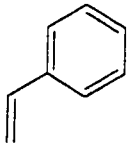
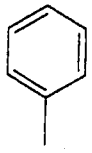
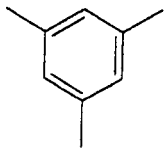
 BrCCBr	106-93-4	dibromoethane	2			
 C(#C)CBr	106-96-7	propargyl bromide	x			
 C(=C)CCl	107-05-1	allyl chloride	x			
 ClCCCl	107-06-2	1,2-dichloroethane	2			
 OCCCl	107-07-3	chloroethanol	x			
 c(cccc1)(c1)Cl	108-90-7	chlorobenzene	2			
 C(=CCCl)CCl	110-57-6	trans-1,4-dichlorobutene	x			
 FC(F)=C(F)F	116-14-3	tetrafluoroethylene	x			
 FC(F)(F)C(F)=C(F)F	116-15-4	hexafluoropropylene	x			
 O=C(N(C(C1=O)(C)C)Cl)N1Cl	118-52-5	1,3-dichloro-5,5-dimethylhydantoin	x			

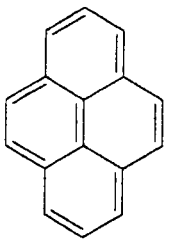
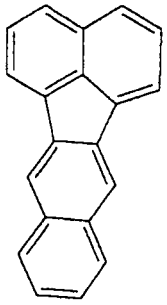
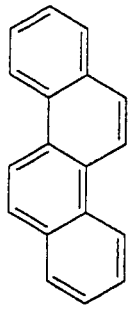
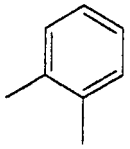
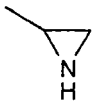
 c(ccc(c1Cl)Cl)(c1)Cl	120-82-1	1,2,4-trichlorobenzene	x			
 C(=C(Cl)Cl)(Cl)Cl	127-18-4	tetrachloroethylene	1	490	230	35
 cis ClCH=CHCl	156-59-2	cis-1,2-dichloroethylene	1	850	500	140
 trans ClCH=CHCl	156-60-2	trans-1,4-dichloroethylene	1	1700	1000	280
 ClC1OC(Cl)C2C1C3(Cl)C(=C(Cl)C2(Cl)C3(Cl)(	297-78-9	isobenzan	x			
 FCCO	371-62-0	ethylene fluorohydrin	x			
 FC(F)=C(C(F)(F)F)C(F)(F)F	382-21-8	perfluoroisobutylene	x			
 O=C(OC)CF	453-18-9	methyl fluoroacetate	2			

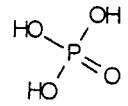
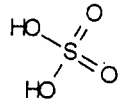
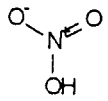
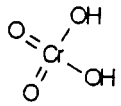
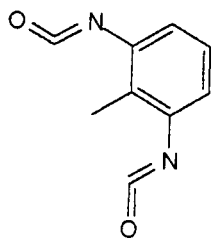
 C(=CCl)Cl	540-59-0	1,2-dichloroethylene MIXTURE	1			
 FC	593-53-3	methyl fluoride	x			
 O=C(C(F)(F)F)C(F)(F)F	684-16-2	hexafluoroacetone	2			
 FCC(F)(F)F	811-97-2	HFC 134a (1,1,1,2-tetrafluoroethane)	1	27000	13000	8000
 Clc2c(ccc(c2)Cl)c1c(cc(cc1)Cl)Cl	1336-36-3	polychlorinated biphenyl	x			
 CC(F)(Cl)Cl	1717-00-6	HCFC 141b (1,1-dichloro-1-fluoroethane)	1	3000	1700	1000
 ClC(C(Cl)C1C2)C(C2(Cl)Cl)(C1(C(Cl)Cl)CCl)C	8001-35-2	camphechlor	x			
 Clc1cccc(c1)Cl	25321-22-6	dichlorobenzene	x			
 ClC(Cl)CCl	25323-89-1	trichloroethane	1	3800	600	230

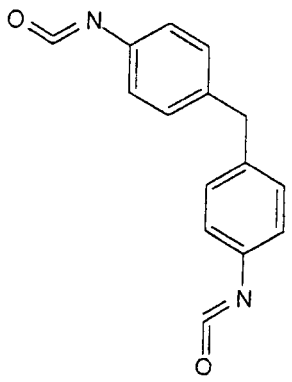
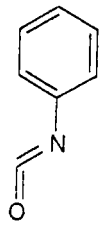
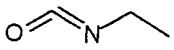
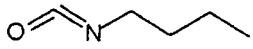
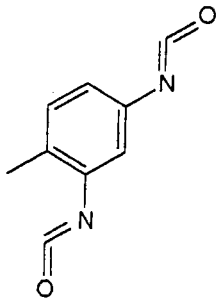
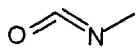
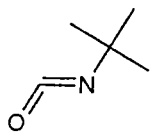
 c1cc(Br)ccc1c(cc2)ccc2C(O)CC(c3ccccc3)C4=	28772-56-7	bromodiolone	x			
 Chemistry 0	163702-07-6	HFE 7100 (methyl nonafluorobutyl ether)	1	15000	8200	2500
 Chemistry 1	163702-08-7	HFE 7100 (methyl nonafluoroisobutyl ether)	1	15000	8200	2500
Hydrides						
Li—H [Li][H]	7580-67-8	lithium hydride	x			
Hydrocarbons (Aliphatic)						
CH_4 C	74-82-8	methane	x			
 C(C)C	74-98-6	propane	2			
 C(C(CC1C2)C1(C)C)(=C2)C	80-56-8	alpha-pinene	x			

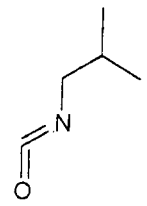
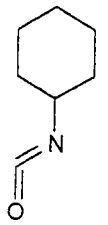
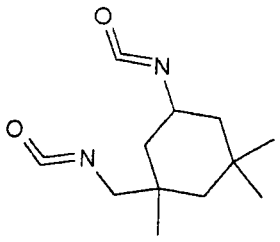
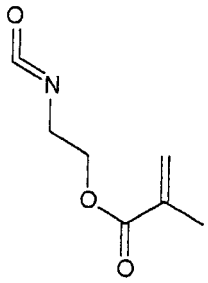
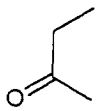
 C(C=C)=C	106-99-0	butadiene	2			
 C(CC)C	106-97-8	butane	2			
 C(CCCC)C	110-54-3	hexane	2			
 C(CCCC1)C1	110-82-7	cyclohexane	2			
 C(CCC1)C1	287-92-3	cyclopentane	x			
 C(C=CC1C2C=C)(C1)C2	3048-64-4	vinylnorbonene	x			
CH	8006-61-9	gasoline	2			
CH	70892-10-3	jet fuels	1	NA	1100	290
Hydrocarbons (Aromatic)						
 c(c(c(cc1)ccc2)c2cc3)(c3cc(c4ccc5)c5)c14	50-32-8	benzo[a]pyrene	2			
 c(c(c(c(c1)ccc2)c2)cc(c3ccc4)c4)(c1)c3	56-55-3	benzo[a]anthracene	x			

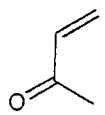
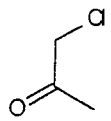
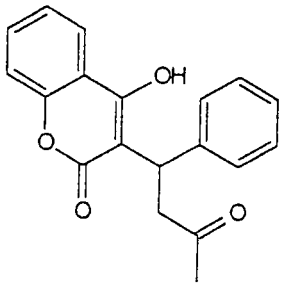
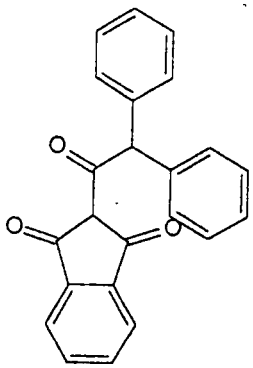
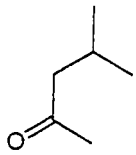
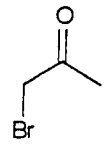
 c(cccc1)c1	71-43-2	benzene	1			
 c(c(cccc1)c1)(cccc2)c2	92-52-4	biphenyl	x			
 c(ccc(c1C)C)(c1)C	95-63-6	trimethylbenzene	x			
 c(cccc1)(c1)C(C)C	98-82-8	cumene	x			
 c(cccc1)(c1)CC	100-41-4	ethyl benzene	x			
 c(cccc1)(c1)C=C	100-42-5	styrene	2			
 c(cccc1)(c1)C	108-88-3	toluene	1	630	190	82
 c(cc(cc1C)C)(c1)C	108-67-8	mesitylene	x			

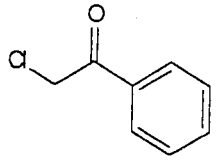
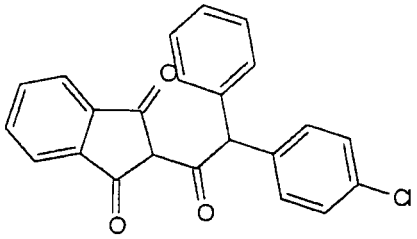
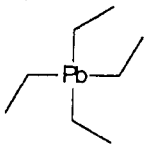
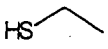
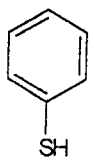
 c(c(c(cc1)ccc2)c2cc3)(c1ccc4)c34	129-00-0	pyrene	x			
 c2ccc1cc3c(cc1c2)c4cccc5cccc3c45	207-08-9	benzo[k]fluoranthene	x			
 c1ccc2ccc3c4ccccc4ccc3c2c1	218-01-9	chrysene	x			
 Cc1ccccc1C	1330-20-7	xylenes	1	930	430	130
Imines						
 N(C1C)C1	75-55-8	propyleneimine	1	23	12	NR
 N(C1)C1	151-56-4	ethyleneimine	1	9.9	4.6	NR
Inorganic Acids						
HCl Cl	7647-01-0	hydrogen chloride gas	1	100	22	1.8

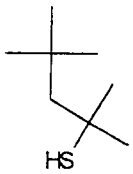
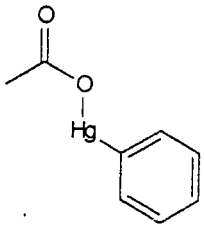
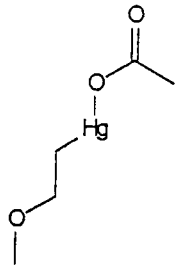
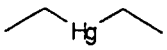
HCl	7647-01-0	hydrochloric acid	1			
 OP(O)(O)=O	7664-38-2	phosphoric acid	2			
HF F	7664-39-3	hydrogen fluoride	1	44	24	1.0
 OS(O)(=O)=O	7664-93-9	sulfuric acid	1			
 O[N+]([O-])=O	7697-37-2	nitric acid	1	22	4.0	0.50
 O=[Cr](=O)(O)O	7738-94-5	chromic acid	x			
IO3H	7782-68-5	iodic acid	x			
H_2S S	7783-06-4	hydrogen sulfide	1	50	28	0.17
Se [Se]	7783-07-5	hydrogen selenide	2			
HI I	10034-85-2	hydrogen iodide	2			
HBr Br	10035-10-6	hydrogen bromide	2			
Isocyanates						
 O=C=Nc(c(c(N=C=O)cc1)C)c1	91-08-7	toluene 2,6-diisocyanate (2,6-TDI)	1	0.51	0.083	0.020hh

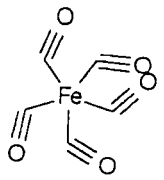
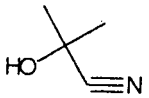
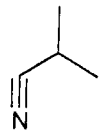
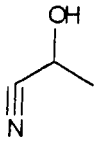
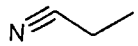
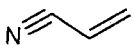
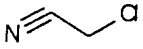
 O=C=Nc(ccc(c1)Cc(ccc(N=C=O)c2)c2)c1	101-68-8	4,4'-methylenediphenyld iisocyanate	2			
 O=C=Nc(cccc1)c1	103-71-9	phenyl isocyanate	x			
 O=C=NCC	109-90-0	ethyl isocyanate	x			
 O=C=NCCC	110-78-1	n-propyl isocyanate	x			
 O=C=NCCCC	111-36-4	n-butyl isocyanate	2			
 O=C=Nc(c(ccc1N=C=O)C)c1	584-84-9	toluene 2,4-diisocyanate (2,4-TDI)	1	0.51	0.32	0.16
 O=C=NC	624-83-9	methyl isocyanate	1	0.20	0.067	NA
 O=C=NC(C)(C)C	1609-86-5	t-butyl isocyanate	x			

