National Advisory Committee (NAC)
for Acute Exposure Guideline Levels (AEGLs) for Hazardous Substances
Final Meeting 4 Highlights
Green Room, 3rd Floor, Ariel Rios Building
1200 Pennsylvania Avenue, NW
Washington, D.C.
December 16-18, 1996

INTRODUCTION

The highlights of the meeting are noted below, and the meeting agenda (Attachment 1) and attendee list (Attachment 2) are attached.

Dr. Roger Garrett welcomed the committee members and provided a brief overview of the NAC/AEGL program for new Committee members. He noted that the Committee should attempt to increase efficiency but not at the expense of quality.

The summary of meeting 3 (September 17-19, 1996) was reviewed and approved with minor changes (Appendix A). Dr. Steve Barbee noted that clarification was needed regarding the AEGL values for hydrogen cyanide. He stated that the Wexler et al. (1974) data should have been used to derive the AEGL-2 values instead of the AEGL-3 values. This change will not affect the selected concentrations and will be reflected in the final draft report to be circulated for public comments. It was noted that the 4-hr and 8-hr AEGL-2 values for arsine as proposed by the NAC/AEGL and listed in the meeting summary should be rounded to the nearest tenth to maintain relational consistency (the arsine values in question were amended accordingly the following day [12/17/96]) (Appendix B). Dr. Doan Hansen noted that for methyl mercaptan, the *n* exponent for temporal scaling was changed from 2.5 to 2.2 resulting in slightly altered values for the 30-minute and 1-hr AEGL-2 and AEGL-3 values.

Dr. Robert Snyder commented that it is the NAC/AEGL that recommends the AEGL values and that ORNL provides data analyses and submits draft documents to the NAC/AEGL.

REPORTS FROM SUBCOMMITTEES AND GENERAL INTEREST ITEMS

Uncertainty Factor Subcommittee

Dr. David Belluck indicated that requests were made to all 50 states regarding how they addressed uncertainty factor application and issues and that 20-25 states had responded thus far. An updated report will be provided at the next NAC/AEGL meeting. Mr. Larry Gephart noted that a report on the use and interspecies variability of the RD_{50} had been provided to Dr. Richard Thomas. Dr. Richard Thomas noted that an overview of uncertainty factor application will be an agenda item at the next (March) meeting.

Time-line for Document Review

A revised time-line for document review to facilitate the effectiveness of the review process and in the use of meeting time was briefly discussed by Dr. George Rusch, NAC/Chair (Attachment 3). It was noted that the Committees' role in document review had been expanded (chemical manager and two secondary reviewers) and that a list of priority chemicals would be made available to the NAC in January 1997 (Attachment 4). Dr. Po-Yung Lu (ORNL) noted that the chemicals and chemical managers for the March meeting had mostly been identified and that the June meeting chemicals were also selected but that chemical

managers had not yet been identified.

Acute Inhalation Toxicity Study Outline
Dr. George Rusch noted that no comments had been received to date regarding the study outline.

Literature Search/Acquisition Considerations
Dr. P.-Y. Lu provided an overview of the literature search/acquisition processes at ORNL for AEGL document preparation. The NAC/AEGL members were encouraged to continue assisting in identifying pertinent literature. Dr. Paul Tobin noted that the exact measured exposure levels are requested from OSHA and will be submitted in the near future. Dr. David Belluck also offered assistance in obtaining very old documents. Dr. Roger Garrett noted that non peer-reviewed data from the private sector is not always easily accessed and that a mechanism needs to be developed to obtain these reports.

Compilation of "Living Document"
Dr. Ernest Falke is in the process of compiling critical data used in deriving AEGL levels (e.g., species, critical effect, reference, scaling procedures, uncertainty factor application, etc.). He noted that special attention should be directed to justifying assumptions and methods used in the derivation of AEGL values. Essentially, we must capture what we have done and why it was done. This will be discussed at the next meeting.

AEGL Document Format
Dr. David Belluck noted that comments regarding document format will be deferred until the next meeting.

AEGL PRIORITY CHEMICALS

Nitric Acid, CAS Reg. No. 7697-37-2

Chemical Manager: Dr. Loren Koller, Orgeon State Univ.
Staff Scientist: Dr. Carol Forsyth, ORNL
Dr. Koller noted that the NO_2 data had been examined relative to revisiting the nitric acid AEGLs. He recommended that the nitric acid AEGLs not be revised and that the report should be considered as complete. The current AEGLs for nitric acid are shown in the table below.

SUMMARY OF PROPOSED AEGL VALUES FOR NITRIC ACID

Classification	30-min	1-hour	4-hour	8-hour	Endpoint
AEGL-1	0.5 ppm 1.3 mg/m^3	0.5 ppm 1.3 mg/m^3	0.5 ppm 1.3 mg/m^3	0.5 ppm 1.3 mg/m^3	Minor irritation in humans
AEGL-2	5 ppm 12.9 mg/m^3	4 ppm 10.3 mg/m^3	3 ppm 7.7 mg/m^3	2 ppm 5.2 mg/m^3	Notable irritation, respiratory effects in humans
AEGL-3	15 ppm 38.7 mg/m^3	13 ppm 33.5 mg/m^3	8 ppm 20.6 mg/m^3	7 ppm 18.1 mg/m^3	Approximate LC_0 in rats

Hydrogen Fluoride, CAS Reg. No. 7664-39-3

Chemical Manager: Mr. Larry Gephart, Exxon Biomedical Sciences
Staff Scientist: Dr. Sylvia Talmage, ORNL

Data were presented and issues discussed regarding the derivation of 10-minute AEGLs for hydrogen fluoride (HF). Mr. Larry Gephart provided a brief overview of the AEGLs previously proposed for HF (August 1996 NAC meeting). These are shown in the table below.

SUMMARY OF PROPOSED AEGL VALUES FOR HYDROGEN FLUORIDE

Classification	10-min	30-min	1-hour	4-hour	8-hour	Endpoint
AEGL-1	2 ppm 1.6 mg/m^3	2 ppm 1.6 mg/m^3	2 ppm 1.6 mg/m^3	1 ppm 0.8 mg/m^3	1 ppm 0.8 mg/m^3	Slight eye and nose irritation in humans (Largent 1960; 1961)
AEGL-2	130 ppm 107 mg/m^3	18 ppm 15 mg/m^3	13 ppm 11 mg/m^3	10 ppm 8 mg/m^3	7 ppm 6 mg/m^3	NOAEL for serious lung effects in rats (PERF 1966)[a], highest concentration for slight eye and nose irritation and reddening of facial skin in humans (Largent 1960; 1961)[b]
AEGL-3	170 ppm 139 mg/m^3	62 ppm 51 mg/m^3	44 ppm 36 mg/m^3	22 ppm 18 mg/m^3	15 ppm 13 mg/m^3	Threshold for lethality in mice (Wohlslagel et al., 1976)

[a] 30-min and 1-hr AEGL-2 values
[b] 4-hr and 8-hr AEGL-2 values

Mr. Larry Gephart and Dr. Walden Dalbey (Mobil Business Resources Corporation) provided data to support a 10-minute AEGL-2 for HF (Attachments 5&6). They provided the results of a study conducted by the Petroleum Environmental Research Forum that was designed to define the HF concentration causing serious effects and estimating the threshold for these effects. Exposure of mouth-breathing rats for 10 minutes to 1764 ppm HF resulted in serious effects including lethality (1/20 animals), 950 ppm caused local irritation but no serious effects, and 271 ppm HF was a NOAEL. The uncertainty factor application included 3 for interspecies variability (HF is a primary irritant, LC_{50} values are similar across species, and the irritation endpoint is appropriate for human health risk assessment), and 3 for intraspecies variability (mouth breathing by test species bypasses nasal scrubbing and maximizes the dose). The approximate arithmetic mean value of the concentrations causing serious effects (1764 ppm) and no serious effects (950 ppm), i.e., 1300 ppm was chosen as the threshold for serious effects for the 10-minute AEGL-2. Based upon this estimated threshold and a total UF of 10 (3 x 3), 130 ppm was proposed as the 10-minute AEGL-2 for HF. The proposed 10-minute AEGL-2 of 130 ppm was accepted by the Committee (Appendix C). A 10-minute AEGL-3 of 170 ppm (1764 ppm/10) and a 10-minute AEGL-1 of 2 ppm (the effect would not change between the 10- and 30-minute time frames) were proposed and accepted by the Committee (Appendix C).

Ammonia, CAS Reg. No. 7664-41-7

Chemical Manager: Mr. Larry Gephart, Exxon Biomedical Sciences
Staff Scientist: Dr. Kowetha Davidson, ORNL

Mr. Larry Gephart provided a brief overview of the AEGL derivation effort for ammonia. Although AEGL-1 levels have been accepted by the Committee, AEGL-2 and AEGL-3 levels are still in the derivation process. Dr. Kowetha Davidson provided an overview (Attachment 7) of the data sets

and previously proposed AEGL values, noting the variability in animal data and the uncertainty in accident reconstruction. Dr. Robert Michaels (RAM-TRAC Corp.) agreed that the animal data are variable and again stated that the conservative accident reconstruction was more appropriate for AEGL estimation (Attachment 8). Dr. Joseph Rodricks* (Environ Corp.) provided an overview of Environ's report addressing proposed AEGLs for ammonia (Attachment 9). He emphasized that the mouse is an especially sensitive species and that the ten Berge extrapolation is applicable to limited exposure durations, concentrations, and chemicals. Mr. Kent Andersen (International Institute of Ammonia Refrigeration) expressed reservations regarding the use of the RD_{50} for derivation of AEGLs (Attachment 10). Dr. Mazzola (DOE) provided an overview (Attachment 11) of the weaknesses and uncertainties of accident reconstruction. Dr. George Rusch recommended that the toxicity data as well as the accident reconstruction data be re-examined and also suggested consideration of the need for longer-term AEGLs for ammonia since lethality usually occurs at short-duration exposures. Dr. Borak noted that glottis closure may not be a valid endpoint for use in AEGL derivation. Discussion ensued regarding the use of human equivalent concentrations and the use of established risk assessment paradigms for AEGL derivations. It was the consensus of the Committee to defer ammonia to the next meeting and that the accident reconstruction modeling may require re-visitation by taking into account Dr. Mazzola's discussion. Additional action items for ammonia included: (1) defining appropriateness of using the RD_{50}; (2) consideration of Environ Corp. comments; (3) assessing the validity of 4-hr and 8-hr AEGLs for ammonia; and, (4) assessing the appropriateness of human equivalent concentrations, especially at high exposure levels.

(*1/28/97 Note: Responses to NAC issues by Dr. Rodricks were transmitted by Dr. James M. Skillen and received on 1/27/97.) (Attachment 21)

Methylhydrazine, CAS Reg. No. 60-34-4

Chemical Manager: Dr. Richard Thomas, ICEH
Chemical Reviewers: Dr. George Rogers, AAPCC; Dr. Kyle Blackman, FEMA
Staff Scientist: Dr. Robert A. Young, ORNL

Dr. Richard Thomas presented a brief overview of the properties and toxicity of methylhydrazine which was followed by a presentation by Dr. Young of the draft AEGL values and a summary of the data sets used for their derivation (Attachment 12). Of special concern was the steep exposure-response relationship indicated by animal data and the apparent low toxicity shown by 10-min exposure of human subjects. Following extensive discussion, it was decided by the Committee that the AEGL-3 be based upon a 1-hr LC_{50} in squirrel monkeys (the most sensitive species) and that the AEGL-2 be adjusted based upon a 3-fold reduction of the AEGL-3 values; a reduction considered adequate for estimating a threshold for serious, irreversible toxic effects. An AEGL-1 was considered to be inappropriate because notable toxicity may occur at concentrations below those that may result in serious toxic effects. A cancer risk assessment indicated that carcinogenic potential would be irrelevant compared to noncarcinogenic toxicity for acute exposures to methylhydrazine. Based upon the above discussion the following AEGL values were accepted by the Committee (Appendix D).