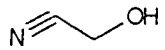
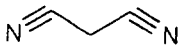
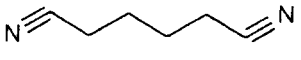
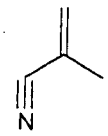
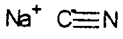
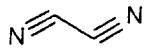
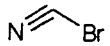
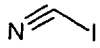
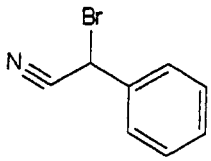
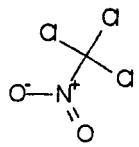
 O=C=NCC(C)C	1873-29-6	isobutyl isocyanate	x			
 O=C=NC(CCCC1)C1	3173-53-3	cyclohexyl isocyanate	2			
 O=C=NCC(CC(N=C=O)CC1(C)C)(C1)C	4098-71-9	isophorone diisocyanate	x			
	6427-21-0	methoxymethyl isocyanate	x			
 O=C(OCCN=C=O)C(=C)C	30674-80-7	methacryloyloxyethyl isocyanate	x			
Ketones						
 O=C(C)C	67-64-1	acetone	2			
 O=C(CC)C	78-93-3	methyl ethyl ketone (2-butanone; MEK)	1	4000	1700	100

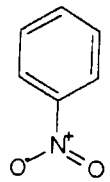
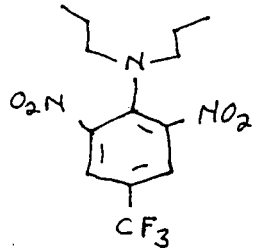
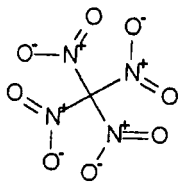
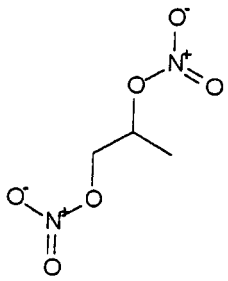
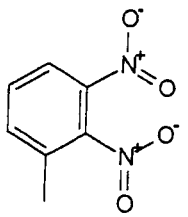
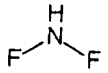
 O=C(C=C)C	78-94-4	methyl vinyl ketone	2			
 O=C(CCl)C	78-95-5	chloroacetone	2			
 c1ccc2C(O)=C(C(c3ccccc3)CC(=O)C)C(=O)Oc	81-81-2	warfarin	x			
 O=C1c2ccccc2C(=O)C1C(=O)C(c3ccccc3)c4cc	82-66-6	diphacinone	x			
 O=C(CC(C)C)C	108-10-1	4-Methyl-2-pentanone	x			
 C=C=O	463-51-4	ketene	2			
 BrCC(=O)C	598-31-2	bromoacetone	x			

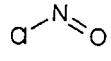
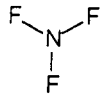
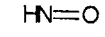
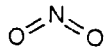
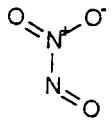
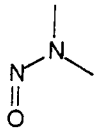
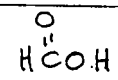
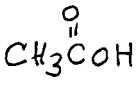
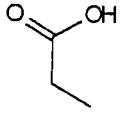
 ClCC(=O)c1ccccc1	1341-24-8	chloroacetophenone	2			
 c1ccccc1C(c2ccc(Cl)cc2)C(=O)C3C(=O)c4ccc	3691-35-8	chlorophacinone	x			
Lead Compounds (not otherwise classified)						
 C[Pb](C)(C)C	75-74-1	tetramethyl lead	1			
 CC[Pb](CC)(CC)CC	78-00-2	tetraethyl lead	x			
Pb [Pb]	7439-92-1	lead and compounds (including lead	2			
Manganese Compounds (not otherwise classified)						
Mn [Mn]	7439-96-5	manganese and compounds	x			
	12108-13-3	manganese, tricarbonylmethyl-cyclopentadienyl	x			
Mercaptans						
HS— SC	74-93-1	methyl mercaptan	1	23	5.0	0.50
 SCC	75-08-1	ethyl mercaptan	2			
 Sc(cccc1)c1	108-98-5	phenyl mercaptan	2			

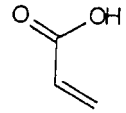
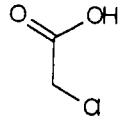
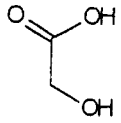
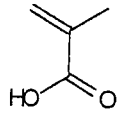
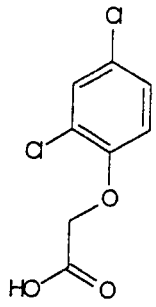
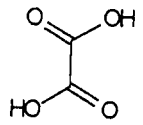
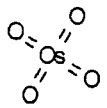
 SCCCCCCCC	111-88-6	n-octyl mercaptan	2			
 SC(CC(C)(C)C)(C)C	141-59-3	t-octyl mercaptan	x			
Mercury Compounds (not otherwise classified)						
 CC(=O)O[Hg]c1ccccc1	62-38-4	phenyl mercuric acetate	2			
 COCC[Hg]OC(=O)C	151-38-2	methoxyethyl mercury	2			
 CC[Hg]CC	627-44-1	diethyl mercury	x			
 [Hg]	7439-97-6	mercury & compounds (including	2			
 [Hg+]C	22967-92-6	methyl mercury	x			
Metal Carbonyls						
Ni (CO)4	13463-39-3	nickel carbonyl	1	0.16	0.021	NR

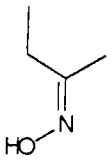
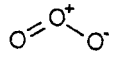
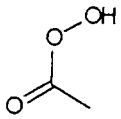
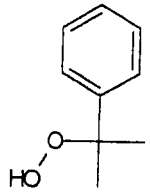
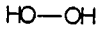
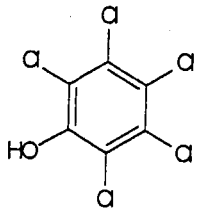
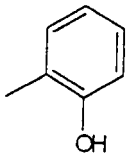
 [Fe](C#[O:])(C#[O:])(C#[O:])(C#[O:])(C#[O:])	13463-40-6	iron pentacarbonyl	1	0.58	0.19	NR
Nickel Compounds (not otherwise classified)						
 [Ni]	7440-02-0	nickel & compounds	2			
NiO	11099-02-8	nickel oxide	2			
Nitriles						
 N#C	74-90-8	hydrogen cyanide	1	15	7.1	2.0
 N#CC	75-05-8	acetonitrile	x			
 N#CC(O)(C)C	75-86-5	acetone cyanohydrin	1	15	5.4	0.84
 N#CC(C)C	78-82-0	isobutyronitrile	1	20	6.6	NR
 N#CC(O)C	78-97-7	lactonitrile	x			
 N#CCC	107-12-0	propionitrile	1	39	7.4	NR
 N#CC=C	107-13-1	acrylonitrile	2			
 N#CCCl	107-14-2	chloroacetonitrile	2			

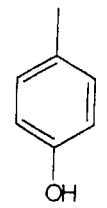
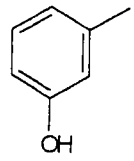
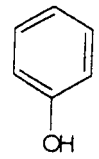
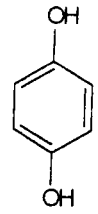
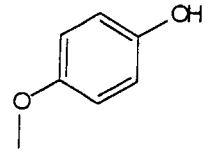
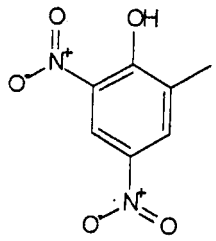
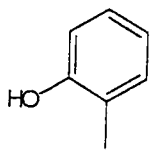
 N#CCO	107-16-4	formaldehyde cyanohydrin	x			
 N#CCC#N	109-77-3	malononitrile	2			
 N#CCCCCC#N	111-69-3	adiponitrile	x			
 N#CC(=C)C	126-98-7	methacrylonitrile	1	3.4	1.1	NR
 [Na+].[C-]#N	143-33-9	sodium cyanide	2			
 N#CC#N	460-19-5	cyanogen	2			
 N#CBr	506-68-3	cyanogen bromide	2			
	506-77-3	cyanogen chloride	1			
 N#Cl	506-78-5	cyanogen iodide	x			
	2698-41-1	o-chlorobenzylidene malononitrile	2			
 N#CC(Br)C1=CC=CC=C1	5798-79-8	bromobenzyl cyanide	x			
Nitro Compounds						
 O=[N+]([O-])C(Cl)(Cl)Cl	76-06-2	chloropicrin	2			

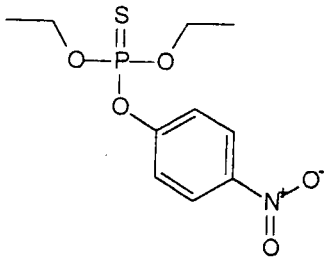
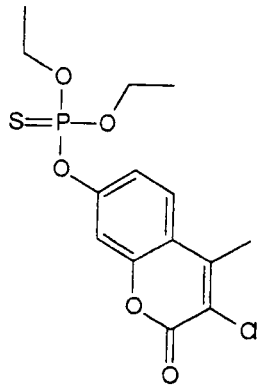
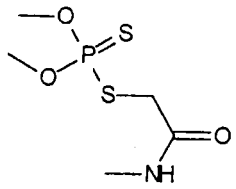
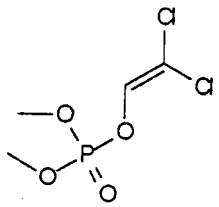
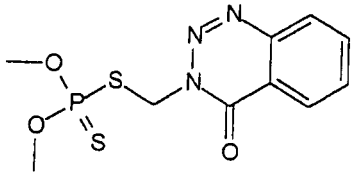
 O=[N+]([O-])c(cccc1)c1	98-95-3	nitrobenzene	x			
	100-14-1	benzene, 1-(chloromethyl)-4-nitro	x			
 CCCN(CCC)c1c(cc(cc1[N+]([O-])=O)C(F)(F)F)	1582-09-8	trifluralin	x			
 O=[N+]([O-])C([N+]([O-])=O)([N+]([O-])=O)[N+]	509-14-8	tetranitromethane	1	1.8	0.91	0.36
 O=[N+]([O-])OCC(O[N+]([O-])=O)C	6423-43-4	Otto Fuel (Propylene glycol dinitrate)	1	13	1.0	0.17
 Cc1cccc([N+]([O-])=O)c1[N+]([O-])=O	25321-14-6	dinitro toluene	x			
Nitrogen Compounds (not otherwise classified)						
 FN(F)	1341-49-7	ammonium fluoride	x			

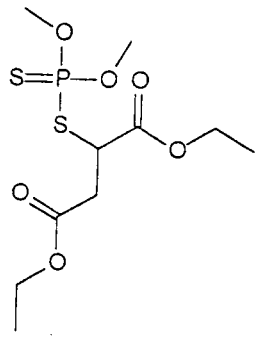
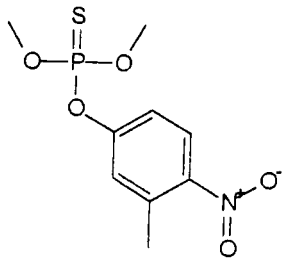
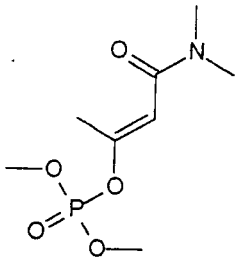
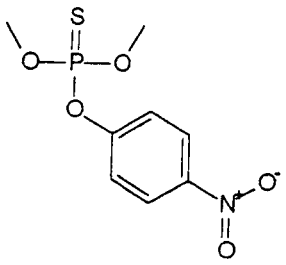
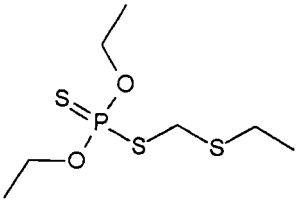
 ClN=O	2696-92-6	nitrosyl chloride	2			
 N(	7664-41-7	ammonia	1	1100	110	25
 FN(F)F	7783-54-2	nitrogen trifluoride	2			
 N=O	10102-43-9	nitric oxide	1	20	12	0.50
 O=N=O	10102-44-0	nitrogen dioxide	1	20	12	0.50
N2O4	10544-72-6	nitrogen tetraoxide	x			
 O=[N+]([O-])N=O	10544-73-7	nitrogen trioxide	x			
Nitroso Compounds						
 O=NN(C)C	62-75-9	nitosodimethyl amine	x			
Organic Acids						
 O=CO	64-18-6	formic acid	x			
 O=C(O)C	64-19-7	acetic acid	x			
 O=C(O)CC	79-09-4	propionic acid	x			