SUMMARY OF PROPOSED AEGL VALUES FOR METHYLHYDRAZINE					
Classification	30-min	1-hour	4-hour	8-hour	Endpoint

AEGL-1	NA	NA	NA	NA	
AEGL-2	2 ppm 3.8 mg/m^3	1 ppm 1.9 mg/m^3	0.2 ppm 0.4 mg/m^3	0.1 ppm 0.2 mg/m^3	Three-fold reduction of AEGL-3
AEGL-3	6 ppm 11.3 mg/m^3	3 ppm 5.6 mg/m^3	0.6 ppm 1.1 mg/m^3	0.3 ppm 0.6 mg/m^3	1-hr LC_{50} of 82 ppm reduced by 3-fold to estimate lethality threshold; UF=30[a]

[a] UF=3 for interspecies variability because mechanism of lethality appears to be similar across species, UF=10 for sensitive populations.

It was noted that in the practical application arena, if hydrazine is known to be present with methylhydrazine, the AEGL-1 for hydrazine (0.1 ppm for all time points) should be used.

Dimethylhydrazine, CAS Reg. No. 57-14-7 (1,1-DMH); 540-73-8 (1,2-DMH)

Chemical Manager: Dr. Richard Thomas, ICEH
Chemical Reviewers: Dr. George Rogers, AAPCC; Dr. Kyle Blackman, FEMA
Staff Scientist: Dr. Robert A. Young, ORNL

Dr. Richard Thomas provided a brief overview of the properties and toxicity of dimethylhydrazines (1,1-dimethylhydrazine and 1,2-dimethylhydrazine) which was followed by a presentation by Dr. Young of the draft AEGL values and a summary of the data sets used to derive draft AEGL values (Attachment 13). As for methylhydrazine, an AEGL-1 was considered to be inappropriate because the odor threshold was above concentrations that could produce effects. The data sets for deriving AEGL-2 and AEGL-3 levels were reviewed by Dr. Young and the draft AEGL-2 and AEGL-3 values were revised slightly. Similar to methylhydrazine, the AEGL values were not driven by excess cancer risk. Both Dr. Young and Dr. Thomas noted that the accepted AEGL-3 values for dimethylhydrazine, methylhydrazine, and hydrazine were relationally consistent with the reported relative toxicity of these chemicals. Additionally, it was noted that for emergency planning purposes, if hydrazine is known to be present, the hydrazine AEGL-1 of 0.1 ppm (for all time points) should be employed. Because of the paucity of toxicity data for 1,2-dimethylhydrazine, it was the consensus of the Committee (Appendix E&F) that the values for 1,1-dimethylhydrazine be used for 1,2-dimethylhydrazine.

SUMMARY OF PROPOSED AEGL VALUES FOR DIMETHYLHYDRAZINE

Classification	30-min	1-hour	4-hour	8-hour	Endpoint
AEGL-1	NA	NA	NA	NA	
AEGL-2	6 ppm 15 mg/m^3	3 ppm 7 mg/m^3	0.8 ppm 2 mg/m^3	0.4 ppm 1 mg/m^3	Behavioral changes and muscle fasciculations in dogs exposed to 360 ppm for 15 minutes (Weeks et al., 1963)[a]
AEGL-3	22 ppm 54 mg/m^3	11 ppm 27 mg/m^3	3 ppm 7 mg/m^3	1.5 ppm 4 mg/m^3	Lethality threshold of 327 ppm estimated from 1-hr LC_{50} for dogs (Weeks et al., 1963)[a]

[a] Uncertainty factor of 30

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

Chemical Manager: Dr. Ernest Falke, USEPA

Chemical Reviewers: Dr. George Alexeeff, Calif. EPA; Dr. Zarena Post, Texas
Staff Scientist: Dr. Cheryl Bast, ORNL

Dr. Falke provided an outline of issues pertaining to the phosphine AEGLs: critical effect, study selection, allometric scaling between laboratory species and humans, uncertainty factor application for inter- and intraspecies variability, temporal scaling, and interpretation of exposure-response curve data (Attachment 14). Dr. Cheryl Bast provided an overview of the draft AEGLs for phosphine (Attachment 15), noting the exceptionally steep exposure-response curve and lack of time and concentration data from human accidents. Following extensive discussion, the Committee decided to base the AEGL-3 on a no-effect-level for death in Sprague-Dawley rats exposed to phosphine for 6 hours. The Committee then decided to base the AEGL-2 on a no-effect-level for renal and pulmonary pathology in Fischer 344 rats exposed to phosphine 6 hours/day, 5 days/week for 13 weeks. Due to a lack of data, and the fact that lethality has been observed in animals exposed to phosphine concentrations below the odor threshold, the Committee decided that derivation of AEGL-1 values was not appropriate for phosphine (Appendix G).

SUMMARY OF PROPOSED AEGL VALUES FOR PHOSPHINE

Classification	30-min	1-hour	4-hour	8-hour	Endpoint
AEGL-1	NA	NA	NA	NA	
AEGL-2	0.4 ppm 0.6 mg/m^3	0.2 ppm 0.3 mg/m^3	0.1 ppm 0.14 mg/m^3	0.1 ppm 0.14 mg/m^3	No-effect level for renal and pulmonary pathology on rats exposed to 3.1 ppm phosphine 6 hr/day, 5 days/week for 13 weeks (Newton et al., 1993). UF=30[a]
AEGL-3	2 ppm 2.8 mg/m^3	1.5 ppm 2.1 mg/m^3	0.7 ppm 0.99 mg/m^3	0.5 ppm 0.7 mg/m^3	No-effect level for lethality in rats exposed to 18 ppm phosphine for 6 hr (Newton, 1991). UF=30[a]

[a]UF=3 for interspecies variability because mechanism of toxicity appears to be similar across species, UF=10 for sensitive populations because children appear to be more sensitive than adults.

Chlorine, CAS Reg. No. 7782-50-5

Chemical Manager: Mr. Larry Gephart, Exxon Biomedical Sciences
Chemical Reviewers: Dr. George Alexeeff, Calif. EPA; Dr. Kyle Blackman, FEMA
Staff Scientist: Dr. Sylvia Talmage, ORNL

Following an introduction by Mr. Larry Gephart, the presentation on chlorine (Cl_2) continued with an overview of the studies (human and animal) and data selection for deriving AEGLs by Dr. Sylvia Talmage (Attachment 16). During the discussion of the human data, the seriousness of an asthmatic attack from exposure to an irritant gas was pointed out by Dr. Jonathan Borak. Therefore, the data from the sensitive individual who suffered the asthmatic attack, exposure to 1 ppm of Cl_2 for 4 hours, was used as the basis for the AEGL-2; the no-effect concentration for this individual, 0.5 ppm for 4 hours, was used as the basis for the AEGL-1. Since human data were used and a sensitive individual was involved, no UFs were applied. The data were scaled across time using the relationship $C^2 \times t = k$.

During discussion of the animal data for the AEGL-3, it was noted that the endpoint was selected based upon study and data quality and not necessarily the most sensitive species; mouse data appeared to provide an overly conservative estimate of lethality that was not consistent with the

overall preponderance of the data. Mice suffered delayed deaths attributed to bronchopneumonia. One-hour LC_0 values for the rat were >200 ppm as was the 30-minute LC_0 for the rabbit. Therefore 200 ppm for one hour, which corresponds to an LC_{20} for the mouse, was chosen as the basis for the AEGL-3. Uncertainty factors of 3 for interspecies (Cl_2 is a direct-acting primary irritant with little difference among species in the response of biological tissue and the irritation endpoint is appropriate for human health risk assessment) and 3 for intraspecies (the mechanism of toxicity is the same for individuals of the same species) differences were applied. The data were scaled across time using the relationship $C^2 \times t = k$. The resulting AEGLs for chlorine were approved by the NCA (Appendix H) and are shown in the table below.

SUMMARY OF PROPOSED AEGL VALUES FOR CHLORINE

Classification	30-min	1-hour	4-hour	8-hour	Endpoint
AEGL-1	1 ppm 3 mg/m^3	1 ppm 3 mg/m^3	0.5 ppm 1.5 mg/m^3	0.5 ppm 1.5 mg/m^3	No-effect level in humans including sensitive individual (Rotman et al., 1983)
AEGL-2	3 ppm 9 mg/m^3	2 ppm 6 mg/m^3	1 ppm 3 mg/m^3	1 ppm 3 mg/m^3	Asthmatic attack in sensitive individual (Rotman et al., 1983)
AEGL-3	31 ppm 90 mg/m^3	22 ppm 64 mg/m^3	11 ppm 32 mg/m^3	8 ppm 23 mg/m^3	LC_0 for rat (MacEwen and Vernot 1972; Zwart and Woultersen 1988), LC_{20} for mouse (O'Neill 1991)

Phosgene, CAS Reg. No. 75-44-5

Chemical Manager: Dr. William C. Bress, ASTHO
Chemical Reviewers: Dr. David Belluck, Minnesota; Mr. Larry Gephart, EXXON
Staff Scientist: Dr. Jim Norris, ORNL

This document will be reviewed in March due to the recently uncovered, key references.

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

Chemical Manager: Dr. Kyle Blackman, FEMA
Chemical Reviewers: Dr. George Alexeeff, Calif. EPA; Dr. Jonathan Borak, ACOEM/ACEP
Staff Scientist: Dr. Kowetha Davidson, ORNL

Dr. Davidson provided an overview of the extensive database for ethylene oxide (EO) (Attachment 17). Several issues were identified regarding EO and included: (1) evaluating toxic vs anesthetic effects and obtaining information on blood:gas partition coefficients; (2) the need for the NAC/AEGL to determine if reproductive/developmental effects are AEGL-2 or AEGL-3 effects; (3) cancer risk issues: data from long-term bioassays may not be appropriate for a direct alkylating agent; and, (4) investigate details of the ampoule exposure case report.

Dr. Bill Snellings (Product Safety, Union Carbide) provided information on the toxicity of EO (Attachment 18) and noted that the only know fatalities from ethylene oxide accidents were associated with the chemical's explosivity. He noted that the TLV has been sequentially lowered over the years, that vomiting may be an important critical effect, that EO may induce dominant lethal effects in female rodents, and that no developmental effects have been shown at <1200 ppm but that exposure to 450 ppm caused hindleg paresis in rodents. Dr. Snellings noted that it is important to

evaluate effects relative to their biological relevance. The Committee requested that Dr. Snellings review the ORNL draft document and Dr. Snellings noted that he would attempt to provide odor threshold data.

Agenda Items

1. Determine if the fetus or pregnant woman should be considered the sensitive population and obtain information on what percent of the population is represented by pregnant women.

2. Dr. Belluck will discuss document formatting.

3. A request from Dr. Eugene Ngai (Solkatronic Chemicals) has been made to consider development of 10-minute AEGLs for compressed gases (Attachment 19). This topic will be discussed by the NAC.

4. A compiltaion of adverse health effect endpoints upon which to base AEGL-2 and AEGL-3 values will be discussed.

5. "Uncertainty" subcommittee report by Dr. Thomas.

6. The "living document" being developed by Dr. Falke regarding rationales for AEGL derivations will be discussed.

7. Consideration of all public comments that convey new and significant information pertinent to the development of AEGLs for ammonia, including any new and significant findings submitted by Ram Trac Corp.

Wrap-Up Comments from all participants:

- good discussions regarding relevant technical issues
- presentation of calculations in documents very helpful
- handouts of overheads very helpful
- document distribution was timely; preferred sequential receipt of documents rather than one large overwhelming package
- timely comments on documents appreciated; as document distribution improves, receipt of comments will hopefully improve as well
- need data on production, use, storage, etc. for chemicals
- because of the dynamics and diversity of the NAC, consistency in methodology application (e.g., uncertainty factor application) is important
- may want 10-minute AEGL routinely
- must make sure to provide rationale for assumptions and adjustments to methodologies
- compile summary of currently derived AEGL "living document"
- quality and good science are critical, productivity and efficiency also important
- include chemical manager on draft document; include exposure-response graphs if possible

Dr. Tobin distributed a chart on the various agencies interactions on the NAC/AEGL project (Attachment 20).

Dr. Garrett provided closing comments regarding the overall effectiveness of the NAC/AEGL and ORNL activities to date. He reiterated the objective and function of the Committee to develop AEGLs for 30 to 40 chemicals per year that are solidly based on good science. He emphasized the point that to attain this level of production together with scientifically defensible values, most of the work must be done in iterative fashion outside of the formal meetings.

To accomplish this, Roger emphasized that it is critical for each chemical manager to accept the "ownership" of the chemicals assigned to them and to serve aggressively as the catalyst and monitor of productive work, the liaison between the Oak Ridge staff scientist and the Committee members, and the key individual for resolving as many of the scientific and technical issues as possible prior to the formal meeting.

Based on his observations of the first four meetings, Roger believes that we have seen examples of very good, average and poor performances of Chemical Managers. He added that if we are to reach our goals, all chemical managers must perform at the upper end of the scale. He speculated that many Committee members may not fully understand the role of the chemical manager and committed himself to providing more definitive guidance. Roger concluded his remarks by emphasizing that the Chemical Manager function represents the "engine" that will drive an efficient and effective process.

Next meeting: March 17-19, 1997, Washington, D.C.

(Minutes were prepared by Drs. Robert Young and Po-Yung Lu, ORNL, and were approved on March 17, 1997.)

List of Attachments

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

1. NAC meeting 4 agenda
2. NAC meeting 4 attendees
3. Time-line for document review - revised from Dr. Rusch
4. Future chemicals for NAC review
5. Data analysis for 10-minute AEGL of HF from Gephart
6. Data analysis for 10-minute AEGL of HF from Dalbey
7. Data analysis of ammonia from Davidson
8. Residual issues of Ammonia Emergency Planning from Michaels
9. Review and technical critique of AEGLs proposed for ammonia from Rodricks
10. Ammonia for RD_{50} documents from Andersen
11. Overview of accident reconstruction from Mazzola
12. Data analysis of methylhydrazine AEGLs from Young
13. Data analysis of dimethylhydrazine AEGLs from Young
14. Data analysis of phosphine from Falke
15. Data analysis of phosphine from Bast
16. Data analysis of chlorine from Talmage
17. Preliminary data analysis of ethylene oxide from Davidson
18. Ethylene oxide LC_{50} values from Snellings
19. Correspondence to Dr. Rusch on compressed gases from Ngai
20. Agencies interactions on the NAC/AEGL from Tobin
21. Skillen/Rodricks response to NAC comments

List of Appendices

A. Final NAC meeting 3 highlights
B. Ballot of arsine modification
C. Ballot of hydrogenfluoride 10-minute AEGLs
D. Ballot of methylhydrazine AEGLs
E. Ballot of 1,2-dimethylhydrazine AEGLs
F. Ballot of 1,1-dimethylhydrazine AEGLs
G. Ballot of phosphine AEGLs
H. Ballot of chlorine AEGLs

Attachment 1

National Advisory Committee for Acute Exposure Guideline Levels for Hazardous Substances

Ariels Rios Building, 3rd Floor, Green Room
1200 Pennsylvania Avenue, N.W., Washington, D.C.

NAC-4 Agenda

Monday, December 16, 1996

10:00 - 10:15 AM	Introduction and approval of NAC-3 minutes
10:15 - 11:15	Technical discussions Uncertainty factors Shorter-term exposure guidance Literature search/acquisition considerations
11:15 - 11:30	**Break**
11:30 - 11:45	Cyanogen chloride (Mark McClanahan/Carol Forsyth)
11:45 - 12:15 PM	Nitric acid (inclusion of nitrogen dioxide) (Loren Koller/Carol Forsyth)
12:15 - 1:15	**Lunch**
1:15 - 1:45	10-min AEGL for hydrogen fluoride (Larry Gephart/Sylvia Talmage)
1:45 - 3:30	Ammonia (Larry Gephart/Kowetha Davidson)
3:30 - 3:45	**Break**
3:45 - 5:00	Methyl hydrazine (Richard Thomas/Bob Young)

Tuesday, December 17, 1996

8:30 - 10:30 AM	1,1- and 1,2-Dimethyl hydrazine (Richard Thomas/Bob Young)
10:30 - 10:45	**Break**
10:45 - 12:00 PM	Phosphine (Ernest Falke/Cheryl Bast)
12:00 - 1:00	**Lunch**
1:00 - 1:30	Phosphine (contd.)
1:30 - 3:30	Chlorine (Larry Gephart/Sylvia Talmage)
3:30 - 3:45	**Break**
3:45 - 5:00	Phosgene (Bill Bress/Jim Norris)

Wednesday, December 18, 1996

8:30 - 10:30 AM	Ethylene oxide (Ken Blackman/Kowetha Davidson)
10:30 - 10:45	**Break**
10:45 - 12:00	Administrative issues
NOON	Adjourn

AEGL, NAC-4, Dec 16-18, 1996

Attachment 2

Committee members

Name	Affiliation
Po-Lyung Yu	ORNL
Tom Sobotka	FDA
Nancy Kim	NYS DOH
Marion Ehrich	Virginia Tech (Virginia Polytechnic Institute & State University)
Loren D Koller	Oregon State University
Zarena Post	Tx Natural Resource Conserv. Commission
Bill Bress	ASTHO, VA. DOH
STEVEN J BARBEE	Olin Corp
John P. Hinz	USAF/AL-OEMW/Brooks AFB
JONATHAN BORAK	ACOEM
Ernest V. Falke	US EPA
Roger [illegible]	US EPA
George Rodgers	AAPCC
[illegible]	Exxon Biomedical
George M. Rusch	Allied Signal Corp
Paul S. Tobin	US EPA
KYLE W. BLACKMAN	FEMA
DAVID A. BELLUCK	MPCA
TOM HORNSHAW	ILL EPA
Robert Snyder	Rutgers Univ.
Richard Thomas	ICEH
Rodn Hansen	DOE/BNL
PATRICIA A. TALCOTT	Univ. Utah
Guy Colonna	NFPA
JIM HOLLER	ATSDR
MARK McCLANAHAN	CDC
RICK NIEMEIER	NIOSH

AEGL, NAC-4, Dec 16-18, 1996
Observers

Name	Affiliation
Wally Dalbey	Mobil
Ron Phillips	The Fertilizer Institute
~~Ford~~ West	TFI
CHRIS LEASON	McKenna & Cuneo
JIM SKILLEN	TFI
Joseph Rodricks	ENVIRON
Rich Kapuscinski	ENVIRON
Barry Hoberman	ENVIRON
Robert Michaels	RAM TRAC Corp, Schenectady NY
Carl Mazzola	Oak Ridge Associated Universities
Kanay Dastur	Dupont
Kathleen Baldor	International Institute of Ammonia Ref.
DANIEL R. KUESPERT	IIAR
KENT ANDERSON	IIAR

AlliedSignal
ENGINEERED
MATERIALS

AlliedSignal Inc.
P.O. Box 1139
Morristown, NJ 07962-1139

Attachment 3

DATE: November 21, 1996

TO: NAC AEGL Committee

FROM: George M. Rusch

SUBJECT: **Time Line for Document Review - Revised**

(At the September 17, 1996 Committee meeting, a few changes to this document were suggested. These have been incorporated in this revised version.)

We have all expressed concern regarding the time available between our initial receipt of the AEGL documents and the meeting at which they are scheduled for review. This has lead to lengthy discussions on several points which might otherwise have been addressed prior to the meeting.

While having two reviewers plus a chemical manager, will help greatly to address many of the questions that have come up during our meeting, it would still be advantageous to have the documents earlier for review. The items listed below were recommendations from the Committee following our discussion:

- Make available a proposed list of priority chemicals to be addressed during the next several meetings. This list should be made publicly available to encourage timely submission of unpublished data.
- Notice and chemical list published in Federal Register: 60 Days Prior to Meeting.
- Proposed Agenda, draft Minutes from prior meeting, draft documents and key reference lists mailed to Committee: 60 Days Prior to Meeting.
- Comments from Reviewers and other interested Committee members sent to Chemical Manager: 40 Days Prior to Meeting.
- Revised Draft and Agenda sent to Committee and other interested parties: 20 Days Prior to Meeting.

Having the draft documents and agenda available 60 days before the meeting would give all interested parties, including members of the public, an opportunity to carefully review them; develop meaningful questions, and get responses well before the meeting. This should help us to focus our discussions during the meeting and review the documents more expeditiously.

Best regards,

GMR:rb

George M. Rusch, Ph.D., D.A.B.T.

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Proposed future chemicals for AEGLs NAC meetings

March 1997

CAS no.	Chemical name	Chemical manager	Chemical reviewer	ORNL staff scientist	Doc. release date	Notes
62-53-3	Aniline	Colonna	Rodgers/Snyder	Talmage		
91-08-7 & 584-84-9	Toluene 2,6-diisocyanate & 2,4-isomer	Barbee	Borak/Hansen	Forsyth		
108-23-6	Isopropyl chloroformate	Hansen	Falke/Post	Bast		
7647-01-0	Hydrogen chloride	Hinz	Gephart/Kim	Bast		
Carry over chemicals: Ammonia, Ethlylene oxide and Phosgene.						
June 1997						
56-23-5	Carbon terachloride	Bress	Hansen/Thomas	Young		
107-11-9	Allyl amine		McClanahan/??	Milanez		
151-56-4	Ethyleneimine	McClanahan	Niemeier/??	Davidson		
624-83-9	Methyl isocyanate	Koller	Belluck/Post	Norris		
7446-09-5	Sulfur dioxide	Koller	Belluck/Ehrich	Bast		
7446-11-9	Sulfur trioxide	Koller	Barbee/??	Bast		
7790-91-2	Chlorine trifluoride		McClanahan/??	Talmage		
19287-45-7	Diborane			Troxel		

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Attachment 4

Septmber 1997						
75-56-9	Propylene oxide			Norris		
79-21-0	Peracetic acid			Davidson		
107-02-8	Acrolein		Hornsaw/Talcot	Bast		
107-18-6	Allyl alcohol		Borak/Niemeier	Forsyth		
107-30-2	Chloromethyl methyl ether			Milanez		
814-68-6	Acryl chloride			Norris		
7784-34-1	Arsenous trichloride			Young		
7726-95-6	Bromine	Post		Talmage		
10294-34-5	Boron trichloride			Troxel		
December 1997 and beyond						
353-42-4	Boron triflouride compound with methyl ether (1:1)					
10049-04-4	Chlorine dioxide					
4170-30-3	Crotonaldehyde					
123-73-9	Crotonaldehyde, (E)					
108-91-8	Cyclohexylamine					
106-89-8	Epichlorohydrin					
107-15-3	Ethylenediamine					
110-00-9	Furan					

13463-40-6	Iron, pentacarbonyl-					
78-82-0	Isobutyronitrile					
126-98-7	Methacrylonitrile					
79-22-1	Methyl chloroformate					
556-64-9	Methyl thiocyanate					
75-79-6	Methyltrichlorosilane					
13463-39-3	Nickel carbonyl					
10102-43-9	Nitric oxide					
8014-95-7	Oleum					
594-42-3	Perchloromethylmercaptan					
10025-87-3	Phosphorus oxychloride					
7719-12-2	Phosphorus trichloride					
110-89-4	Piperidine					
107-12-0	Propionitrile					
109-61-5	Propyl chloroformate					
75-55-8	Propyleneimine					
7783-60-0	Sulfur tetrafluoride					
75-74-1	Tetramethyllead					
509-14-8	Tetranitromethane					
75-77-4	Trimethylchlorosilane					

A study was conducted to assess the concentration-response of effects resulting from single HF exposures which were 2 or 10 minutes in duration. (Dalbey, W. 1996). Additional 60-minute exposures were performed for comparison.

Groups of 20 female Sprague-Dawley rats were exposed to HF for 2, 10 or 60 minutes for substudies A through Q as described in Table 1. Each group of HF-exposed animals were compared to on identical group of sham-exposed controls. Endpoints emphasized effects on the respiratory tract, the anticipated target site, but other organs were also evaluated. Ten rats were used for bronchoalveolar lavage (BAL), hematology, and serum chemistry; the remaining 10 were used for pulmonary function tests, histopathology, and organ weights. All animals were observed for clinical signs of toxicity immediately after exposure and before sacrifice on the following day. Based on preliminary results, sacrifice at ~1 day after exposure provided data on the time of peak effects from HF. One substudy (I) was included to follow possible progression of any lesions observed on the day after exposure; half of the animals were sacrificed at both 3 and 14 weeks after exposure. Substudies R-U were performed solely for assessing mortality. Nose breathing rats (plus mouth-breathing animals in substudies R and T) were not sacrificed on the day after exposure, but were observed for 2 weeks instead. Mortality in these groups was compared to published data on nose-breathing rats and also allowed direct comparison of mouth-breathing and nose-breathing groups.