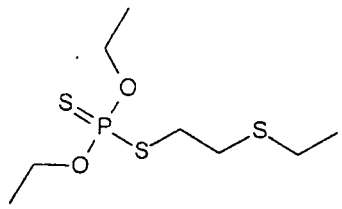
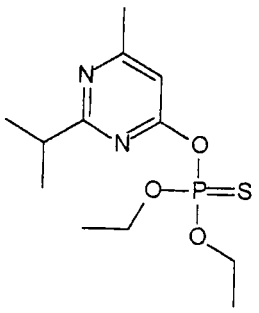
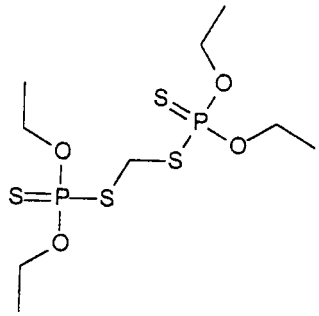
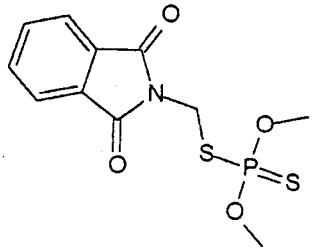
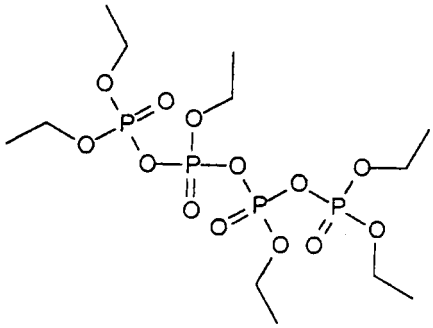
 O=C(O)C=C	79-10-7	acrylic acid	1	180	20	1.0
 O=C(O)CCl	79-11-8	mono-chloroacetic acid	1	ID	6.6	ID
 O=C(O)CO	79-14-1	glycolic acid	x			
 O=C(O)C(=C)C	79-41-4	methacrylic acid	2			
 O=C(O)COc(c(cc(c1)Cl)Cl)c1	94-75-7	2,4-dichlorophenoxy acid	x			
 O=C(O)C(=O)O	144-62-7	oxalic acid	x			
Osmium Compounds (not otherwise classified)						
 O=[Os](=O)(=O)=O	20816-12-0	osmium tetroxide	2			
Oximes						

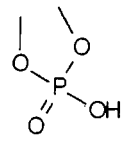
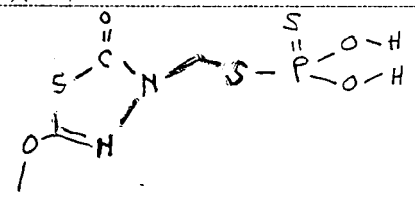
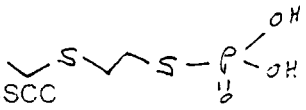
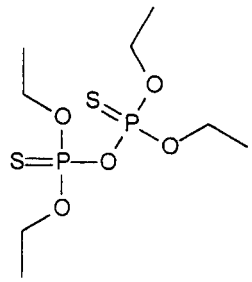
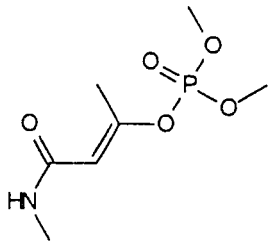
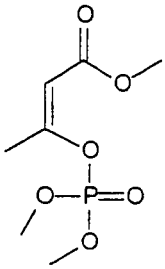
 N(O)=C(CC)C	96-29-7	2-Butanone oxime	x			
Oxygen Compounds (not otherwise classified)						
 O#C	630-08-0	carbon monoxide	1	330	83	NR
 O=[O+][O-]	10028-15-6	ozone	2			
Peroxides						
 O=C(OO)C	79-21-0	peracetic acid	1			
 O(O)C(c(cccc1)c1)(C)C	80-15-9	cumene hydroperoxide	x			
 OO	7722-84-1	hydrogen peroxide	2			
Phenols						
 Oc(c(c(c(c1Cl)Cl)Cl)Cl)c1Cl	87-86-5	pentachlorophenol	x			
 Oc(c(ccc1)C)c1	95-48-7	o-cresol	x			

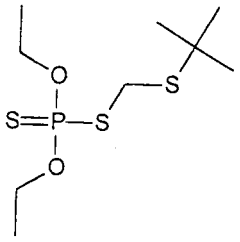
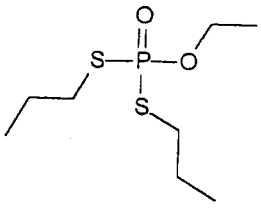
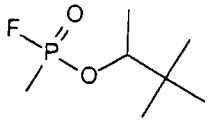
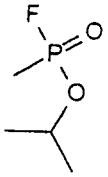
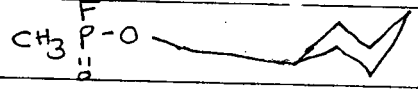
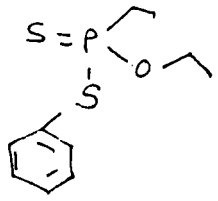
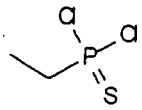
 Oc(ccc(c1)C)c1	106-44-5	p-cresol	x			
 Oc(cccc1C)c1	108-39-4	m-cresol	x			
 Oc(cccc1)c1	108-95-2	phenol	1	47	15	4.5
 Oc(ccc(O)c1)c1	123-31-9	hydroquinone	x			
 O(c(ccc(O)c1)c1)C	150-76-5	p-methoxyphenol	x			
 O=[N+]([O-])c(cc([N+]([O-])=O)c(O)c1C)c1	534-52-1	4,6-dinitro-o-cresol	x			
 Oc1ccccc1C	1319-77-3	cresol	2			
	4418-66-0	phenol, 2,2'-thiobis(4-chloro-6-methyl-)	x			

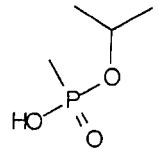
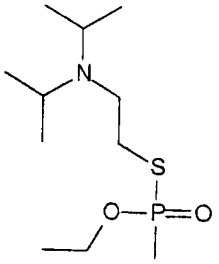
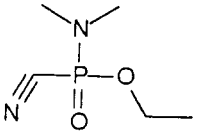
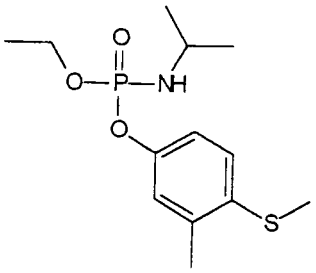
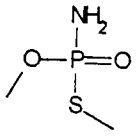
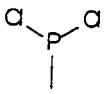
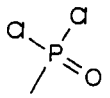
Phosphate & Thiophosphate Esters						
 CCOP(=S)(OCC)Oc1ccc(cc1)[N+]([O-])=O	56-38-2	parathion	2			
 S=P(OCC)(OCC)Oc1ccc2C(C)=C(Cl)C(=O)Oc	56-72-4	coumaphos	x			
 O=C(NC)CSP(OC)(OC)=S	60-51-5	dimethoate	x			
 O=P(OC)(OC)OC=C(Cl)Cl	62-73-7	dichlorovos	x			
 S=P(OC)(OC)SCN1N=Nc2ccccc2C1(=O)	86-50-0	azinphos-methyl	2			

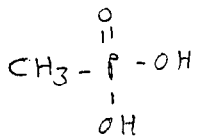
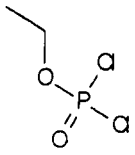
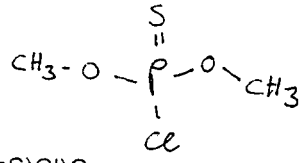
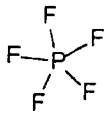
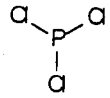
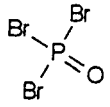
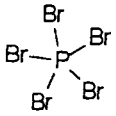
 CCOC(=O)CC(SP(=S)(OC)OC)C(=O)OCC	121-75-5	malathion	x			
 COP(=S)(OC)Oc1ccc([N+]([O-])=O)c(C)c1	122-14-5	fenitrothion	x			
 COP(=O)(OC)OC(C)=CC(=O)N(C)C	141-66-2	dicrotophos	x			
 COP(=S)(OC)Oc1ccc(cc1)[N+]([O-])=O	298-00-0	methyl parathion	2			
 CCOP(=S)(OCC)SCSCC	298-02-2	phorate	2			

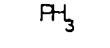
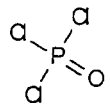
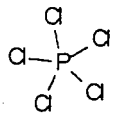
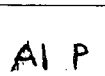
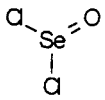
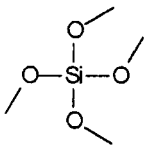
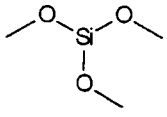
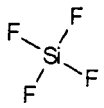
 CCOP(=S)(OCC)SCCSCC	298-04-4	disulfoton	2			
 O(P(OCC)(Oc(nc(nc1C)C(C)C)c1)=S)CC	333-41-5	diazinon	x			
 CCOP(=S)(OCC)SCSP(=S)(OCC)OCC	563-12-2	ethion	x			
 COP(=S)(OC)SCN2C(=O)c1ccccc1C2=O	732-11-6	phosmet	x			
 O=P(OP(OCC)(OCC)=O)(OCC)OP(OP(OCC)(	757-58-4	hexaethyl tetraphosphate	x			

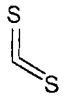
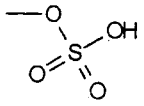
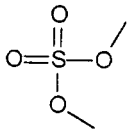
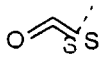
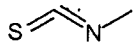
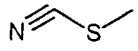
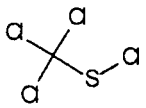
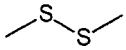
 O=P(OC)(OC)O	813-78-5	dimethylphosphate	x			
 S=P(OC)(OC)SCN1C(=O)SC(OC)=N1	950-37-8	methidathion	2			
 O=P(OC)(OC)SCCSCC	919-86-8	demeton S-methyl	x			
 CCOP(=S)(OCC)OP(=S)(OCC)OCC	3689-24-5	tetraethyl dithiopyrophosphate (Sulfoteb)	2			
 b	6923-22-4	monocrotophos	2			
 O=P(OC)(OC)OC=C(C)C(=O)OC	7786-34-7	mevinphos	2			

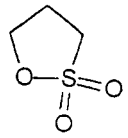
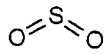
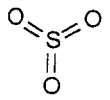
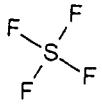
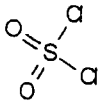
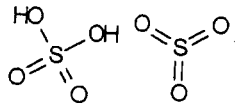
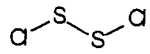
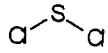
 CCOP(=S)(OCC)SCSC(C)(C)C	13071-79-9	terbuphos	2			
 CCCSP(=O)(OCC)SCCC	13194-48-4	ethoprophos	x			
Phosphonate Esters						
 CC(OP(C)(F)=O)C(C)(C)C	96-64-0	Soman (GD)	1	0.017	0.0022	0.000018
 CC(C)OP(C)(F)=O	107-44-8	Sarin (GB)	1	0.022	0.0060	0.00048
	329-99-7	cyclohexylmethyl fluoridate (GF)	1	0.18	0.0024	0.00022
 S=P(OCC)(Sc1ccccc1)CC	944-22-9	fonophos	2			
 S=P(CC)(Cl)Cl	993-43-1	ethylphosphonodithioic dichloride	x			

 O=P(O)(C)OC(C)C	1832-54-8	isopropyl methyl phosphonic acid	x			
 O=P(C)(OCC)SCCN(C(C)C)C(C)C	50782-69-9	VX	1	0.0030	0.000090	0.000007
 CCOP(=O)(C#N)N(C)C	77-81-6	Tabun (GA)	1	0.039	0.0053	0.00042
 CCOP(=O)(NC(C)C)Oc1ccc(SC)c(C)c1	22224-92-6	fenamiphos	x			
 COP(N)(=O)SC	10265-92-6	methamidophos	2			
Phosphorus Compounds (not otherwise classified)						
 P(C)(Cl)Cl	676-83-5	methyl phosphonous dichloride	x			
 CP(Cl)(Cl)=O	676-97-1	methyl phosphonic dichloride	x			