Table 1
Exposure Regimen for the Study by Dalbey (1996)

	Duration of Exposure to HF		
PPM x MIN	**2 MINUTES**	**10 Minutes**	**60 Minutes**
~1,200	0 - 593 ppm	N - 135 ppm	Q - 20 ppm
~2,800	L - 1589 ppm	K - 271 ppm	M - 34 ppm J - 48 ppm
~4,000			H - ~74 ppm
~9,500	E - 4887 ppm	B - 950 ppm	
14,000	G-6392 ppm	I - 1454 ppm (recovery)	
~17,000	D-8621 ppm	F - 1669 ppm A - 1764 ppm	
38,470		R - 3847 ppm	
~70,000		T - 7014 ppm	U - 1224 ppm
122,340			S - 2039 ppm

All groups are mouth-breathing (i.e., exposed via oral cannula) except the nose-breathing groups indicated by underlining.

Concentration-related mortality was noted with 2-minute exposures of 4887 ppm HF or greater and with 10-minute exposures of 1764 ppm for mouth-breathing animals. In nose-breathing animals, no HF-related mortality occurred with concentrations as high as >7,000 ppm for 10-minute exposures and there was only 10% mortality with 2,039 ppm for 60 minutes, although many of the surviving animals were virtually moribund.

The primary sites of damage following acute mouth-breathing exposures appeared to be limited to the respiratory tract, particularly the trachea and bronchi. There was also evidence of effects in the lower lung with mouth-breathing exposure to the highest concentrations of HF. With nose-breathing groups, the effects were generally limited to the nose; apparently the HF did not pass through the nose in sufficient amounts to affect the posterior sections of the respiratory tract. The ventral meatus was the site most affected in nose-breathing animals, followed by the nasoturbinates. The nasal septum was least affected. Necrosis and acute inflammation were noted in the nose; fibrinopurulent exudate was not. No significant lesions were noted in other organs microscopically and no changes were observed in most of the other endpoints.

A definite concentration-response was observed in mouth breathing rats exposed for 2-minutes to HF. At 8621 and 4887 ppm, mortality was observed in 1/20 and 2/20 animals, respectively. Other evidence of serious toxicological effects observed in animals in these groups included evidence of histopathological damage in the lung (e.g., necrosis of the bronchial mucosa). Transient effects, including changes in BAL indices and flow at 25% FVC during forced exhalation were observed at 1589 ppm. Histopathological effects in the mid-trachea were also observed at this concentration. However, similar marginal effects in terms of incidence and severity were also observed in controls and may have resulted from cannulation. No effects were observed at 593 ppm.

A concentration-response was also observed in mouth breathing rats exposed for 10 minutes to HF. Treatment-related mortality in 1/20 animals and serious toxicological effects, including histopathological damage in the lung and trachea, were observed at 1764 ppm. At 950 ppm, small increases in myeloperoxidase and PMNs in the BAL were observed along with histologic changes in the trachea. These morphological changes were marginal, being similar in incidence and severity to controls. No treatment-related effects were observed at 271 ppm.

In mouth breathing rats exposed to HF for 60 minutes , minor increases in lung volumes were observed across the upper part of the deflation pressure-volume curve. No histologic changes were noted in the respiratory tract and it was not clear that the change in the PV curve was an adverse effect. No effects were observed at 20 ppm for 60 minutes.

In nose breathing rats exposed to 1669 ppm for 10 minutes (substudy "F"), a 67% and 69% decreased in respiratory rate was observed during the first minute of exposure and at 6 minutes of exposure, respectively. An increase in compliance and decrease in pulmonary resistance were also observed; other pulmonary function measures were not effected. Red nasal discharge was observed in 7/20 animals in this group. Histologic findings included hemorrhage, inflammation, and necrosis in the nasal septum, nasoturbinates, and ventral meatus. No histologic effects were observed in the lung. All twenty animals survived the exposure.

In substudy "I" on recovery, the effects of HF noted at the 1-day sacrifices were not observed in the animals at either sacrifice at 3 or 14 weeks after exposure. However, the weights of the liver, spleen, and thymus were decreased at week 3, but not at week 14. These significant differences were associated with a significant decrease in the mean body weight compared to controls. The acute lesions essentially had resolved and the tissues appeared to be repaired following the recovery period.

Reference

Dalbey, W. (1996). Evaluation of the Toxicity of Hydrogen Fluoride at Short Exposures Times. Petroleum Environmental Research Foundation Report 92-09.

PROPOSED 10-MINUTE AEGL-2 FOR HF
AEGL COMMITTEE MEETING

December 16, 1996

L. A. Gephart

96MR 1047

SELECTION OF KEY STUDY

- RECOMMEND STUDY IN RATS REPORTED BY DALBY (1996)
  - Designed to evaluate AEGL-2 effects
  - Included 10-minute exposures
  - Employed sensitive model (cannulated rat)
  - Included multiple, sensitive biological endpoints
    - + Pulmonary function
    - + Bronchoalveolar lavage
    - + Hematology and serum chemistry
    - + Histopathology
    - + Nasal resistance (nose breathing groups)

RESULTS

- SERIOUS EFFECTS OBSERVED AT 1764 PPM
  - Histopathological effects in the lung
  - Pronounced function/biochemical alterations
- MARGINAL EFFECTS AT 950 PPM
  - No histopathological changes in the lungs or bronchi
  - Histological changes in trachea similar to control
  - Functional/biochemical changes minimal
- THRESHOLD FOR SERIOUS EFFECTS AT ~ 1300 PPM

UNCERTAINTY FACTOR CONSIDERATIONS

- ARE WE USING A THRESHOLD, OR A NOAEL?
  - We are using a NOAEL (950 ppm)
- DO WE HAVE INFORMATION ON A SINGLE SPECIES OR FOR MULTIPLE SPECIES?
  - We have data for multiple species
- ARE THE DATA CONSISTENT ACROSS SPECIES?
  - When differences due to exposure measurement are accounted for, the data are fairly consistent across species
- DO WE EXPECT MAN TO BE UNIQUELY MORE OR LESS SENSITIVE THAN THE TEST SPECIES?
  - No - Lab animals and humans respond similarly to respiratory irritants; cannulation used to simulate human mouth breathing

UNCERTAINTY FACTOR CONSIDERATIONS (cont'd)

- IS THE ENDPOINT ACCURATELY DEFINED BY OUR DEFINITION OR IS IT A MORE OR LESS SERIOUS EFFECT?
  - The endpoint used meets our definition i.e. a NOAEL from a study designed to assess AEGL 2 effects - the endpoints evaluated included extensive lung histology, pulmonary function, etc.
- WAS THE STUDY ON WHICH THE AEGLs WERE BASED WELL-DESIGNED, CONDUCTED AND REPORTED?
  - Yes, the study was designed to establish short-term AEGLs and we have the full report
- DO WE NEED TO EXTRAPOLATE THE EXPOSURE DURATION?
  - No, the study exposure duration = AEGL time frame

CONCLUSIONS

- CONDITIONS SUPPORT USE OF LOWER UNCERTAINTY FACTOR
  - Used NOAEL rather than a threshold
  - Have data for multiple species and results are consistent
  - Endpoint of concern has lower response variability
  - Used data from cannulated animal
  - Used data from a study that was well-designed and reported
  - Did not need to extrapolate
- UNCERTAINTY FACTOR RECOMMENDATION
  - 3X intra-species UF
  - 3X intra-species UF
  - 10X total UF
- 10-MINUTE AEGL-2 RECOMMENDATION
  - 130 ppm (if based on "threshold" for serious effects
  - 95 ppm (if based on NOAEL)

HF

PROPOSED 10-MINUTE AEGL-3

- Threshold for lethality ≈ 1764 ppm (Dalbey, 1996)
  - 1/20 animals exposed for 10 minutes via oral cannula died

- No deaths in nasal breathing animals exposed for 10-minutes to 1669 ppm, and 1454 ppm (recovery group)

- Other supporting data
  - 5-min LC_{10} in rats: 12, 440 ppm (Higgins, 1972)
  - 5-min LC_{50} in rats: 14, 640 ppm (Haskell, 1988)

- Apply 10 x Uncertainty Factor to 1700

- AEGL-3 = 170 ppm

A 10-MINUTE "AEGL-2" FOR HF DERIVED FROM PERF PROJECT 92-09

Presented to the AEGL Committee, December, 1996

by Walden Dalbey, Ph.D., DABT
Product Stewardship and Toxicology, Mobil

Developed in january, 1996, by Representatives of AlliedSignal, CITGO, Elf Atochem North America, Exxon, Mobil, Phillips, Texaco

Attachment 6

EXPERIMENTAL DESIGN TO EVALUATE NONLETHAL EFFECTS OF HF

	Duration of Exposure		
	2 Min.	10 Min.	60 Min
Mouth-Breathing	593 ppm	135 ppm	20 ppm
	1589 ppm	271 ppm	48 ppm
	4887 ppm	950 ppm	
	8621 ppm	1764 ppm	
Nose-Breathing	6392 ppm	1669 ppm	34 ppm
MB Recovery		1454 ppm	
Mortality	3847 ppm*	1224 ppm	
	7014 ppm*	2039 ppm	

NB underlined, others MB
20 control and 20 exposed female rats/substudy
Sacrifice on day following exposure except recovery (3 and 14 wk) and mortality (2 wk)
* MB and NB exposed simultaneously

ENDPOINTS FOLLOWING EXPOSURE TO HF

- BREATHING FREQUENCY AND RELATIVE TIDAL VOLUME DURING EXPOSURE

- NASAL RESISTANCE (NB GROUPS)

- PULMONARY FUNCTION:
  - PULMONARY RESISTANCE
  - LUNG VOLUMES
  - CO DIFFUSING CAPACITY
  - QUASISTATIC PRESSURE-VOLUME CURVES
  - MAXIMAL FORCED EXHALATION

- BRONCHOALVEOLAR LAVAGE:
  - LAVAGED CELLS
  - G-6-PDH
  - ACID PHOSPHATASE
  - MYELOPEROXIDASE
  - SIALIC ACID
  - LDH
  - ALK. PHOSPHATASE
  - β-GLUCURONIDASE
  - PROTEIN

- HEMATOLOGY, SERUM CHEMISTRY, STANDARD NECROPSY AND 7 ORGAN WEIGHTS

- HISTOPATHOLOGY OF RESPIRATORY TRACT AND MAJOR ORGANS

DERIVATION OF "SHORT-TERM EXPOSURE VALUE" FOR 10 MIN

- BASED ON DEFINITION OF ERPG-2 / AEGL-2

- TWO SEPARATE STEPS
  - DEFINE CONCENTRATION CAUSING "SERIOUS" EFFECT WITH 10-MIN EXPOSURE
  - DIVIDE THAT CONCENTRATION BY UNCERTAINTY FACTORS (UF) TO EXTRAPOLATE TO PEOPLE

EXAMPLES OF DATA RELATED TO CONCENTRATION CAUSING "SERIOUS" EFFECTS

1,764 PPM

5% MORTALITY

BAL PROTEIN ↑ 664%, LDH ↑ 36%, SIALIC ACID ↑ 549%, MPO ↑ 3083%, PMNs ↑ 1971%

Fmax/FVC ↓ 22%, FEV0.1/FVC ↓ 22%

WET LUNG WEIGHT ↑ 21%, THYMUS ↓ 28%

TRACHEA: FIBRINOPURULENT EXUDATE, ACUTE INFLAMMATION, AND MUCOSAL NECROSIS

LUNG: ACUTE FOCAL ALVEOLITIS, FOCAL NECROSIS OF BRONCHIAL MUCOSA

950 PPM

NO MORTALITY

BAL PROTEIN ↑ 174%, MPO ↑ 201%, PMNs ↑ 161%

OTHER ENDPOINTS ~ CONTROLS

271 PPM

NO TREATMENT-RELATED EFFECTS

ESTIMATED THRESHOLD CONCENTRATION FOR SERIOUS EFFECTS

- DEFINITE SERIOUS EFFECTS AT 1,764 PPM
  - PRONOUNCED FUNCTIONAL/BIOCHEMICAL ALTERATIONS
  - SEVERE HISTOPATHOLOGICAL EFFECTS BEYOND POINT OF ENTRY
  - UNEQUIVOCAL TREATMENT-RELATED LESIONS IN TRACHEA
- MARGINAL EFFECTS AT 950 PPM
  - NO DETECTABLE INVOLVEMENT OF LUNGS OR BRONCHI
  - FUNCTIONAL/BIOCHEMICAL CHANGES RELATIVELY MARGINAL
  - HISTOLOGICAL CHANGES IN TRACHEA NEAR CONTROL
- THRESHOLD ESTIMATED AS ARITHMETIC MEAN: 1,357 PPM
- CORROBORATED BY EXPOSURE TO 1,454 PPM AND EVALUATION AT 3 AND 14 WEEKS WITH NO ADVERSE EFFECTS.... NO LASTING EFFECTS EXPECTED WITH 1,357 PPM

UNCERTAINTY FACTOR FOR TIME = 1

- 10-MINUTE LAB EXPOSURES = 10-MINUTE ACCIDENTAL EXPOSURES

UNCERTAINTY FACTOR FOR INTERSPECIES DIFFERENCES = 3

- PRIMARY IRRITANT WITHOUT METABOLIC ACTIVATION: REDUCED INTERSPECIES DIFFERENCES
- PUBLISHED LC50s ~ SAME ACROSS SPECIES, INCLUDING PRIMATES.
- MEASURED ENDPOINTS REFLECT CLINICAL CHANGES OF CONCERN IN PEOPLE. EXTRAPOLATION IS DIRECT, NOT FROM LETHALITY TO CLINICAL CHANGES.
- UF OF 3 WAS CHOSEN (RATHER THAN 1) TO BE CONSERVATIVE.

UNCERTAINTY FACTOR FOR INTRASPECIES DIFFERENCES ~3 WITH MB MODEL

- MB MODEL REPRESENTS A RELATIVELY SENSITIVE INDIVIDUAL BECAUSE OF DIRECT DELIVERY OF HF TO TRACHEA.
- PROTECTIVE SCRUBBING ACTION OF NOSE AND/OR MOUTH ELIMINATED
- REFLEX DEPRESSION OF RESPIRATION DURING EXPOSURE TO AN IRRITANT WAS ELIMINATED, MAXIMIZING DOSE TO THE RESPIRATORY TRACT
- ANIMALS WERE NOT ANESTHETIZED DURING EXPOSURE. BREATHING AND CONSEQUENT DEPOSITION OF HF WERE NOT DEPRESSED.
- MB ANIMALS WERE MORE SENSITIVE THAN NB IN TERMS OF MORTALITY AND MEASURED ENDPOINTS. BY INFERENCE, SENSITIVITY IS GREATER THAN MOST OTHER SPECIES FOR MORTALITY.

THRESHOLD OF SERIOUS EFFECTS / AGGREGATE UF OF 10 = PROPOSED VALUE

- UF FOR INTERSPECIES AND INTRASPECIES DIFFERENCES TOGETHER = 10
- 1,357 PPM / 10 ~ 130 PPM
- VALUE OF 130 PPM DOES NOT IMPLY LACK OF IRRITATION DURING OR AFTER EXPOSURE.
- MOST PEOPLE SHOULD NOT HAVE "SERIOUS" OR IRREVERSIBLE DAMAGE.

ACUTE EXPOSURE GUIDELINE LEVELS (AEGLs) FOR AMMONIA

PRELIMINARY REPORT

PREPARED BY

KOWETHA A. DAVIDSON, Ph.D., D.A.B.T.
OAK RIDGE NATIONAL LABORATORY
OAK RIDGE, TENNESSEE

DECEMBER 1996

Managed by Lockheed Martin Energy Research Corporation, for the U.S. Department of Energy under Contract No. DE-AC05-84OR21400

Attachment 7

PROPOSED AEGL VALUES FOR AMMONIA

Classification	Exposure Duration					Endpoint (Reference)
	5 min	30 min	1 hour	4 hours	8 hours	
AEGL-3 (lethality)	3400 ppm (2380 mg/m^3)	1400 ppm (980 mg/m^3)	990 ppm (693 mg/m^3)	300 ppm (210 mg/m^3)	200 ppm (140 mg/m^3)	Lethality/LC_{50} (entire database)
	4000 ppm* (2800 mg/m^3)	1700 ppm (1190 mg/m^3)	1200 ppm (840 mg/m^3)	same	same	
AEGL-2 (disabling)	340 ppm (238 mg/m^3)	140 ppm (98 mg/m^3)	100 ppm (70 mg/m^3)	50 ppm (35 mg/m^3)	35 ppm (25 mg/m^3)	Offensive odor, intolerable irritation (entire database)
	500 ppm* (350 mg/m^3)	200 ppm (140 mg/m^3)	150 ppm (105 mg/m^3)	75 ppm (53 mg/m^3)	50 ppm (35 mg/m^3)	Irritation to eyes, nose, throat, chest, offensive odor (entire database)
AEGL-1 (nondisabling)	25 ppm (18 mg/m^3)	25 ppm (18 mg/m^3)	25 ppm (23 mg/m^3)	25 ppm (23 mg/m^3)	25 ppm (23 mg/m^3)	Odor detection

*Values proposed in first draft (April 1996) with addition of 5-min values

COMPARISON OF ACUTE LETHALITY (LC_{50}) DATA IN DIFFERENT SPECIES						
Species	LC_{50} ©		Exp. Time (t)	$C^{2.02} \times t$		Reference
	mg/m^3	ppm		$mg/m^3 \cdot min$	ppm • min	
Rat	28,130	39,382	10 min	9.71E+09	1.92E+10	Appelman et al., 1982
Mouse	7,060	9,884	10 min	5.95E+08	1.17E+09	Silver and McGrath, 1948
Rat	19,960	27,944	20 min	9.71E+09	1.92E+10	Appelman et al., 1982
Mouse	21,430	30,002	30 min	1.68E+10	3.32E+10	Hilado et al., 1978
Rat	14,170	19,838	40 min	9.72E+09	1.92E+10	Appelman et al., 1982
Rat	11,590	16,226	60 min	9.72E+09	1.92E+10	Appelman et al., 1982
Mouse	4,230	5,922	60 min	1.27E+09	2.50EE+09	Kapeghian et al., 1982

LOWEST EXPERIMENTAL CONCENTRATIONS CAUSING DEATH				
Species	Concentration (ppm)	Exposure time (min)	% Mortality	Reference
Mouse	8,723	10	25	Silver and McGrath, 1948
Mouse	19,048	30	25	Hilado et al., 1977
Mouse	3,950	60	25	Kapeghian et al., 1982
Mouse	4,380	240[a]	25	Kapeghian et al., 1985
Rat	33,433	10	10	Appelman et al., 1982
Rat	26,155	20	30	Appelman et al., 1982
Rat	18,047	40	20	Appelman et al., 1982
Rat	14,114	60	30	Appelman et al., 1982
Cat	1,000	10	5	Dodd and Gross, 1980

[a]No observation period after exposure.

ESTIMATES OF LETHAL CONCENTRATIONS OF AMMONIA BASED ON ANIMAL DATA					
Probability of Mortality	Species	Exposure Time (min)	Experimental Concentration[a]		HEC[b]
			mg/m^3	ppm	ppm
0.1 (LC_{10})	Rat	5	30,092	43,032	119,199
		30	12,380	17,703	49,037
		60	8,780	12,555	34,777
		240	4,416	6,315	17,493
		480	24,025	4,479	12,407
0.01 (LC_{01})	Rat	5		34,356	95,166
		30	9,884	14,134	39,151
		60	7,010	10,024	27,766
		240	3,526	5,042	13,966
		480	2,500	3,575	9,903
0.001 ($LC_{0.1}$)	Rat	5	20,378	29,141	80,721
		30	8,384	11,989	33,210
		60	5,945	8,501	23,548
		240	2,990	4,276	11,845
		480	2,121	3,033	8,401

ESTIMATES OF LETHAL CONCENTRATIONS OF AMMONIA BASED ON ANIMAL DATA (Continued)					
Probability of Mortality	Species	Exposure Time (min)	Experimental Concentration [a]		HEC[b]
			mg/m^3	ppm	ppm
0.1 (LC_{10})	Mouse	5	8,169	11,682	33,930
		30	3,421	4,892	14,209
		60	2,443	3,493	10,145
		240	1,246	1,782	5,176
		480	890	1,273	3,697
0.01 (LC_{01})	Mouse	5	6,853	9,800	28,464
		30	2,870	4,104	11,920
		60	2,050	2,932	8,516
		240	1,045	1,494	4,339
		480	746	1,067	3,099
0.001 ($LC_{0.1}$)	Mouse	5	6,028	8,620	25,037
		30	2,525	3,611	10,488
		60	1,803	2,578	7,488
		240	919	1,314	3,816
		480	656	938	2,724

FOOTNOTES

[a]Concentration derived using ten Berge et al. (1986) regression coefficients: b_0 = 47.8, b_1 = 4.64, and b_2 = 2.30 (rat); b_0 = 54.5, b_1 = 5.95, and b_2 = 2.89 (mouse).
[b]HEC (human equivalent concentration) calculated based on regional gas dose ratio (RGDR) , which is the ratio of the minute volume/surface area of the pulmonary region for animals and humans; min. vol. =13.8 L/min for human, 236.96 mL/min for the rat, and 34.94 mL/min for the mouse, pulmonary surface area = 54 m^2 for humans, 0.34 m^2 for the rat, and 0.05 m^2 for the mouse.

RATIONALE FOR USING THE RAT DATA TO DERIVE AGEL-3 VALUES

- Substantial uncertainties are associated estimating exposures from gas dispersion models.
- The Kapeghian et al. (1982) mouse study was well-conducted using adequate numbers of animals exposed for only one duration (60 min); the Appelman et al (1982) rat study was also well-conducted using adequate numbers of animals exposed four durations (10, 20, 40, and 60 min).
- Because mice appear to be more sensitive than other mammalian species to respiratory irritants, there is some doubt that the mouse is the most relevant species to use for estimating mortality responses in humans.