 CP(O)(O)=O (PHOSPHONATE)	993-13-5	methyl phosphonic acid	2			
Zn3P2	1314-84-7	zinc phosphide	x			
Cl2P-CH2CH3	1498-40-4	ethylphosphonous dichloride	x			
 O=P(OCC)(Cl)Cl	1498-51-7	ethylphosphonodichloridate	x			
 O(P(OC)(=S)Cl)C	2524-03-0	dimethylphosphorochloridothioate	x			
 P(F)(F)(F)(F)F	7647-19-0	phosphorus pentafluoride	2			
 ClP(Cl)Cl	7719-12-2	phosphorus trichloride	1	0.88	NA	NA
 P	7723-14-0	phosphorus	x			
 BrP(Br)(Br)=O	7789-59-5	phosphorus oxybromide	x			
 BrP(Br)(Br)(Br)Br	7789-69-7	phosphorus pentabromide	x			

 P	7803-51-2	phosphine	1	3.6	2.0	NA
 ClP(Cl)(Cl)=O	10025-87-3	phosphorus oxychloride	1	0.85	NA	NA
 ClP(Cl)(Cl)(Cl)Cl	10026-13-8	phosphorus pentachloride	x			
 P#[Al]	20859-73-8	aluminum phosphide	2			
Selenium Compounds (not otherwise classified)						
 F[Se](F)(F)(F)(F)F	7783-79-1	selenium hexafluoride	2			
 [Se](Cl)(Cl)=O	7791-23-3	selenium oxychloride	x			
Silicon Compounds (not otherwise classified)						
 CO[Si](OC)(OC)OC	681-84-5	tetramethoxy silane	x			
 CO[Si](OC)OC	2487-90-3	trimethoxysilane	x			
 [Si]	7803-62-5	silane	2			
 [Si](F)(F)(F)F	7783-61-1	silicon tetrafluoride	x			

Sulfur Compounds (not otherwise classified)						
 C(=S)=S	75-15-0	carbon disulfide	2			
 S(C)C	75-18-3	dimethyl sulfide	x			
 O=S(=O)(OC)O	75-93-4	methyl sulfate	x			
 O=S(=O)(OC)OC	77-78-1	dimethyl sulfate	2			
OCCSCCO	111-48-8	thiodiglycol	x			
 O=C=S	463-58-1	carbonyl sulfide	2			
$(ClCH_2CH_2)_2S$ ClCCSCCCl	505-60-2	sulfur mustard	1	0.32	0.015	0.010
 N(=C=S)C	556-61-6	methyl isothiocyanate	x			
 N#CSC	556-64-9	methyl thiocyanate	2			
 S(C(Cl)(Cl)Cl)Cl	594-42-3	perchloromethyl mercaptan	1			
 S(SC)C	624-92-0	dimethyl sulfide	2			

 O=S(=O)(OCC1)C1	1120-71-4	1,3-propane sultone	x			
 O=S=O	7446-09-5	sulfur dioxide	1			
 S(=O)(=O)=O	7446-11-9	sulfur trioxide	1			
 S(F)(F)(F)F	7783-60-0	sulfur tetrafluoride	1			
 O=S(=O)(Cl)Cl	7791-25-5	sulfuryl chloride	2			
 O=S(=O)(O)O.O=S(=O)(=O)	8014-95-7	oleum	1			
 ClSSCl	10025-67-9	disulfur dichloride	x			
 ClSCl	10545-99-0	sulfur dichloride	2			
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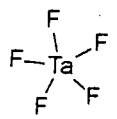
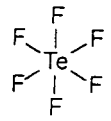
 [Ta](F)(F)(F)(F)F	7783-71-3	tantalum V fluoride	x			
Tellurium Compounds (not otherwise classified)						

 [Te](F)(F)(F)(F)(F)F	7783-80-4	tellurium hexafluoride	2			
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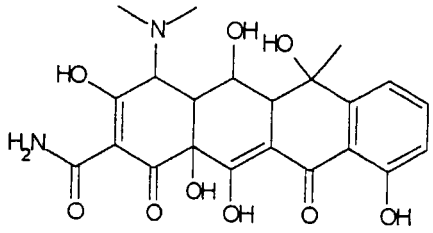 O=C(N)C(=C(O)C(N(C)C)C(C1(O)C(O)=C(C2C	79-57-2	terramycin	2			
Thallium Compounds (not otherwise classified)						
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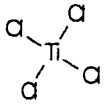
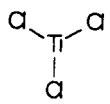
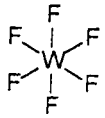
Titanium Compounds (not otherwise classified)						
 Cl[Ti](Cl)(Cl)Cl	7550-45-0	titanium tetrachloride	2			
 [Ti](Cl)(Cl)Cl	7705-07-9	titanium chloride	x			
	7783-63-3	tatanium III fluoride	x			
Tungsten Compounds (not otherwise classified)						
 [W](F)(F)(F)(F)(F)F	7783-82-6	tungsten hexafluoride	x			
Vanadium Compounds (not otherwise classified)						
V [V]	7440-62-2	vanadium & compounds	x			
Zinc Compounds (not otherwise classified)						
Zn [Zn]	7440-66-6	zinc & compounds	x			

Appendix A

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

December 3-5, 2001

Final Meeting 23 Highlights

Holiday Inn Riverwalk
217 N. St Mary's Street
San Antonia, Texas 78205

INTRODUCTION

George Rusch, NAC/AEGL Chair, opened the meeting with brief remarks and along with AEGL Program Director, Roger Garrett, welcomed the committee members and guests. Thanks were expressed to John Hinz and Eric Stephens, Director, Air Force Institute for Environmental Safety and Occupational Health Risk Analysis (AFIERA) for hosting the meeting and Lacey Young for providing the excellent support prior to and during the NAC/AEGL-23 meeting.

John Hinz and Lacey Young briefly described the meeting logistics and evening activities for the NAC/AEGL-23 meeting. Eric Stephens, Director of AFIERA, welcomed the NAC/AEGL Committee members and guests and presented an overview of AFIERA (Attachment 1). The AFIERA mission statement includes the following points: (1) Enhance mission effectiveness, protect health, improve readiness and reduce costs (Air Force Health Protection) and (2) Assess and manage risks (Radiological, Biological, Chemical & Operational). He briefly highlighted the ongoing research project on JP-8 Jet Fuel. The research findings from the AFIERA research team will be incorporated into the JP-8 TSD and be reviewed at the meeting.

The highlights of the NAC/AEGL-22 meeting were reviewed and briefly discussed. John Morawetz submitted a brief note on carbon tetrachloride (Attachment 2) for inclusion in the revised highlights of NAC/AEGL-22. Afterwards, a motion was made by Bob Benson and seconded by Marinelle Payton to accept the draft meeting highlights with two minor changes. The motion was passed unanimously (Appendix B). The revised highlights of NAC/AEGL-22 are attached (Appendix A).

The highlights of the NAC/AEGL-23 meeting are presented below along with the meeting agenda (Attachment 3) and the attendee list (Attachment 4). Ballots were taken during the meeting and are incorporated into the appropriate chemical specific section as Appendices.

Visit by NAS/COT/AEGL Subcommittee

Dan Krewski, Chair, and John Doull from the COT/NAS/AEGL Subcommittee attended the NAC/AEGL-23 meeting. Dan Krewski praised the productive working relationships with EPA, NAC/AEGL, and ORNL and commented that the technical quality of the TSDs is excellent in general. NAS plans to have two more volumes of AEGL documents published in 2002. Later, Dan and John made the following specific remarks associated with the AEGLs development:

(1) Scientific validity of procedures: need transparency in the area of quantitative, qualitative, and completeness of data review. How do you get to the decision? Even though you never have enough data to do a perfect job you must look at the weight of the evidence and use valid extrapolation procedures. (Can't spend 8 hours on one topic, though.)

(2) AEGL-1 Values: we really need numbers for all chemicals; otherwise the emergency planners and others in the field will use AEGL-2 values. Liked the *Odor Annoyance* paper by Doorn, Ruijen and van Harreveld because it separates odor data from pure irritation data; however, they cautioned that it "bends" the definition for AEGL-1.

(3) AEGL values may be too low. If values don't agree with or are way out of line with previously derived numbers published by NAS for similar chemicals and scenarios, the NAC/AEGL creates a big problem for the NAS. The AEGL PROCESS NEEDS CREDIBILITY. One must look at the "real world" vs worst-case. Don't be so overly conservative that no one will believe the numbers.

(4) PK/PD Modeling: Jim Bruckner (AEGL/COT Subcommittee member) wants to see pharmacokinetic/pharmacodynamic modeling used more often. These data should help in the evaluation of actual dose to the target tissue(s).

(5) Benchmark Dose (BD) Calculations: BD is replacing NOELs as the standard analysis technique. Some questions remain to be addressed - "How do you go from BD to RfD (NOEL)?" Still, the committee would like to see more of this approach.

(6) Categorical Regression Analysis: discussion at the COT/NAS/AEGL August 2001 meeting led by Judy Strickland was impressive. It's recognized that we don't always have enough data to do this, but the committee would like to see more of this approach in the future.

John Doull brought up the possibility of visiting these and other major issues at a workshop that would be sponsored by The Academy at the request of the NAC/AEGL committee. Dan Krewski added that there is much interest in the work of this committee from overseas, Canada, EU. ...etc.
He also commented on a "data-needs" section for AEGLs.

TOPICAL ITEMS FOR DISCUSSION

GUIDANCE FOR THE USE OF ODOR IN AEGL-1 DEVELOPMENT

Due to a car accident, the originally scheduled presentation by Ton van Harreveld on Monday was postponed to Tuesday. Ton van Harreveld is the Managing Director of Ordournet Company. The revised paper of "*Guidance for the Application of Odor in the Derivation of AEGL-1*" by Reind van Doorn, Marc Ruijten, and Ton van Harreveld was distributed before the meeting to the NAC/AEGL, COT/NAS/AEGL and guests so that they could participate in the discussion (Attachment 5). Ton focused his presentation on why application of odor should be considered as an AEGL-1 endpoint and how the proposed methodology fit into the AEGL Standing Operating Procedures (AEGL SOPs). A few AEGL-1 values based on the proposed methodology were presented for comparison with the current AEGL values. Reasons for development of the AEGL-1 based on odor are briefly summarized below:

Any individual can perceive unusual odor as a threat, especially in the context of chemical incidents. Awareness of exposure might cause anxiety and manifest itself by somatic symptoms of arousal, such as dyspnea, sweating and hyperventilation. Although these symptoms are normal physiologic responses to frightening occurrences, they could lead to avoidance behavior (e.g., closing windows, seeking contact with environmental agencies and/or health authorities). Therefore, health professionals would be greatly served by the availability of practically applicable information about the odor annoyance potential of compounds, as much as they need information about irritative and toxic properties of these compounds.

Notification (i.e., informing the public about properties of the unusual odor) can modulate appraisal of odor and the resulting behavior. This guidance provides criteria for the derivation of a 'Level of Odor Annoyance' (LOA) for emergency exposure. If this LOA is lower than the concentration which causes other responses, such as irritation, it is considered the best estimate for an AEGL-1. By default, the LOA can be obtained by multiplying the odor threshold, C_0 by 12 (LOA= 12* C_0).

MONITORING DEVICES LINKED TO AEGL VALUES

Lisa K. Stallsworth, Straughan Technical, presented the Gastec Gas Detection System (Attachment 6). The advantages of detector tubes over electronic devices are: they are always ready and easy to use; they require no power source and no calibration. The detector tubes are thin glass tubes filled with an inert support on which is impregnated a chemical. The chemical will react colorimetrically with the contaminant of interest. The length of stain of color change is proportional to the contaminant concentration.

Interchangeability refers to using a pump from one manufacturer and a tube from another manufacturer. It is prohibited or strongly discouraged by many national and international standardization organizations as pointed out by Lisa.

Gastec was the first company to attain all Safety Equipment Institute certifications (tubes and pumps and manufacturing facilities). Gastec has developed several types of tubes and accessaries for various applications.

Lisa stressed that Gastec's tubes are useful for emergency response because they are easy to use, Gastec has more tubes (over 250) and applications (over 500) which have been developed to detect all ranges for many ERPG and AEGL chemicals, and Gastec will custom design tubes for more of these chemicals if a market can be proven (chemicals must be in the gas/vapor phase; chemicals with low vapor pressures are not well detected on colorimetric tubes).