RATIONALE FOR USING THE MOUSE DATA TO DERIVE AGEL-3 VALUES

- Substantial uncertainties are associated estimating exposures from gas dispersion models
- ten Berge et al. (1986) combined two mouse studies (Silver and McGrath, 1948; Kapeghian et al., 1982) to derive their regression coefficients.
- The mouse is the most sensitive species, and the relative sensitivity of humans to rodents is unknown.
- Dosimetric adjustment of exposure concentrations is not used
- An interspecies uncertainty factor is not used

AEGL-3 VALUES DERIVED USING RAT AND MOUSE DATA					
	Concentration (ppm)				
	5 min	30 min	1 hour	4 hours	8 hours
Mouse data, LC_{01}, no HEC adj., UF = 3	3,267	1,368	977	498	356
Rat data, $LC_{0.1}$, HEC, UF = 20	4,036	1,661	1,177	592	420
Rat data, LC_{01}, HEC, UF = 30	3,172	1,305	925	466	330
Rat data, LC_{10}, HEC, UF = 30	3,973	1,635	1,159	583	414

SUMMARY OF NONDISABLING AND REVERSIBLE EFFECTS OF INHALING AMMONIA			
Conc.	Duration of Exposure	Effect[a]	Reference
30 ppm	10 min	moderately intense to penetrating odor; barely detectable irritation	MacEwen, 1970
34 ppm	5 min	nasal dryness	Industrial Bio-Test Lab, 1973
50 ppm	5 min	nasal dryness	Industrial Bio-Test Lab, 1973
50 ppm	10 min	highly penetrating odor; moderate irritation	MacEwen, 1970
50 ppm	30 min	moderately intense odor; moderate irritation to eyes and nose, mild irritation to throat and chest, slight urge to cough, slight general discomfort	Verberk, 1977
50 ppm	1 h	highly intense odor; moderate irritation to eyes, nose, throat, and chest, mild urge to cough, slight general discomfort	Verberk, 1977
50 ppm	2 h	highly intense odor; moderate irritation to eyes, nose, throat, and chest, mild urge to cough, mild general discomfort	Verberk, 1977
72 ppm	5 min	nasal, eye, and throat irritation	Industrial Bio-Test Lab, 1973
80 ppm	30 min	highly intense odor; highly intense eye and nose irritation, moderate throat and chest irritation; mild urge to cough, moderate general discomfort	Verberk, 1977
80 ppm	1 h	highly intense odor; moderate eye, nose, throat, and chest irritation, mild urge to cough, moderate general discomfort	Verberk, 1977
80 ppm	2 h	highly intense odor; highly intense eye, nose, throat, and chest irritation, highly intense urge to cough, and moderate general discomfort	Verberk, 1977

SUMMARY OF NONDISABLING AND REVERSIBLE EFFECTS OF INHALING AMMONIA (Continued)			
Conc.	Duration of Exposure	Effect	Reference
110 ppm	30 min	highly intense odor; highly intense eye, nose, throat, and chest irritation, mild urge to cough, moderate general discomfort	Verberk, 1977
110 ppm	1 h	highly intense odor; highly intense eye, nose, throat, and chest irritation, moderate urge to cough, moderate general discomfort	Verberk, 1977
110 ppm	2 h	highly intense odor; highly intense eye, nose, throat, chest irritation, urge to cough, and general discomfort	Verberk, 1977
140 ppm	30 min	highly intense odor; unbearable eye, nose, throat, and chest irritation, mild urge to cough, moderate general discomfort	Verberk, 1977
140 ppm	1 h	highly intense odor; unbearable eye, nose, throat, and chest irritation, moderate urge to cough, moderate general discomfort	Verberk, 1977
140 ppm	2 h	highly intense odor; unbearable eye and nose, highly intense throat and chest irritation, highly intense urge to cough, unbearable general discomfort	Verberk, 1977
143 ppm	5 min	nose, eye, throat, and chest irritation, lacrimation	Indust. Bio-Test Lab, 1973
500 ppm	15-30 min	nose and throat irritation, nasal dryness and stuffiness, excessive lacrimation, hyperventilation, unbearable	Silverman et al., 1949
570 ppm	single breath	threshold for reflex glottis closure, 21-30-year old subjects	Erskine et al., 1993
1000 ppm	single breath	threshold for reflex glottis closure, 60-year old subjects	Erskine et al., 1993
1000 ppm	NR	immediate urge to cough	Silverman et al., 1949
1790 ppm	single breath	threshold for reflex glottis closure, 86-90-year old subjects	Erskine et al., 1993

RATIONALE FOR RECOMMENDING 150 PPM AS THE AEGL-2, 60-MIN VALUE

- The nonexpert subjects exposed to 140 ppm for 60 min were not disabled.
- The subjects who left the exposure chamber required no assistance to do so.
- Irritant effects of exposure were reversed immediately upon termination of exposure, and there were no effects on respiratory function
- None of the nonexpert subjects exposed to 110 ppm left the exposure chamber before the 2-hour termination of the study, although some reported their perception of eye, nose, and throat irritation as offensive (4 on a scale of 0-5).

RATIONALE FOR RECOMMENDING 100 PPM AS THE AEGL-2, 60-MIN VALUE

- Some of the nonexpert subjects exposed to 140 ppm left the exposure chamber in less than 60 min.
- Some of the nonexpert subjects exposed to 140 ppm reported their perception of eye, nose, and throat as unbearable (5 on a scale of 0-5).
- Some of the nonexpert subjects exposed to 110 ppm reported their perception of eye, nose, and throat as offensive (4 on a scale of 0-5).

Robert A. Michaels, PhD, CEP, President
Toxicology & Risk Assessment Consulting

Residual Issues of Ammonia Emergency Planning: Comments by Robert A. Michaels to *the National Advisory Committee on Acute Exposure Guideline Levels*

15 November 1996

RAM TRAC Corporation

Project Director:

Robert A. Michaels, PhD, CEP
Board Certified Environmental Assessor
Chair, ABCEP Certification Review Board
Elected Life Member, New York Academy of Sciences
Admitted Member, American College of Toxicology
Admitted Member, Society of Toxicology

AEGL-3

Appropriate Role of Accident Reconstruction Data

Page 38 of ORNL's September draft, titled *"Acute Exposure Guideline Levels (AEGLs) for Ammonia"* states that *"[b]ecause of the uncertainties associated with gas dispersion models, animal data are preferred over the estimate from the gas dispersion models for deriving AEGL-3 values."* However, gas dispersion modeling is used routinely to predict exposure levels for permit applications and other purposes, because such modeling can and does incorporate factors to account for inevitable uncertainties about exposure levels. Further, use of such models to predict exposure prospectively vs. retrospectively is a distinction without a difference. Moreover, the degree of uncertainty associated with using gas dispersion models should diminish as the modeled concentrations increase, giving more confidence in the Potchefstroom ammonia levels than in, say, trace factory emissions modeled over a full year or longer. Thus, at the highest concentration levels, HGSYSTEM gives equal values for the upper and lower concentration range, reflecting relatively little uncertainty, and greater differences between upper- vs. lower-bound concentrations in the lower concentration ranges.

Nonetheless, I have not argued that the Potchefstroom accident reconstruction data are of sufficiently high quality to be used to derive AEGL-3 values. Rather, I have argued that numerous sources of data are available, but that each considered individually is inadequate. Consequently, I have examined multiple, independent data sources.[1] This weight-of-evidence approach is standard for the U. S. EPA. It reflects the validity of using studies which are individually questionable in a meta-analysis to strengthen the conclusions that might be drawn from individual, imperfect, and often mutually inconsistent studies. In my view, the appropriate role of accident reconstruction data is to add meta-analytic strength to other lines of evidence which are not definitive individually.

In precisely this context, accident reconstruction data were endorsed by ORNL and NAC AEGL when, at first, the data appeared to lend consistency to the ORNL use of animal bioassay data to derive AEGL-3 values. Only when I upwardly corrected the WHAZAN model results based upon using HGSYSTEM did criticism of gas dispersion modeling develop. Indeed, a recurrent theme in

[1] George Alexeef of NAC AEGL suggested that the rat bioassay data and accident reconstruction data might not be truly independent because both were derived by members of the same research team. The attempt of a research team to corroborate conclusions drawn from one line of evidence by testing a hypothesis using another line of evidence does not undermine the independence of the two lines of evidence. Rather, it illustrates the willingness of the research team to place its conclusions in jeopardy, so that if they emerge unscathed, they will be objectively stronger.

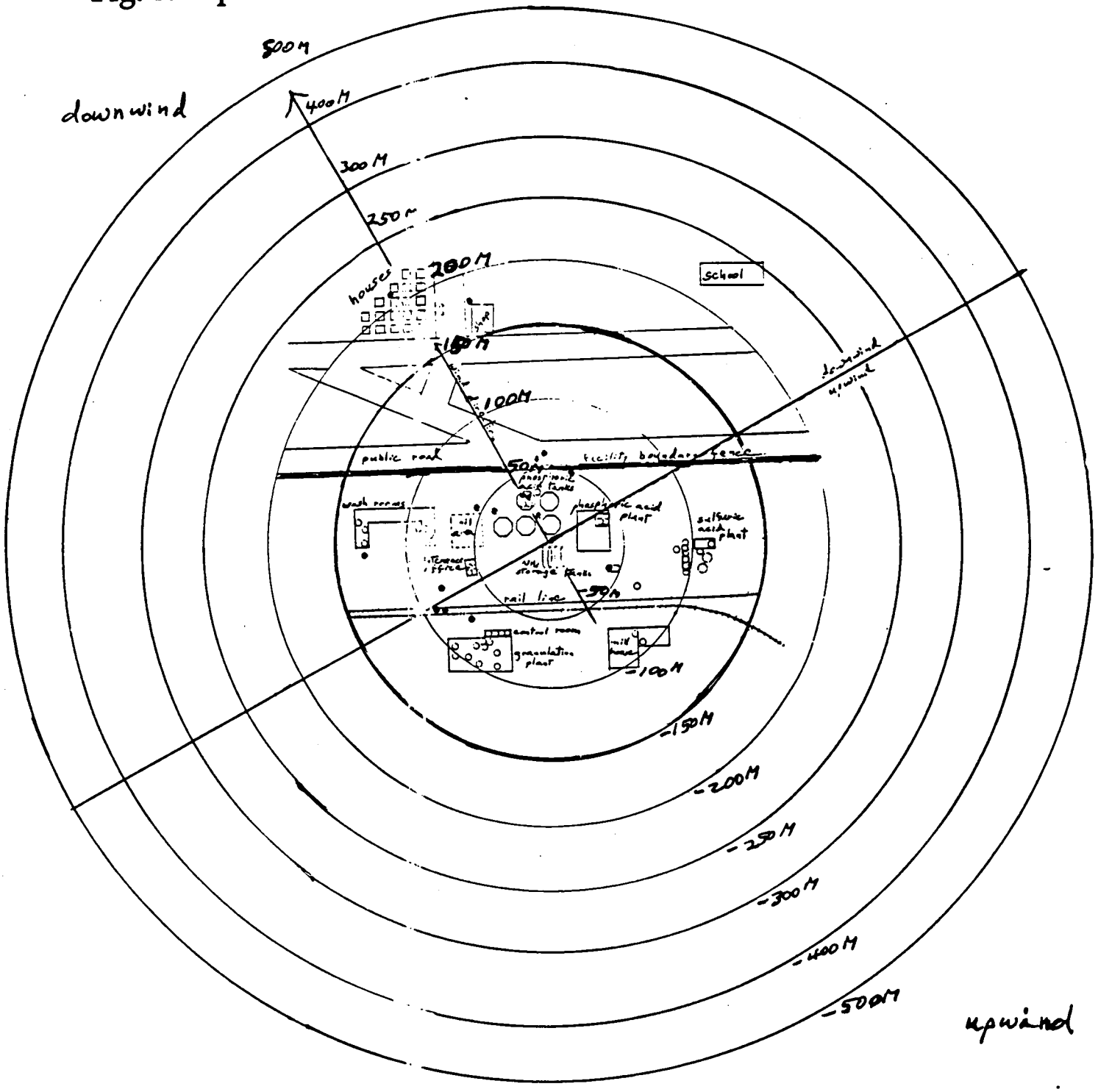
ORNL's September draft document objects to RAM TRAC's use of gas dispersion modeling results to calculate an LC_{50} value without taking into consideration the fact that some individuals were indoors. However, my oral and written presentations at the September NAC AEGL meeting (and my presentations at previous NAC AEGL meetings) emphasized that I shared ORNL's concerns, and rejected use of the calculated LC_{50} value in favor of the LC_0. The LC_0 was derived based upon knowledge that people were outdoors, and that all people outdoors survived their exposure to ammonia at the modeled LC_0 concentrations. Nonetheless, to be safe, I divided the LC_0 in half based upon a 'benign bubble' scenario, which presumes that people will utilize evasive strategies to reduce their exposure to ammonia below modeled concentrations. NAC AEGL's response was that we do not know how many people were present nor, indeed, do we know if any people were present in outdoor areas further from the accident center, where the modeled LC_0 concentration was found.

Further Potchefstroom Accident Analysis

To respond to the above criticism RAM TRAC has conducted a more detailed analysis of the Potchefstroom accident. Additional information was derived from Lonsdale (1975). Lonsdale reported that an inquest was conducted into the Potchefstroom accident, and that *"about 350 people were working in the plant at the time of the incident"* (page 126). With six fatalities among members of the general public, this brings the presumed minimum number of people present to 356, assuming that no members of the general public were present except those (six individuals) who died. This is a conservative assumption, given that the fatality rate among employees equaled 3.4 percent (18 - 6 = 12; 12/350 = 3.4 percent). If members of the general public suffered the same 3.4-percent fatality rate as employees generally located closer to the accident center, the number of members of the general public in the accident zone would be 175 (calculation: 6 fatalities/0.034 fatality rate = 175 people, including 175 - 6 = 169 survivors). Thus, a conservative estimate of the number of people in the accident zone is approximately 525 (350 + 175), including those sheltered indoors and those outdoors. However, the analysis conservatively assumes that only 356 people were present in the accident zone.