REVIEW OF PRIORITY CHEMICALS FOR AEGL VALUES

METHYL ETHYL KETONE
CAS Reg. No. 78-93-3

Chemical Manager: Mark McClanahan, CDC
Staff Scientist: Sylvia Talmage, ORNL

The chemical review was presented by Sylvia Talmage (Attachment 7). Methyl ethyl ketone (MEK) is a widely used volatile solvent with a rich data base of clinical and laboratory animal studies. Two studies with human volunteers exposed to 100, 200, or 350 ppm were evaluated for the AEGL-1; the exposure times were 5 minutes (Nelson et al. 1943) and 4 hours (Dick et al. 1992). Although a concentration of 200 ppm was judged unobjectionable in both studies, slight nose and throat irritation were noted at 100 ppm in the Nelson et al. (1943) study. Therefore, 100 ppm was selected as the threshold for sensory irritation. The safety of this value is supported by numerous clinical studies in which volunteers were routinely exposed to 200-400 ppm for up to 4 hours. Because this is a threshold value, slight irritation should not increase in intensity with time, and population response to slight irritation should not vary greatly, an intraspecies uncertainty factor of 1 was applied. Because accommodation to slight irritation occurs, the 100 ppm concentration was used across all AEGL-1 exposure durations. Furthermore, MEK is rapidly metabolized and will not accumulate in the blood or in the body which further supports using the same value for all the time intervals. A motion was made by David Belluck and seconded by Steve Barbee to adopt the 100 ppm concentration for all AEGL-1 time points. The motion passed [YES:16; No:2; Abstain:0] (Appendix C).

The AEGL-2 was based on the chronic study of Cavender et al. (1983) in which rats were exposed to 5000 ppm for 5 days/week for 90 days. No lesions were reported in this study, but the concentration is close to the threshold for neurotoxicity as evidenced by somnolence in another repeated exposure study in which rats were exposed to 6000 ppm for several weeks (Altenkirch et al. 1978). Because this was a no-effect repeated-exposure study, no interspecies uncertainty factor was applied. Because the threshold for narcosis differs by no more than 2- to 3-fold among the general population, an intraspecies uncertainty factor of 3 was applied to protect sensitive

individuals. Because the threshold for narcosis is concentration dependent, the resulting 1700 ppm concentration was applied across all AEGL-2 exposure durations. A motion was made by Bob Snyder and seconded by John Hinz to adopt the 1700 ppm concentration for all time points. The motion passed [YES:13; No:2; Abstain:3] (Appendix C)

The AEGL-3 values were based on two different studies. The 10- and 30-minute values were based on a study with mice in which a 30-minute exposure to 31,426 ppm reduced the respiratory rate by 50% but resulted in no deaths (Hansen et al. 1992). Because a 30-minute exposure of rats to 3 times this concentration (92,239 ppm) also resulted in no deaths (Klimisch 1988), the 31,426 ppm value was adjusted by an interspecies uncertainty factor of 1. Because the threshold for narcosis differs by no more than 2- to 3-fold among the general population, an intraspecies uncertainty factor of 3 was applied to protect sensitive individuals. The resulting value of 10,000 ppm was used for the 10-minute and 30-minute AEGL-3 exposure durations. The longer-term values were based on an MLE_{01} of 7500 ppm calculated by Fowles et al. (1999) from a 4-hour study with rats exposed to several concentrations for 4 hours (La Belle and Brieger 1955). In this study the 4-hour LC_{50} was 11,700 ppm and the highest concentration resulting in no deaths was 7850 ppm for 4 hours. The 7500 ppm concentration was divided by an intraspecies uncertainty factor of 3. The resulting value of 2500 ppm was used for both the 4-hour and 8-hour AEGL-3 values because MEK would reach equilibrium in the body prior to this time period. The 4-hour 2500 ppm value was time scaled to the 1 hour time using the default n value of 3 for scaling to shorter time intervals. It was moved by John Hinz and seconded by Loren Koller that we adopt AEGL-3 values for methyl ethyl ketone for 10 minutes to 8 hours of 10,000 ppm, 10,000 ppm, 4000 ppm, 2500 ppm, and 2500 ppm. In response to John Morawetz's concern that 10,000 ppm is close to the lower explosive limit of 17,000 ppm, it was stated by George Rusch, NAC/AEGL Chair, that a note to that affect will be clearly indicated in the final discussion and rationale. The motion passed [YES:15; NO: 2; Abstain:0] (Appendix C)

SUMMARY OF AEGL VALUES FOR METHYL ETHYL KETONE [ppm (mg/m^3)]

Classification	10-minute	30-minute	1-hour	4-hour	8-hour	Endpoint
AEGL–1	100 (293)	100 (293)	100 (293)	100 (293)	100 (293)	Threshold for irritation in humans
AEGL–2	1700 (4980)	1700 (4980)	1700 (4980)	1700 (4890)	1700 (4980)	Threshold for narcosis in repeated exposure study - rat
AEGL–3	10,000[a,b] (29,300)	10,000[a,b] (29,300)	4,000[c] (11,720)	2500[c] (7325)	2500[c] (7325)	[a]No deaths (30 minutes) - rats; MLE_{01} (4 hours) - mice

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

JET PROPELLANT FUEL-8 (JP-8)

A series of presentations was made to inform the NAC/AEGL Committee on the status of action items from the earlier meeting when the Jet Fuel-8 TSD was first reviewed at the NAC/AEGL-13, March 1999. John Hinz made brief introductory remarks on the "Issues & Answers" to the JP-8 AEGLs development (Attachment 8). A sequence of presentations followed: (1) Epidemiology Study by Roger Gibson, (2) Health Effect Studies by Walter Kozumbo, (3) Potential Respiratory Irritation Studies by John Hinz and finally (4) TSD presentation by Sylvia Talmage.

Epidemiology Study: Lt. Col. Roger Gibson, Air Force

Lt Col. Gibson briefed the NAC/AEGL on the current status of epidemiology studies of military personnel exposed to JP-8. The investigation was undertaken in response to complaints regarding the increased irritancy of JP-8 compared to the previously used JP-4 aviation fuel (Attachment 9).

During 2000, the USAF led an investigation into the impact of acute JP-8 occupational exposure among active duty service members. The study was conducted at multiple USAF installations in the continental United States. Using an observational short-term cohort epidemiological model, biologic specimens and performance measures were collected from subjects prior to and after a four-hour work period (Attachment 9).

Results showed that JP-8 constituents were detected at significantly higher levels in the urine, breath and skin of those exposed to JP-8 compared to those unexposed. JP-8 constituents were also found at higher, but not statistically significant, levels in the blood of exposed workers. Exposed workers scored significantly more poorly on neurocognitive test batteries, had increased balance problems, and showed significantly reduced response to eye-blink conditioning (hippocampal function) testing. Exposed workers reported significantly more health symptoms and believed their work was harming their health. However, no differences were noted in health encounters (medical visits) among exposed and unexposed workers.

The results of this acute exposure study indicate workers acquire a JP-8 body burden during routine occupational operations and these exposures mildly impact neurological function. More study is needed to establish the long-term impact of exposure (Attachment 9).

Health Effect Studies: Walter Kozumbo, Air Force Research Laboratory

Walt Kozumbo described ongoing studies and results of recent studies regarding the effects of JP-8 aerosols on the lungs and immune system of the mouse (Attachment 10).
A number of effects were observed in animals inhaling JP-8 aerosol. They consisted of changes in pulmonary function and reductions in immune organ weights, in immune T cell numbers and in immune T cell functions. The lowest concentrations of JP-8 aerosol that have produced effects in the lungs and immune systems of mice were at 50 mg/m^3 for lung edema and 100 mg/m^3 for effects on thymus immune cells. JP-8 and JP-8+100 (a newer JP-8-derived fuel) were found to be equally toxic and their effects were dose-dependent.

JP-8 applied to skin of mice was more irritating than its predecessor, JP-4 jet fuel, and induced dermal elevations in TNFalpha, IL-1 and iNOS. A topical application to mice of 50 μL per day for 5 days or of 300 μL at one time resulted in systemic T cell suppression that was preceded by elevated blood levels of interleukin-10 and prostaglandins PGE2, biologically active cellular mediators with immunosuppressive activities. In mice, the administration of antibodies against IL-10 or of a commercially available cyclooxygenase II inhibitor (Celebrex) prevented the immunosuppressive activities induced by dermal exposure to JP-8. Thus far, preliminary studies have also shown that pre-exposure to JP-8 aerosol enhances both the growth of tumor cells and the severity of influenza infectivity in mice (1, 2; unpublished data). Finally, molecular studies on cultured cells have indicated that JP-8 exposure at a 10,000-fold dilution is highly cytotoxic, with the induction of apoptotic responses in lung and immune cells and necrotic responses in epidermal cells.

Initial studies at other laboratories are expected to produce results in the near future. These studies include:

1. Mouse lung proteomic responses above and below the JP-8 toxicity threshold
2. Genotoxic effects on blood and bone marrow cells from dermal and aerosol exposures to JP-8
3. Quantitative structure activity relationships (QSAR), cluster analysis and cytokine release from human keratinocytes in assessing the relative toxicity of JP-8 mixture components
4. Mathematical modeling of JP-8 disposition in the lung
5. Whole body toxicokinetic modeling of JP-8 mixture components

This research aims to disclose potentially toxic interactions of JP-8 with biological tissues, to understand the molecular mechanisms mediating and inhibiting these toxicities, and, ultimately, to apply novel computational and molecular approaches to the task of identifying specific components in JP-8 that are toxic. Accomplishing these objectives will enable improvement of health safety standards; development of safer fuels, of protective strategies and of rapid monitoring devices; reductions in health effects and in concomitant medical and legal costs; and, finally, enhancement of human performance during sustained military actions.

Sensory Irritation Study in Mice -- Comparative and Quantitative Characterization of JP-8's Potential for Respiratory Tract Sensory Irritation: John Hinz, AFIERA

John Hinz discussed the recently completed respiratory irritation study (Attachment 11) and distributed the ExxonMobil final report by Dr. Fred Whitman (Attachment 12). This study addressed the comparative irritancy of JP-4, JP-8 and JP-8+100 and was performed in response to the request at the NAC/AEGL meeting held in New Orleans in March, 1999. To address this request, AFIERA, in concert with Army and Navy colleagues, designed a study based on ASTM's "Standard Method E 981-84" to characterize and compare the relative potency of three jet fuels to cause respiratory tract sensory irritation.
These fuels (JP-4, JP-8 and JP-8+100) were administered for 30 minute periods by means of a head-only exposure system to groups of four male Swiss-Webster mice. Test atmospheres laden with these fuels were presented as vapor-only (JP-4) or as a vapor/aerosol mixtures (JP-8, JP-8+100). Analytical sampling data revealed differences in the distribution and relative proportions

of the hydrocarbon species contained in the vapor and aerosol phases. Generally, compounds with carbon numbers in the range of C11-C12 represented the principal constituents in the aerosol phase.

Each fuel was tested over a range of air concentrations (685 - 11,430 mg/m^3 for JP-4, 681 - 3,565 mg/m^3 for JP-8, and 777 - 2,356 mg/m^3 for JP-8+100) that resulted in minimal to severe decreases in respiratory rate. All three fuels evoked breathing patterns that were characteristic of upper airway sensory irritation at all exposure levels. Within the context of this study, there was no apparent evidence of pulmonary (deep lung) irritation or narcosis at any exposure level. The concentration that reduced the respiratory rate by 50% (RD_{50}) was calculated for each fuel: JP-4 = 4842 mg/m^3; JP-8 = 2876 mg/m^3; JP-8+100 = 1629 mg/m^3. The relative irritancy of these fuels may be ranked as follows: JP-8+100 > JP-8 > JP-4. Alarie observed that 10% of the RD_{50} estimates the threshold of effect for respiratory irritation. This value for JP-8 is approximately 290 mg/m^3, a starting point for determining an AEGL-1 for this fuel. Values for AEGL-2 can be obtained from JP-8's RD_{50} in concert with other exposure data on this fuel. There was no mortality data in the available scientific literature upon which to predicate values for AEGL-3.

This study constitutes Phase I of a two-phase program to compare and characterize the potential of selected jet fuels to cause respiratory tract sensory irritation. Phase II will test the following fuels: JP-5, -7, -TS, -10, and a light marine diesel.