The affected area was divided into 16 accident zones, including eight upwind and eight downwind (Figure 1). Figure 1 depicts the Potchefstroom facility, bounded on one side by a fence and public road. The locations of individuals, where known, is indicated by circles, open for survivors and closed for fatalities. The numbers are approximate because of lack of clarity and possibly inconsistencies in three available accident maps. However, uncertainty about the number of employees located in a zone was compensated for in a conservative manner by distributing all such employees to the zone within the Potchefstroom plant exhibiting the lowest concentration, whereas greater dispersion of employees throughout the plant would have been more likely. Uncertainty about the distribution of members of the general public was also compensated for in a conservative manner,

Fig. 1. Upwind and Downwind Potchefstroom Accident Zones



specifically, by assuming that no such individuals were present in the affected area. This is conservative because it exclusively eliminates survivors (probably in excess of 169 survivors, as explained above) from the modeled population.

Upper-bound and lower-bound concentrations of airborne ammonia were modeled in all six zones of the Potchefstroom plant (-150 M to + 150 M), and in five of 10 zones outside the plant (150 M to 500 M). Only lower-bound ammonia concentrations are tabulated and used for the reconstruction (Table 1). Only five-minute time-weighted average (TWA) concentrations were used in the reconstruction. Inasmuch as the ammonia cloud persisted for close to 10 minutes, use of five-minute TWA concentrations requires no extrapolation beyond the modeled accident duration. The procedure is also conservative in assuming that individuals exposed to ammonia at the modeled concentrations for five minutes were exposed to clean air afterwards, whereas dispersion modeling indicates that their exposure to ammonia after five minutes would have abated gradually rather than abruptly.[2]

Table 1 also calculates probit values and expected fatality rates in each modeled zone based upon the ORNL and NAC AEGL assumption that the human dose-response curve is the same as that of mice, with Ten Berge coefficients of $b_0 = -54.5$, $b_1 = 5.95$, $b_2 = 2.89$, and $b_1/b_2 = n = 2$. A detailed analysis of available accident maps was used to quantify the number of people indoors. Half of employees whose location was unknown were assumed to be outdoors, and half indoors, though few indoor refuges appear to have been present, as indicated by available accident maps. Table 2 shows that all employees and nearly all members of the general public who were outdoors should have died if humans are as sensitive to ammonia as mice. This conclusion is based upon conservatively using only the *lower bound* concentration of ammonia estimated by the HGSYSTEM model; most probable exposure levels are higher. The number fatalities under this conservative scenario is 172 expected, compared with 18 observed. Thus, the death rate should have been a full order of magnitude higher than 18/356 observed under ORNL and NAC AEGL assumptions.

[2] A more conservative approach to distributing employees was rejected, specifically, assuming that employees either were located in the community surrounding the plant, or had escaped to the community after the explosion but before the ammonia cloud reached them. These scenarios were rejected for three reasons. First, individuals were unable to run far once the ammonia cloud was upon them. Second, Lonsdale (1975) reported that *"[t]he immediate resulting gas cloud from the failure was about 150 meters in diameter"* (page 126, emphasis added), which would have encompassed the entire plant (with a diameter of about three football field lengths). Third, escape from the plant to the community was blocked by a boundary fence along the public road, at which one individual was found dead, apparently unable to cross the barrier.

Table 1. Fatality Risks Posed By Ammonia At Inhalation Exposure Durations of 2, 5, 30, and 60 Minutes*

accident zone	fatality risk				probit value				Ten Berge regression coefficients			n
	2-min.	5-min.	30-min.	60-min.	2-min.	5-min.	30-min.	60-min.	b0	b1	b2	(b1/b2)
(meters)	...	...	...	...	...	...	...	...	...	...	...	...
-150	1.00	1.00	1.00	1.00	20.7056	23.3537	28.5319	30.5350	-54.5	5.95	2.89	2
-100	1.00	1.00	1.00	1.00	22.3837	25.0318	30.2099	32.2131	-54.5	5.95	2.89	2
-50	1.00	1.00	1.00	1.00	24.3760	27.0241	32.2023	34.2055	-54.5	5.95	2.89	2
50	1.00	1.00	1.00	1.00	24.3760	27.0241	32.2023	34.2055	-54.5	5.95	2.89	2
100	1.00	1.00	1.00	1.00	22.3837	25.0318	30.2099	32.2131	-54.5	5.95	2.89	2
150	1.00	1.00	1.00	1.00	20.7056	23.3537	28.5319	30.5350	-54.5	5.95	2.89	2
200	1.00	1.00	1.00	1.00	18.7025	21.3506	26.5288	28.5320	-54.5	5.95	2.89	2
250	1.00	1.00	1.00	1.00	16.9231	19.5712	24.7494	26.7526	-54.5	5.95	2.89	2
300	1.00	1.00	1.00	1.00	14.5425	17.1906	22.3688	24.3720	-54.5	5.95	2.89	2
400	1.00	1.00	1.00	1.00	10.5564	13.2045	18.3827	20.3859	-54.5	5.95	2.89	2
500	0.16	0.38	1.00	1.00	2.0435	4.6915	9.8697	11.8729	-54.5	5.95	2.89	2

accident zone	ammonia concentration				ammonia concentration				scaling factors			
	2-min	5-min	30-min	60-min	2-min	5-min	30-min	60-min	2-min	5-min	30-min	60-min
(meters)	mg/cu M)	mg/cu M)	mg/cu M)	mg/cu M)	(ppm)	(ppm)	(ppm)	(ppm)	...	...	...	...
-150	220,331	88,132	14,689	7,344	75,975	30,390	5,065	2,533	1	1	1	1
-100	292,119	116,847	19,475	9,737	100,729	40,292	6,715	3,358	1	1	1	1
-50	408,302	163,321	27,220	13,610	140,792	56,317	9,386	4,693	1	1	1	1
50	408,302	163,321	27,220	13,610	140,792	56,317	9,386	4,693	1	1	1	1
100	292,119	116,847	19,475	9,737	100,729	40,292	6,715	3,358	1	1	1	1
150	220,331	88,132	14,689	7,344	75,975	30,390	5,065	2,533	1	1	1	1
200	157,351	62,941	10,490	5,245	54,258	21,703	3,617	1,809	1	1	1	1
250	116,678	46,671	7,779	3,889	40,233	16,093	2,682	1,341	1	1	1	1
300	78,204	31,282	5,214	2,607	26,967	10,787	1,798	899	1	1	1	1
400	40,021	16,008	2,668	1,334	13,800	5,520	920	460	1	1	1	1
500	9,570	3,828	638	319	3,300	1,320	220	110	1	1	1	1

Table 2. Evaluation of Potchefstroom, South Africa Ammonia Release Incident Relative To Human Lethality Concentrations*

time from release	exposure duration	modeled lower-bound ammonia concentration										
(seconds)	(seconds)	(ppm)	(ppm)	(ppm)	(ppm)	(ppm)	(ppm)	(ppm)	(ppm)	(ppm)	(ppm)	(ppm)
distance from accident:	...	-150 to -100 M	-100 to -50 M	-50 to 0 M	0 to 50 M	50 to 100 M	100 to 150 M	150 to 200 M	200 to 250 M	250 to 300 M	300 to 400 M	400 to 500 M
0	...	...	...	...	...	...	...	...	...	...	...	...
5	7.5	...	...	641,000	641,000	...	...	...	...	...	...	...
15	12.5	...	365,000	365,000	365,000	365,000	...	...	...	...	...	...
30	17.5	220,000	220,000	220,000	220,000	220,000	220,000	...	...	...	...	...
50	15	136,000	136,000	136,000	136,000	136,000	136,000	136,000	...	...	...	...
60	15	109,000	109,000	109,000	109,000	109,000	109,000	109,000	...	...	...	...
80	20	79,600	79,600	79,600	79,600	79,600	79,600	79,600	79,600	...	...	...
100	20	62,200	62,200	62,200	62,200	62,200	62,200	62,200	62,200	62,200	...	...
120	40	49,800	49,800	49,800	49,800	49,800	49,800	49,800	49,800	49,800	...	...
180	60	25,300	28,100	28,100	28,100	28,100	28,100	28,100	28,100	28,100	27600	...
240	60	...	4,200	14,100	15,800	15,800	15,800	15,800	15,800	15,800	15800	6600
300	60	...	...	1,100	7,600	8,900	9,100	9,100	9,100	9,100	9100	8700
360	60	...	...	...	1,300	2,900	4,400	5,400	5,800	5,900	5900	5900
420	60	...	...	...	...	...	1,100	1,900	2,800	3,400	4000	4100
480	60	...	...	...	...	...	...	...	...	1,300	2300	2900
540	60	...	...	...	...	...	...	...	...	...	...	1500
600	60	...	...	...	...	...	...	...	...	...	...	...
660	60	...	...	...	...	...	...	...	...	...	...	...
720	...	...	...	...	...	...	...	...	...	...	...	...

time-weighted average (twa) ammonia concentrations

initial exposure	(sec.)	67.5	60	67.5	67.5	60	67.5	70	80	60	60	60
twa	(ppm)	135,067	201,458	250,296	250,296	201,458	135,067	93,014	60,350	53,933	27,600	6,600
total exposure	(sec.)	188	260	328	388	380	428	410	380	420	360	360
twa	(ppm)	73,979	72,513	74,263	64,235	53,309	37,106	29,563	22,432	16,790	10,783	4,950
peak	(ppm)	220,000	365,000	641,000	641,000	365,000	220,000	136,000	79,600	62,200	27,600	8,700
1-minute	(ppm)	151,950	201,458	281,583	281,583	201,458	151,950	108,517	80,467	53,933	27,600	6,600
2-minute	(ppm)	75,975	100,729	140,792	140,792	100,729	75,975	54,258	40,233	26,967	13,800	3,300
5-minute	(ppm)	30,390	40,292	56,317	56,317	40,292	30,390	21,703	16,093	10,787	5,520	1,320
30-minute	(ppm)	5,065	6,715	9,386	9,386	6,715	5,065	3,617	2,682	1,798	920	220
60-minute	(ppm)	2,533	3,358	4,693	4,693	3,358	2,533	1,809	1,341	899	460	110

analysis of fatality risks, by zone

peak conc. mortality risk	...	...	...	...	...	...	...	...	...	...	...	...
2-min. mortality risk	...	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.16
5-min. mortality risk	...	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.38
30-min. mortality risk	...	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
60-min. mortality risk	...	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
estimated number exposed	356	293	25	5	5	12	8	3	5	0	0	0
fraction outdoors	0.48	0.50	0.20	0.20	1.00	0.42	0.50	0.50	0.50	0.50	0.50	0.50
number outdoors	172	146	5	1	5	5	4	3	3	0	0	0
number of fatalities	172	146	5	1	5	5	4	3	2	0	0	0
fatality rate**	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	...	...	...
number injured/hospitalized	65	...	...	...	...	...	...	...	...	...	...	...
injury rate**	0.18	(relative to total exposed)			...	...	...	...	...	...	...	...
injury rate**	0.38	(relative to number outdoors)			...	...	...	...	...	...	...	...

*Assumes Ten Berge coefficient n = 2 for humans, as reported for mice and rats.

**Fatality rate based upon individuals outdoors; injury rates based upon individuals outdoors (0.38) or indoors plus outdoors (0.18).