Chemical Manager: John Hinz, AFIERA
Staff Scientist: Sylvia Talmage, ORNL

A review of the new data on JP-8, developed since 1999, was presented by Sylvia Talmage (Attachment 13). Although JP-8 is a complex mixture of aliphatic and aromatic hydrocarbons, for the purposes of AEGL development, the vapor and vapor/aerosol of the whole fuel was treated as a single entity. Studies addressing sensory irritation, neurotoxicity, reproductive and developmental toxicity, immunotoxicity, and carcinogenicity and using primarily rodent species were available for consideration. Exposure durations ranged from acute to chronic. The AEGL-1 was based on the sensory irritation study of Whitman (2001). In this study, the 30-minute RD_{50} of male Swiss Webster mice was 2876 mg/m^3. According to Alarie (1981), 0.1 x the mouse RD_{50} elicits "some" sensory irritation in humans but can be tolerated for hours. Therefore, the 290 mg/m^3 value was applied to all AEGL-1 exposure durations. The value is supported by the lack of adverse health effects in rodents exposed to 1000 mg/m^3 in several repeated exposure and subchronic studies (Briggs 2001, Mattie et al. 1991, Rossi et al. 2001). Adjusting the 1000 mg/m^3 value by an interspecies uncertainty factor of 1 (no species differences were noted and the exposures were repeated) and by an intraspecies uncertainty factor of 3 (no susceptible populations were identified) results in a similar value, 330 mg/m^3. The repeated nature of the support studies corroborates the use of a single value for all AEGL-1 exposure durations. A motion was made to accept the 290 mg/m^3 for all exposure durations by Bob Benson and seconded by Glen Leach. The motion passed [YES: 15; NO: 5; Abstain: 0] (Appendix D).

The AEGL-2 was based on several acute studies with rodents in which sensory irritation was evident and is supported by the repeated, no-effect exposure studies. Exposure to 3430 mg/m^3 of

vapor for 4 hours (Wolfe et al. 1996), 3565 mg/m^3 vapor/aerosol for 30 minutes (Whitman et al. 2001), 4440 mg/m^3 of aerosol for 4 hours, and 5000 mg/m^3 of JP-5 aerosol for 1 hour (MacEwen and Vernot 1985) resulted in sensory irritation. The 5000 mg/m^3 concentration was the threshold for central nervous system depression in both rats and mice. The lowest concentration, 3430 mg/m^3 was adjusted by an interspecies uncertainty factor of 1 (no species differences were evident) and by an intraspecies uncertainty factor of 3 (no susceptible populations were identified and the threshold for central nervous system depression differs by no more than 2- to 3-fold in the general population. The resulting value is 1100 mg/m^3. Because no adverse health effects were identified in rodent studies with repeated exposures to 1000 mg/m^3 (6 hrs/day, 5 days/weeks, for 6 weeks), the 1100 mg/m^3 value can be used for all AEGL-2 exposure durations. Based on this discussion, a motion was introduced by Loren Koller and seconded by Ernie Falke to accept 1100 mg/m^3 as AEGL-2 for all exposure durations. The motion was approved [YES: 17; NO: 1; Abstain: 0] (Appendix D).

The above AEGL-2 studies utilized the highest JP-8 vapor/aerosol exposures that could be generated. No studies resulted in lethality. Therefore, an AEGL-3 was not determined.
A motion was made by John Morawetz and seconded by George Alexeeff not to develop AEGL-3 values due to insufficient data. The motion passed unanimously (Appendix D).

A question was raised concerning the benzene content of JP-8 and carcinogenicity. The benzene content of neat JP-8, one of the more volatile components of JP-8, is <0.005% by volume. A discussion comparing the potential exposure to benzene at the 8-hour AEGL-2 of 1100 mg/m^3 to established standards and guidelines for benzene will be incorporated into Section 8.2 of the TSD. Also it was noted that the derived values should be applied to the vapor or vapor/aerosol of JP-8 and not to a pure aerosol.

SUMMARY OF AEGL VALUES FOR JET PROPELLANT FUEL 8 (mg/m^3)[a]

Classification	10-minute	30-minute	1-hour	4-hour	8-hour	Endpoint
AEGL–1	290	290	290	290	290	sensory irritation - mouse
AEGL–2	1100	1100	1100	1100	1100	severe irritation - rat and mouse
AEGL–3	Not determined	Not determined	Not determined	Not determined	Not determined	[b]No data

[a] The values apply to JP-8 vapor or vapor/aerosol and not to the pure aerosol; the values do not apply to JP-8+100.
[b] Lethal concentrations were not attained in the available studies.

REVIEW OF CHEMICALS WITH ISSUES FROM PREVIOUS MEETINGS

XYLENES: PBPK Modeling

The Xylene AEGL's 2 and 3 values (1,4, and 8 hours) were determined from a study that used rats exposed to 1300 ppm of mixed xylenes for 4 hours (Carpenter et al 1975). Thus, extrapolation to 10 and 30 minute values would most likely be inaccurate. Therefore, a toxicokinetic approach (PBPK model) was considered in calculating the AEGL 2 and 3 values for 10 and 30 minutes. Dr. Ursula Gundert-Remy presented 10 and 30 minute data for AEGL's 2 and 3 using the PBPK model. Several assumptions were made using this model including that data from m-xylene represents the mixture of all xylenes and the kinetics are linear in the concentration/dose range at 10 and 30 minutes. Assumptions were also made concerning the concentration, toxicological endpoint, and effects of the substance. Kinetics were based on data from human volunteers.

The data from three studies were used. The calculations were performed using the NONMEM program (Attachment 14). It was assumed that the inhalation volume and frequency were constant. Calculations were derived for the mean concentrations and at 2 and 3 standard deviations (SD) for the 10 and 30 minute values for both AEGL's 2 and 3. A motion was made by Bob Benson and seconded by Ernie Falke to accept the AEGL-2 & 3 values with 2 SD. Thus, the values proposed for AEGL-2 were: 10 minutes - 980 ppm and 30 minutes - 480 ppm. The values proposed for AEGL-3 were: 10 minutes - 2100 ppm and 30 minutes - 1000 ppm. The motion was approved for AEGL-2 values [YES:16; NO: 4; Abstain: 0] and for AEGL-3 [YES:20; NO: 0; Abstain:0] (Appendix E).

Dr. Ursula Gundert-Remy will provide justifications to be incorporated into the TSD.

NAC/AEGL RESPONSES TO *FEDERAL REGISTER* COMMENTS TO THE PROPOSED AEGL VALUES

METHANOL
CAS Reg. No. 67-56-1

Chemical Manager: Ernie Falke, U. S. EPA
Staff Scientist: Peter Griem, FoBiG

Comments from the *Federal Register Notice* (FR) of May 2, 2001, on the proposed AEGL-2 values for methanol were received and discussed. This is a continuation of the discussion of methanol's AEGL-1 values from the last meeting of NAC/AEGL-22 which was held over due to an internal EPA issue. After Roger Garrett made brief remarks on the resolution of the issue, NAC/AEGL continued the discussion on AEGL-2 levels. Bob Benson noted that all other public comments regarding methanol were addressed at the September meeting. Mark McClanahan proceeded to make a proposal to approve the AEGL values as published in the Federal Register Notice of May 2, 2001 and elevate the methanol from Proposed to Interim status. The motion was seconded by Bob Benson. The motion was approved [YES:14; NO:3; Abstain:1] (Appendix F).

PERCHLOROMETHYL MERCAPTAN
CAS Reg. No. 594-42-3

Chemical Manager: Zarena Post, Texas
Staff Scientist: Claudia Troxel, ORNL

The status of perchloromethyl mercaptan (PCMM) was reviewed by Chemical Manager Zarena Post. She summarized that values had been voted on and accepted by the NAC/AEGL-19 in December of 2000, and the proposed AEGL values were published in the FR of May 2001. A letter of comment was received from Tomen Agro in response to the FR request for comments, and comments were discussed at the NAC/AEGL-21, June 2001 meeting. One of the comments Tomen Agro made was that data were inadequate to set AEGL values for PCMM. A letter was sent to Tomen Agro to give them the opportunity to supply any additional existing data they might have or propose to collect more. Tomen Agro replied that they had no additional data, and proposed an alternate calculation method (Attachment 15). The proposed alternate calculation was not in accordance with the NAC/AEGL committee's SOP. After the summary was presented, a motion was made by Zarena Post and seconded by John Hinz to elevate the AEGLs of PCMM from Proposed to Interim status. The motion was approved unanimously(Appendix G).

Review of AEGL-1 Values:

ETHYLENIMINE
CAS Reg. No. 151-56-4
&
PROPYLENIMINE
CAS Reg. No. 75-55-8

Chemical Manager: Mark McClanahan, CDC
Staff Scientist: Kowetha Davidson, ORNL

Mark McClanahan presented the proposed AEGL-1 values for ethylenimine and propylenimine (Attachment 16 and 17). For ethylenimine the proposed derivation entailed the using a factor of 2 to divide the AEGL-2 values to obtain the AEGL-1 values. This factor was equal to the average factor for the ratio between AEGL-3 and AEGL-2 for the compound. Because the propylenimine AEGL -1 and -2 values are directly derived from those of ethylenimine, any decision made about ethylenimine directly influences these propylenimine AEGL values as well. The committee members expressed discomfort with rationale for deriving the factor and suggested looking at the factor between AEGL-2 and AEGL-1 for other similar nitrogen containing compounds. The deliberations were suspended until these data were available. With these data, deliberations resumed, the ratios ranging from 21 to 1.5 from the shortest to longest exposure times. The

committee expressed no interest in deriving a factor from these data. As an alternative factor Mark suggested using 3, a value which has been used to derive AEGL-2 values from AEGL-3 values for some chemicals. Mark also presented the level of annoyance (LOA) of 8 ppm value. This value was provided by Reind van Doorn in the following material:

AIHA (1989) presents two sources that report odor thresholds for ethylenimine. Carpenter (1948) reports a threshold of 2.0 ppm. This study was rejected by AIHA because of passive exposure. Berzins (1967) reports a value of 0.68-1.9 ppm. Methodology was critiqued as insufficient. The best choice in this case would be the lowest value, because the bias introduced by older testing methodology is always towards higher odor thresholds. There is no kw determined according to VDI 3882 available. Therefore a default value of 2.33 is recommended and the LOA defaults to 12 standardized odor units. Based on this approach a LOA-derived AEGL-1 for ethylenimine would be approximately 8 ppm (15 mg/m3). Depending on the definitive AEGL-2 and AEGL-3 values, odor may not a significant criterion for derivation of the AEGL-1 for ethylenimine.

For propyleneimine, no odor thresholds were found in Devos (1990) or in AIHA

Based on this information, Mark's recommendation to the committee was to retain the AEGL-1 values for both chemicals unchanged from those currently approved by the NAC/AEGL Committee. The NAC/AEGL Chair, George Rusch, asked for a vote by the simple show of hands; the recommendation was unanimously supported to retain the existing designation of NR (not recommended) for AEGL-1 values for both compounds (Appendix H and I).

Review of 10-minutes AEGL Values

HYDRAZINE
CAS Reg. No. 302-01-2

Chemical Manager: Richard Thomas, ICEH
Staff Scientist: Bob Young, ORNL

George Rusch briefly presented the chemical toxicity information on hydrazine (Attachment 18). The discussion focused on the development of 10-minutes AEGL values. The AEGL-1 was based on monkeys exposed continuously by the inhalation route to 0.4 ppm (days 1-10 of 90-days exposure). They exhibited flushing of the face and eye irritation (House 1964). Because of the extremely reactive and irritative nature of hydrazine, the severity of the toxic effect depends on the chemical concentration rather than on exposure time. Therefore, the same AEGL-1 value, 0.1 ppm, was set for all time periods. The AEGL-2 was based on rats exposed for 1 hour to 750 ppm of hydrazine. The rats exhibited reversible nasal lesions following removal from exposure (Latendress et al 1995). The AEGL-2 value was extrapolated from 1 hour to the other exposure durations using n=3 and a UF of 60 (interspecies 10; intraspecies 3; and a modifying factor of 2 due to sparse data). The 10-minute AEGL-2 value is 23 ppm. The 10-minute AEGL-3 was extrapolated from a rat lethality study (HRC 1993). The lethality threshold was estimated, by a threefold reduction of the 1-hr $LC_{50,}$ as 1064 ppm; this value was adjusted by a UF of 30 (interspecies 10; and intraspecies 3) and time-scaled using n=3. The 10-minute AEGL-3 was calculated as 64 ppm. The above 10-minutes AEGL values were proposed by Mark McClanahan

and seconded by John Hinz. The motion passed [YES:15; NO: 2; Abstain: 0] (Appendix J).

METHYL HYDRAZINE
CAS Reg. No. 60-34-4

Chemical Manager: Richard Thomas, ICEH
Staff Scientist: Bob Young, ORNL

George Rusch briefly introduced the chemical toxicity information for methyl hydrazine (Attachment 19). He pointed it out that no numeric AEGL-1 values were developed due to (1) the lack of adequate data, (2) an inadequate margin of safety exists between the derived AEGL-1 and AEGL-2 values because significant irritation and possible toxic effects may occur at concentration at or below the odor threshold. The AEGL-3 was based on the 1-hour LC_{50} of 82 ppm in female squirrel monkeys; the lethality threshold was estimated as a 3-fold reduction of the LC_{50}, 27.3 ppm. A total of UF of 10 was applied (interspecies of 3 based on the fact that toxicities to the squirrel monkey, dog, rat, and mouse differed by a factor of three and interspecies of 3 due to steep dose-response curve and mechanism of toxicity). A value of n=1 was used for temporal time scaling. The lethality data for the species tested indicated a near linear relationship between concentration and time (n = 0.97 and 0.99 for monkeys and dogs, respectively). The resulting 10-minute AEGL-3 value is 16 ppm. The 10-minute AEGL-2 value was derived from a 3-fold downward adjustment of the 10-minute AEGL-3 value, 5.3 ppm. A motion was made Steve Barbee and seconded by Mark McClanahan to accept the above proposal. The motion passed [YES: 16; NO: 1; Abstain: 0] (Appendix K).

DIMETHYL HYDRAZINE
CAS Reg. No. 151-56-4

Chemical Manager: Richard Thomas, ICEH
Staff Scientist: Bob Young, ORNL

George Rusch briefly presented the chemical toxicity information on dimethyl hydrazine (DMH) (Attachment 20). George noted that no numeric AEGL-1 values were developed due to (1) the lack of adequate data, and (2) an inadequate margin of safety exists between the derived AEGL-1 and AEGL-2 values because significant irritation and possible toxic effects may occur at concentrations at or below the odor threshold, similar to monomethyl hydrazine. The AEGL-2 values were based on the exposure of dogs to 1,1-DMH at 360 ppm for 15 minutes. The dogs exhibited behavioral changes and muscle fasciculations (Weeks et al., 1963). Extrapolation was based on C^n x t=K (ten Berge, 1986), using n=1 and a total uncertainty factor of 30 (interspecies of 3 and intraspecies of 10) to obtain 18 ppm as the 10-minute value. The AEGL-3 value was derived from a 1-hour LC_{50} study in dogs (Weeks et al., 1963) by establishing a lethality threshold of 327 ppm. The 10-minute AEGL-3 was derived in the same manner (n=1, UF = 30) as the AEGL-2 to obtain 65 ppm. A motion was made by Loren Koller and seconded by John Hinz to accept the above proposal. The motion passed [YES:17; NO: 1; Abstain: 0] (Appendix L).

Literature review of Benzene and Trichloroethylene

A brief literature overview of benzene and trichloroethylene was presented by Marcel T.M. van Raaij. Basically, he described the key attributes of benzene (Attachment 21). Benzene has been used as a solvent in industry since late 1800; it is produced from coal tar and crude oil; it is a constituent of gasoline; it has vapor pressure (95 mm Hg @ 25 °C); and inhalation is the primary route of exposure. The toxicity of benzene is well characterized by CNS depression (acute) and bone marrow toxicity (chronic). It is a human carcinogen. Marcel outlined possible endpoints for AEGL-2 development in the area of CNS effects, hematotoxicity, chromosome aberrations, and embryo/fetotoxicity. He solicited inputs from NAC/AEGL committee which endpoint should be considered the most relevant for AEGL-2 development and what would be the rationale? The presentation was supplemented by Robert Snyder, Chemical Manager and subject expert. Bob described the postulated role of benznetriol in bone marrow depression and recent human studies from China on chromosome damage with benzene exposure. The studies can be important references while we are considering the most relevant endpoints for AEGL values (Attachment 22).

The presentation, continued by Marcel, focused on trichloroethylene. Trichloroethylene is another well-documented chemical. It is a volatile liquid (69 mm Hg @ 25 °C) and inhalation is the primary route of exposure. There are several possible endpoints for considering the developments of AEGL values (Attachment 23).

Administrative Matters

The next meeting, NAC/AEGL-24, has been set for April 9-11, 2002, in Washington, D.C. More information about the lodging will be provided soon by Po-Yung Lu. The tentative NAC/AEGL-25 meeting is proposed for June 17-19, 2002 , either in Washington, D.C. or Rutgers University (hosted by Bob Snyder); and the NAC/AEGL-26 meeting is also tentatively set for September 10-12, 2002, in Washington, D.C.

The meeting highlights were prepared by 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.

Attachment 1. Over view of AFIERA
Attachment 2. NAC/AEGL-22 meeting highlight comments by John Morawetz
Attachment 3. NAC/AEGL-23 meeting agenda
Attachment 4 . NAC/AEGL-23 attendee list
Attachment 5. Revised version of "*Guidance for the Application of Odor in the Derivation of AEGL-1*"
Attachment 6. Technical information of Gastec Gas Detection System
Attachment 7. Data Analysis of Methyl ethyl ketone
Attachment 8. JP-8"Issues & Answers"
Attachment 9. Jet Fuel-8, Epidemiology Study
Attachment 10. Jet Fuel-8, Health Effect Studies
Attachment 11. Jet Fuel-8, Potential Respiratory Irritation Studies
Attachment 12. ExxonMobil Final report on sensory irritation study in mice
Attachment 13. Data Analysis of Jet Fuel-8
Attachment 14. PBPK Data Analysis of Xylenes
Attachment 15. Federal Register Comments of Perchloromethylmercaptan from Tomem Agro
Attachment 16. Data Analysis of Ethylenimine
Attachment 17. Data Analysis of Propylenimine
Attachment 18. Data Analysis of Hydrazine
Attachment 19. Data Analysis of Methyl hydrazine
Attachment 20. Data Analysis of Dimethyl hydrazine
Attachment 21. Benzene progress report
Attachment 22. Recent studies on benzene exposure
Attachment 23. Trichloroethylene progress report

LIST OF APPENDICES

Appendix A. Revised meeting high lights of NAC/AEGL-22
Appendix B. Ballot for Approval of NAC/AEGL-22 meeting highlights
Appendix C. Ballot for Methyl ethyl ketone
Appendix D. Ballot for Jet Fuel-8
Appendix E. Ballot for Xylenes
Appendix F. Ballot for Methanol
Appendix G. Ballot for Perchloromethylmercaptan
Appendix H. Ballot for Ethylenimine
Appendix I. Ballot for Propyleneimine
Appendix J. Ballot for Hydrazine
Appendix K. Ballot for Methyl hydrazine
Appendix L. Ballot for Dimethyl hydrazine

NAC/AEGL Meeting 24: April 9-11,2002

Chemical: AMMONIA (10 MIN. ONLY) **CAS Reg. No.:** 7664-41-7

NAC Member	AEGL 1	AEGL 2	AEGL 3	NAC Member	AEGL 1	AEGL 2	AEGL 3
George Alexeeff	Y	N	Y	Nancy Kim	Y	Y	Y
Steven Barbee	Y	Y	Y	Loren Koller	Y	Y	Y
Lynn Beasley	Y	Y	Y	Glenn Leach	Y	Y	Y
David Belluck	Y	Y	Y	Mark McClanahan	Y	Y	Y
Robert Benson	Y	Y	Y	John Morawetz	Y	N	Y
Jonathan Borak	A	A	A	Richard Niemeier	A	A	A
William Bress	Y	Y	Y	Marinelle Payton	A	A	A
George Cushmac	Y	Y	Y	Zarena Post	A	A	A
Al Dietz	A	A	A	George Rodgers	Y	Y	Y
Ernest Falke	Y	Y	Y	George Rusch, Chair	Y	Y	Y
Larry Gephart	Y	Y	Y	Robert Snyder	Y	Y	Y
John Hinz	Y	Y	Y	Thomas Sobotka	Y	Y	Y
Jim Holler	Y	Y	Y	Kenneth Still	A	A	A
Thomas Hornshaw	Y	Y	Y	Richard Thomas	Y	Y	Y
DOAH	Y	Y	Y	TALLY	22/22	20/22	22/22

PPM, (mg/m³)	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1	25 ,( )	,( )	,( )	,( )	,( )
AEGL 2	~~220~~ 270 ,( )	,( )	,( )	,( )	,( )
AEGL 3	~~3300~~ 2700 ,( )	,( )	,( )	,( )	,( )

AEGL 1 Motion: Koller **Second:** Falke

AEGL 2 Motion: ↓ **Second:** ↓

AEGL 3 Motion: ↓ **Second:** ↓

Approved by Chair: [signature] **DFO:** Paul S. Tobin **Date:** 4/9/02

NAC/AEGL Meeting 24: April 9-11,2002

Chemical: FLUORINE **CAS Reg. No.:** 7782-41-4

NAC Member	AEGL 1 †	AEGL 2 *	AEGL 3 ‡	NAC Member	AEGL 1	AEGL 2 *	AEGL 3 ‡
George Alexeeff	N	P	P	Nancy Kim	Y	Y	Y
Steven Barbee	Y	Y	Y	Loren Koller	Y	Y	Y
Lynn Beasley	Y	Y	Y	Glenn Leach	Y	Y	Y
David Belluck	Y	Y	Y	Mark McClanahan	Y	Y	Y
Robert Benson	P	P	P	John Morawetz	N	P	P
Jonathan Borak	Y	Y	Y	Richard Niemeier	A	A	A
William Bress	Y	Y	Y	Marinelle Payton	A	A	A
George Cushmac	Y	Y	Y	Zarena Post	P	P	P
Al Dietz	A	A	A	George Rodgers	N	Y	Y
Ernest Falke	Y	Y	Y	George Rusch, Chair	Y	Y	Y
Larry Gephart	Y	Y	Y	Robert Snyder	Y	Y	Y
John Hinz	Y	Y	Y	Thomas Sobotka	Y	Y	Y
Jim Holler	Y	Y	Y	Kenneth Still	A	A	A
Thomas Hornshaw	Y	Y	Y	Richard Thomas	Y	Y	Y
Doan Hansen	Y	Y	Y	TALLY	20 3 2		

† Vote on AEGL-1,2,3 10' and AEGL-1 30'-8 hr

PPM, (mg/m³)	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1	1.7 ,( )	1.7 ,( )	1.7 ,( )	1.7 ,( )	1.7 ,( )
AEGL 2	20 ,( )	,( )	,( )	,( )	2.3* ,( )
AEGL 3	36 ,( )	,( )	,( )	,( )	5.7‡ ,( )

AEGL 1 Motion: McClanahan Second: Koller

AEGL 2 Motion: ↓ Second: ↓

AEGL 3 Motion: ↓ Second: ↓

Approved by Chair: [signature] DFO: [signature] Date: 2/9/02

NAC/AEGL Meeting 24: April 9-11,2002

Chemical: METHYL MERCAPTAN **CAS Reg. No.:** 74-93-1

NAC Member	AEGL 1 *	AEGL 2	AEGL 3	NAC Member	AEGL 1 *	AEGL 2	AEGL 3
George Alexeeff		A	A	Nancy Kim		Y	Y
Steven Barbee		Y	Y	Loren Koller		Y	P
Lynn Beasley		Y	Y	Glenn Leach		Y	Y
David Belluck		N	Y	Mark McClanahan		N	N
Robert Benson		Y	Y	John Morawetz		Y	Y
Jonathan Borak		A	A	Richard Niemeier		A	A
William Bress		Y	Y	Marinelle Payton		A	A
George Cushmac		Y	Y	Zarena Post		Y	Y
Al Dietz		A	A	George Rodgers		Y	Y
Ernest Falke		Y	Y	George Rusch, Chair		Y	Y
Larry Gephart		Y	Y	Robert Snyder		Y	Y
John Hinz		A	Y	Thomas Sobotka		Y	Y
Jim Holler		Y	Y	Kenneth Still		A	A
Thomas Hornshaw		Y	Y	Richard Thomas		A	Y
Doan Hansen		Y	Y	TALLY		19/21	21/22

PPM, (mg/m³)	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1 *	26 ,( )	26 ,( )	21 ,( )	13 ,( )	8.6 ,( )
AEGL 2	59 ,( )	59 ,( )	47 ,( )	30 ,( )	19 ,( )
AEGL 3	120 ,( )	86 ,( )	68 ,( )	43 ,( )	22 ,( )

AEGL 1 Motion: * Falke Second: Benson

AEGL 2 Motion: Falke Second: Benson

AEGL 3 Motion: Barbee Second: Kim

* Table discussion of CH_3SH AEGL-1

Approved by Chair: George M. Rusch DFO: Paul S. Tobin Date: 4/10/02

NAC/AEGL Meeting 24: April 9-11,2002

(AEGL-2+3 LEVELS) (AEGL-1 VALUES)

Chemical: PHOSPHORUS TRICHLORIDE ^ **CAS Reg. No.:** 7719-12-2

NAC Member	AEGL 1	AEGL 2	AEGL 3	NAC Member	AEGL 1	AEGL 2	AEGL 3
George Alexeeff	A	A	A	Nancy Kim	N	Y	N
Steven Barbee	Y	Y	Y	Loren Koller	Y	Y	Y
Lynn Beasley	A	A	Y	Glenn Leach	A	A	A
David Belluck	Y	Y	Y	Mark McClanahan	Y	Y	Y
Robert Benson	Y	Y	Y	John Morawetz	N	Y	P
Jonathan Borak	A	A	A	Richard Niemeier	A	A	A
William Bress	N	Y	Y	Marinelle Payton	A	A	A
George Cushmac	Y	Y	Y	Zarena Post	Y	Y	Y
Al Dietz	A	A	A	George Rodgers	N	Y	Y
Ernest Falke	Y	Y	Y	George Rusch, Chair	P	Y	Y
Larry Gephart	P	Y	Y	Robert Snyder	N	Y	Y
John Hinz	Y	Y	Y	Thomas Sobotka	Y	Y	Y
Jim Holler	Y	Y	Y	Kenneth Still	A	A	A
Thomas Hornshaw	P	Y	Y	Richard Thomas	Y	Y	Y
Dean Hansen	Y	Y	Y	TALLY	13/16	21/21	20/21

PPM, (mg/m³)	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1	0.78 , ( )	0.78 , ( )	0.62 , ( )	0.39 , ( )	0.26 , ( )
AEGL 2	2.5 , ( )	2.5 , ( )	2.0 , ( )	1.3 , ( )	0.83 , ( )
AEGL 3	7.0 , ( )	7.0 , ( )	5.6 , ( )	3.5 , ( )	1.8 , ( )

AEGL 1 Motion: Benson Second: McClanahan

AEGL 2 Motion: Benson Second: Thomas

AEGL 3 Motion: Gephart Second: Hinz

Approved by Chair: George M Rusch DFO: Paul S. Tobin Date: 4/10/02

ELEVATE TO INTERIM

Appendix F

NAC/AEGL Meeting 24: April 9-11,2002

Chemical: ACRYLIC ACID RAISE TO INTERIM **CAS Reg. No.:** 79-10-7

NAC Member	AEGL 1	AEGL 2	AEGL 3	NAC Member	AEGL 1	AEGL 2	AEGL 3
George Alexeeff	Y-BY	N	Y	Nancy Kim		Y	Y
Steven Barbee	SHOW HANDS	Y	Y	Loren Koller		Y	Y
Lynn Beasley	- NONE	Y	Y	Glenn Leach		Y	Y
David Belluck	voted	Y	Y	Mark McClanahan		Y	Y
Robert Benson	NO. (16 YES)	Y	Y	John Morawetz		N	Y
Jonathan Borak		A	A	Richard Niemeier		A	A
William Bress		Y	Y	Marinelle Payton		A	A
George Cushmac		Y	Y	Zarena Post		N	Y
Al Dietz		A	A	George Rodgers		Y	Y
Ernest Falke		Y	Y	George Rusch, Chair		Y	Y
Larry Gephart		Y	Y	Robert Snyder		Y	Y
John Hinz		N	P	Thomas Sobotka		A	A
Jim Holler		A	A	Kenneth Still		A	A
Thomas Hornshaw		Y	Y	Richard Thomas		A	A
DOAN HANSEN		Y	Y	TALLY		17/20	20/20

1940 2001/21

PPM, (mg/m³)	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1	1.0 ,( )	1.0 ,( )	1.0 ,( )	1.0 ,( )	1.0 ,( )
AEGL 2	68 ,( )	68 ,( )	46 ,( )	21 ,( )	14 ,( )
AEGL 3	480 ,( )	260 ,( )	180 ,( )	85 ,( )	58 ,( )

AEGL 1 Motion: G. Rusch (Show of hands) **Second:** _____

AEGL 2 Motion: Snyder **Second:** Barbee

AEGL 3 Motion: Rodgers * Barbee **Second:** Belluck Falke

Approved by Chair: George M. Rusch **DFO:** Paul S. Tobin **Date:** 4/11/02

NAC/AEGL Meeting 24: April 9-11,2002

Raise to Interim

Chemical: BORON TRIFLUORIDE (DIMETHYL ETHER COMPLEX) **CAS Reg. No.:** 353-42-4

NAC Member	AEGL 1	AEGL 2	AEGL 3	NAC Member	AEGL 1	AEGL 2	AEGL 3
George Alexeeff				Nancy Kim			
Steven Barbee				Loren Koller			
Lynn Beasley				Glenn Leach			
David Belluck				Mark McClanahan			
Robert Benson				John Morawetz			
Jonathan Borak				Richard Niemeier			
William Bress				Marinelle Payton			
George Cushmac				Zarena Post			
Al Dietz				George Rodgers			
Ernest Falke				George Rusch, Chair			
Larry Gephart				Robert Snyder			
John Hinz				Thomas Sobotka			
Jim Holler				Kenneth Still			
Thomas Hornshaw				Richard Thomas			
Doan Hansen				TALLY			

UNANIMOUS

PPM, (mg/m^3)	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1	, ( )	, ( )	, ( )	, ( )	, ( )
AEGL 2	, ( )	, ( )	, ( )	, ( )	, ( )
AEGL 3	, ( )	, ( )	, ( )	, ( )	, ( )

AEGL 1 Motion: McClanahan **Second:** Thomas

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

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

Approved by Chair: [signature] **DFO:** Paul S. Tobin **Date:** 4/10/02

NAC/AEGL Meeting 24: April 9-11,2002

METHYL NONAFLUOROISOBUTYL ETHER Raise to Interim

Chemical: (HFE-7100 COMPONENT) **CAS Reg. No.:** 163702-08-7

NAC Member	AEGL 1	AEGL 2	AEGL 3	NAC Member	AEGL 1	AEGL 2	AEGL 3
George Alexeeff				Nancy Kim			
Steven Barbee				Loren Koller			
Lynn Beasley				Glenn Leach			
David Belluck				Mark McClanahan			
Robert Benson				John Morawetz			
Jonathan Borak				Richard Niemeier			
William Bress				Marinelle Payton			
George Cushmac				Zarena Post			
Al Dietz				George Rodgers			
Ernest Falke				George Rusch, Chair			
Larry Gephart				Robert Snyder			
John Hinz				Thomas Sobotka			
Jim Holler				Kenneth Still			
Thomas Hornshaw				Richard Thomas			
Doan Hansen				TALLY			

UNANIMOUS

PPM, (mg/m³)	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1	,( )	,( )	,( )	,( )	,( )
AEGL 2	,( )	,( )	,( )	,( )	,( )
AEGL 3	,( )	,( )	,( )	,( )	,( )

AEGL 1 Motion: McClanahan **Second:** Thomas

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

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

Approved by Chair: _____ **DFO:** _____ **Date:** 4/10/02

NAC/AEGL Meeting 24: April 9-11,2002

Raise to Interim

Chemical: URANIUM HEXAFLUORIDE **CAS Reg. No.:** 7783-81-5

NAC Member	AEGL 1	AEGL 2	AEGL 3	NAC Member	AEGL 1	AEGL 2	AEGL 3
George Alexeeff				Nancy Kim			
Steven Barbee				Loren Koller			
Lynn Beasley				Glenn Leach			
David Belluck				Mark McClanahan			
Robert Benson				John Morawetz			
Jonathan Borak				Richard Niemeier			
William Bress				Marinelle Payton			
George Cushmac				Zarena Post			
Al Dietz				George Rodgers			
Ernest Falke				George Rusch, Chair			
Larry Gephart				Robert Snyder			
John Hinz				Thomas Sobotka			
Jim Holler				Kenneth Still			
Thomas Hornshaw				Richard Thomas			
Joan Hansen				TALLY			

URANIUS

PPM, (mg/m^3)	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1	, ( )	, ( )	, ( )	, ( )	, ( )
AEGL 2	, ( )	, ( )	, ( )	, ( )	, ( )
AEGL 3	, ( )	, ( )	, ( )	, ( )	, ( )

AEGL 1 Motion: McClanahan **Second:** Thomas

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

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

Approved by Chair: _____ **DFO:** _____ **Date:** 4/11/02

NAC/AEGL Meeting 24: April 9-11,2002

Chemical: TRICHLOROETHYLENE **CAS Reg. No.:** 79-01-6

NAC Member	AEGL 1	AEGL 2	AEGL 3	NAC Member	AEGL 1	AEGL 2	AEGL 3
George Alexeeff	Y	Y	N	Nancy Kim	Y	Y	N
Steven Barbee	Y	Y	Y	Loren Koller	Y	N	Y
Lynn Beasley	Y	Y	Y	Glenn Leach	Y	Y	Y
David Belluck	Y	Y	Y	Mark McClanahan	Y	N	Y
Robert Benson	Y	Y	Y	John Morawetz	Y	Y	N
Jonathan Borak	A	A	A	Richard Niemeier	A	A	A
William Bress	Y	Y	Y	Marinelle Payton	A	A	A
George Cushmac	Y	Y	Y	Zarena Post	Y	Y	N
Al Dietz	A	A	A	George Rodgers	Y	N	Y
Ernest Falke	Y	Y	Y	George Rusch, Chair	Y	Y	Y
Larry Gephart	Y	Y	Y	Robert Snyder	Y	N	Y
John Hinz	Y	Y	Y	Thomas Sobotka	P	N	N
Jim Holler	Y	Y	Y	Kenneth Still	A	A	A
Thomas Hornshaw	Y	N	Y	Richard Thomas	Y	N	Y
Doan Hansen	Y	Y	Y	TALLY	23/23	17/24	18/23

24/11

PPM, (mg/m³)	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1	260 ,( )	180 ,( )	130 ,( )	84 ,( )	77 ,( )
AEGL 2	960 ,( )	620 ,( )	450 ,( )	270 ,( )	240 ,( )
AEGL 3	10,000 ,( )	~~4100~~ ,( )	~~5900~~ ,( )	~~2300~~ ,( )	~~1500~~ ,( )
		6100	3800	1500	970

AEGL 1 Motion: Bress **Second:** Hinz

AEGL 2 Motion: Benson **Second:** Hinz

AEGL 3 Motion: Snyder **Second:** Thomas

Approved by Chair: George M Rusch **DFO:** Paul S. Tobin **Date:** 4/10/02

NAC/AEGL Meeting 24: April 9-11,2002

Chemical: FURAN **CAS Reg. No.:** 110-00-9

NAC Member	AEGL 1	AEGL 2	AEGL 3	NAC Member	AEGL 1	AEGL 2	AEGL 3
George Alexeeff		Y	Y	Nancy Kim		Y	Y
Steven Barbee		P	P	Loren Koller		A	A
Lynn Beasley		Y	Y	Glenn Leach		Y	Y
David Belluck		Y	Y	Mark McClanahan		A	A
Robert Benson		N	N	John Morawetz		Y	Y
Jonathan Borak		A	A	Richard Niemeier		A	A
William Bress		N	N	Marinelle Payton		A	A
George Cushmac		Y	Y	Zarena Post		Y	Y
Al Dietz		A	A	George Rodgers		Y	Y
Ernest Falke		N	N	George Rusch, Chair		Y	Y
Larry Gephart		Y	Y	Robert Snyder		Y	Y
John Hinz		N	N	Thomas Sobotka		A	A
Jim Holler		A	A	Kenneth Still		A	A
Thomas Hornshaw		Y	Y	Richard Thomas		A	A
Dean Hansen		N	N	TALLY		13/18	13/18

13519

PPM, (mg/m³)	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1	NR, ( )	, ( )	, ( )	, ( )	, ( )
AEGL 2	12 , ( )	8.5 , ( )	6.8 , ( )	1.7 , ( )	0.85 , ( )
AEGL 3	35 , ( )	24 , ( )	19 , ( )	4.8 , ( )	2.4 , ( )

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

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

AEGL 3 Motion: Hornshaw **Second:** Rodgers

Approved by Chair: _____ **DFO:** _____ **Date:** 4/11/02