Changes Needed To ORNL Document

Mulder and Van der Zalm. ORNL states that the report of Mulder and Van der Zalm (1967) estimates the lethal concentration of ammonia to be 10,000 ppm (ORNL, page 14). However, Mulder and Van der Zalm did not say this, but refuted it. Specifically, they reject the Henderson and Haggard 5,000-to-10,000-ppm five-to-10-minute lethality value (which the original source and related documents shows to be actually a 30-minute value). Mulder and Van der Zalm stated that the subject was exposed to *"multiple times 10,000 ppm."* In this case, the subject died. However, his death was perhaps unnecessary, inasmuch as he failed to seek medical attention, continued work for three hours, and suffered fatal heart failure six hours post-exposure. His exposure level appears to have been, at least sporadically, to a high fraction of the full 330,000-ppm saturated vapor displaced from inside the tank he was refilling, while failing to wear respiratory protection. ORNL should (after multiple requests made already) correct its draft text to reflect the actual content and context of the Mulder and Van der Zalm report.

Silverman, *et al.* (1949). Regarding the Silverman, *et al.* (1949) study involving exposure of seven individuals to ammonia at 500 ppm, ORNL states that *"500 ppm was tolerated via nose breathing for 30 minutes by only 2/6 subjects, because of irritation of the upper respiratory tract"* (page 39). This statement is misleading, implying that adverse upper respiratory effects such as bronchial irritation and bronchoconstriction might have occurred. It further implies that volunteers might have terminated their exposure to ammonia when they terminated their nasal breathing pattern. In contrast, Silverman, *et al.* actually state:

> *"only two subjects were able to continue nasal breathing throughout the 30-minute exposure, the others changing to mouth breathing on account of nasal dryness and irritation."*

On page 41 ORNL states, incorrectly, that *"[t]he study by Silverman, et al. (1949) showed that exposure to 500 ppm was tolerated for 30 minutes by only 2/7 subjects."* This should be corrected.

ORNL states that *"the RD_{50} (the concentration causing 50% depression in the respiratory rate in mice (300 ppm) would be rapidly incapacitating to humans. Therefore 300 ppm is recommended for the AEGL-3, 4-h exposures"* (ORNL, page 39 and again on page 41). However, ORNL cites conflicting data on page 10 (and then disregards it) from Silverman, *et al.* indicating that, far from depressing the respiratory rate as predicted from mouse data, ammonia at 500 ppm elevated the breathing rate of volunteers:

> *"[t]he most significant physiologic change in response to ammonia was the increase in respiratory minute volume, amounting to 50 to 250 per cent over control values."*

ORNL should correct or justify its text to address the issues of misleading text regarding upper respiratory effects, *and the failure of mouse data to reflect human response as indicated by the* RD_{50}.

Glottis closure reflex. ORNL misinterprets the glottis closure data of Erskine, *et al.* (1993), stating that *"[t]his study indicated that elderly people may be more susceptible to lower respiratory tract effects than young people"* (ORNL page 13) because their glottis closure reflex occurs at a higher ammonia concentration. This would, of course, admit ammonia in a narrow band of concentrations into the lungs of elderly people while excluding those concentrations from the lungs of young people, with possible adverse effects upon the elderly. However, this difference in glottal closure reflex does not suggest that concentrations which are either above or below the glottis closure reflex of *both* young and elderly people would be more detrimental to elderly people.

The glottis closure reflex may be interpreted as degraded in elderly people, along with their reflexes generally, but this does not mean that elderly people are more sensitive to ammonia. Another interpretation, which I do not advocate though it may be true, is that the higher glottis closure level does not represent reflex degradation in elderly people. Rather, it might suggest that elderly people are *less* sensitive to ammonia, and therefore that they more closely resemble the 'expert' group of volunteers in the Verberk study. Either way, ORNL's conclusion about the significance of glottis closure is technically unjustified because neither interpretation implies greater sensitivity of elderly people to ammonia.

Sublethal injury rate at Potchefstroom. ORNL, citing Lonsdale (1975), states that, in the Potchefstroom accident, *"eighteen people died and an unknown number were injured"* (page 4). However, Lonsdale actually states that *"[i]n addition to the 18 deaths, approximately 65 people required medical treatment in hospital and an unknown number were treated by private doctors"* (page 126). This is significant, because it increases the documented size of the population of ammonia-exposed, surviving individuals.

No need to downwardly adjust time-weighted average concentrations at Potchefstroom. ORNL and NAC AEGL should critically evaluate ORNL's criticisms of RAM TRAC's alleged failure (in reconstructing the Potchefstroom accident) to downwardly adjust HGSYSTEM-modeled ammonia concentrations in air using the (simplified) Ten Berge equation, $C^n t$ = constant, with n = 2. The assumption that n = 2 (or any other value) is appropriate for inferring a fatality rate from a concentration, or a concentration from a fatality rate, when the value of one of these two parameters is undetermined. In the Potchefstroom accident, however, both the concentration and fatality rate in each modeled zone were determined. Neither parameter should be adjusted from its determined value

merely to validate the *assumption* that n = 2; indeed, determining the parameter value would be redundant if it could be reliably calculated from a relationship like that of Ten Berge, with n = 2. Nonetheless, the n = 2 assumption was applied by RAM TRAC in extrapolating from five minutes to 1/2-, one-, four-, and eight-hour durations, though the Potchefstroom data suggest that this value of n, derived from animal bioassay data, may be too high. ORNL's text in multiple places should retract the criticism and acknowledge the conservativeness of RAM TRAC's use of n = 2 for longer durations.

Failure of ORNL document to consider Ten Berge coefficient b_0. In reconstructing the Potchefstroom accident, the ammonia concentration was determined from the HGSYSTEM model, and the fatality rate from a detailed inquest following the accident. If n fails to equal 2 in the reconstruction, that is understandable, given the way n was determined from mouse and rat data. In fact, n was determined using probit analysis of mouse and rat bioassay data. The probit function is a dose-response curve whose shape is defined by three parameters, creatively known as b_0, b_1, and b_2; where $b_1/b_2 = n$ (in the Ten Berge equation):

$$\text{Probit } (Y) = b_0 + b_2 \ln [C^n t].$$

RAM TRAC oral and written comments show that, even if one assumes that $b_1/b_2 = n = 2$, great uncertainty about the dose-response curve for human exposure to ammonia persists nonetheless because the probit function also depends upon b_0, which was not considered by the ORNL draft document.

Uncertainty About Animal Bioassay Data

ORNL, using the simplified form of Ten Berge's equation ($C^n t$ = constant) failed to address b_0, implicitly assuming the same b_0 value for humans as for mice. However, RAM TRAC has performed a sensitivity analysis which shows that the $LC_{0.1}$ (one-per-thousand fatality concentration) depends exponentially rather than linearly upon b_0. Thus, a 10-percent change in b_0 (in either direction) from mice to humans produces a 250-percent change in the $LC_{0.1}$ value used for AEGL-3 derivation. Further, Ten Berge's article reports differences in the value of b_0 of over 50 percent within a single species (rats), depending upon sex and possibly other factors (strain, for example). Variability in estimates of Ten Berge coefficients, including b_0, are quantified in Table 3. Figure 2 depicts the covariation of the ammonia $LC_{0.1}$ with Ten Berge coefficients b_0, b_1, and b_2, producing significant differences in the dose-response curves for rats, depending upon sex (within a study) and between studies (both sexes combined). Figure 2 also shows the significantly lower dose-response curve of mice relative to all of the rat data. However, Figure 2 does not isolate the individual effect of b_0. To do this, Figure 3 holds constant the values of b_1, and b_2 while allowing b_0 to vary in accordance with the values used in Figure 2, and as reported by Ten Berge, *et al.* (1986).

Table 3. Ten Berge Regression Coefficients for Ammonia*

species	b0	b1	b2		n	
...	...	...	...	lower 95-percent confidence limit	...	upper 95-percent confidence interval
male + female rats	-47.9	4.65	2.30	...	2.02	...
male rats	-76.2	7.17	3.71	...	1.93	...
females rats	-62.6	5.91	2.76	...	2.14	...
mice	-54.5	5.95	2.89	...	2.06	...
mean	*-60.3*	*5.92*	*2.92*	*1.6*	*2.04*	*2.4*

*Source: Ten Berge, W. F. Concentration-time mortality response relationship of irritant and systemically acting vapours and gases. Journal of Hazardous Materials, 13:301-9, 1986.

Fig. 2. Covariation of the Ammonia LC-0.1 with Ten Berge Regression Coefficients b0, b1, and b2; where b1/b2 = n = 2

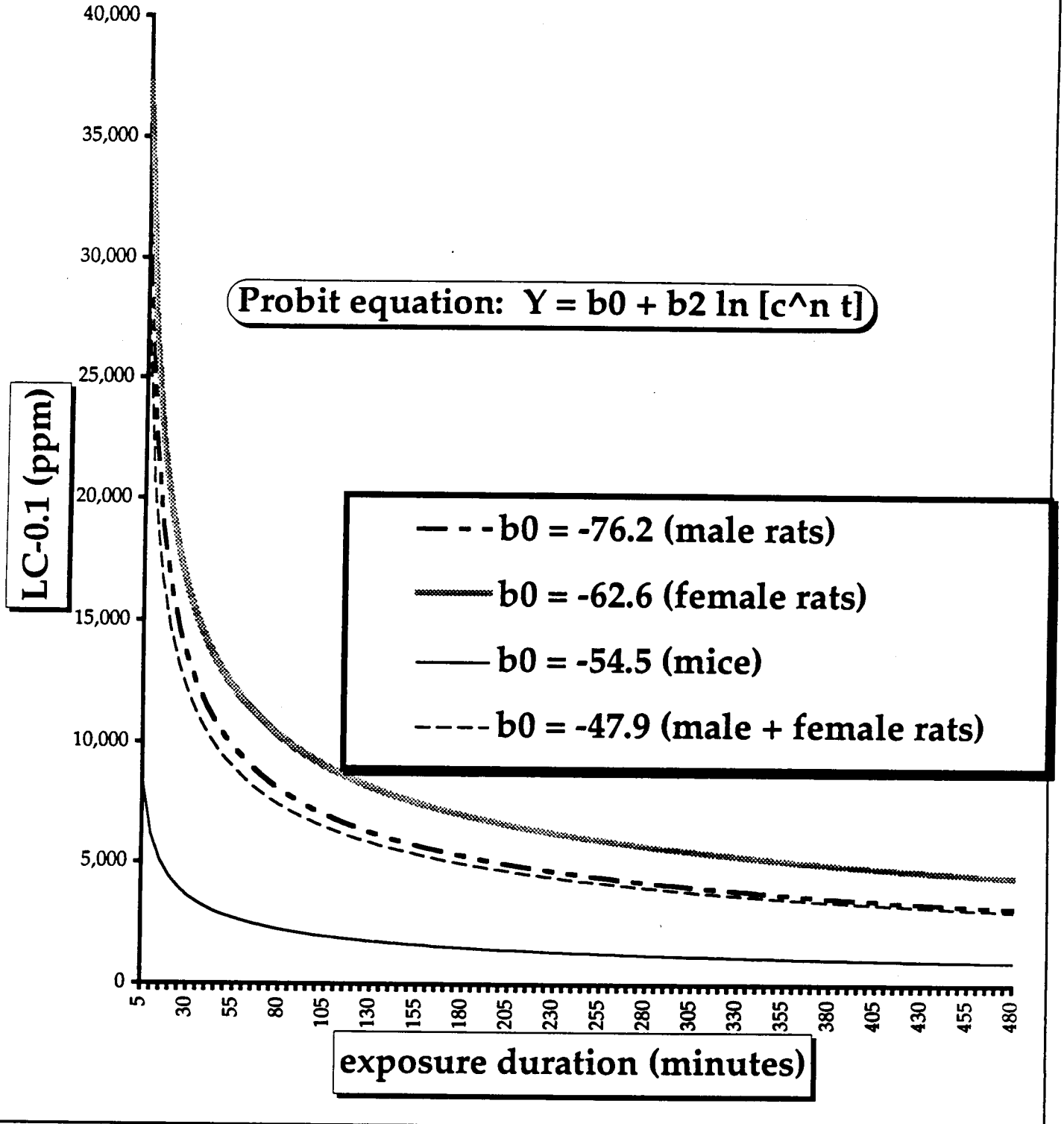


Fig. 3. Ammonia LC-0.1 Exponential Response To Linear Variation of the Ten Berge Regression Coefficient b0, with Invariant b1/b2 = n = 2

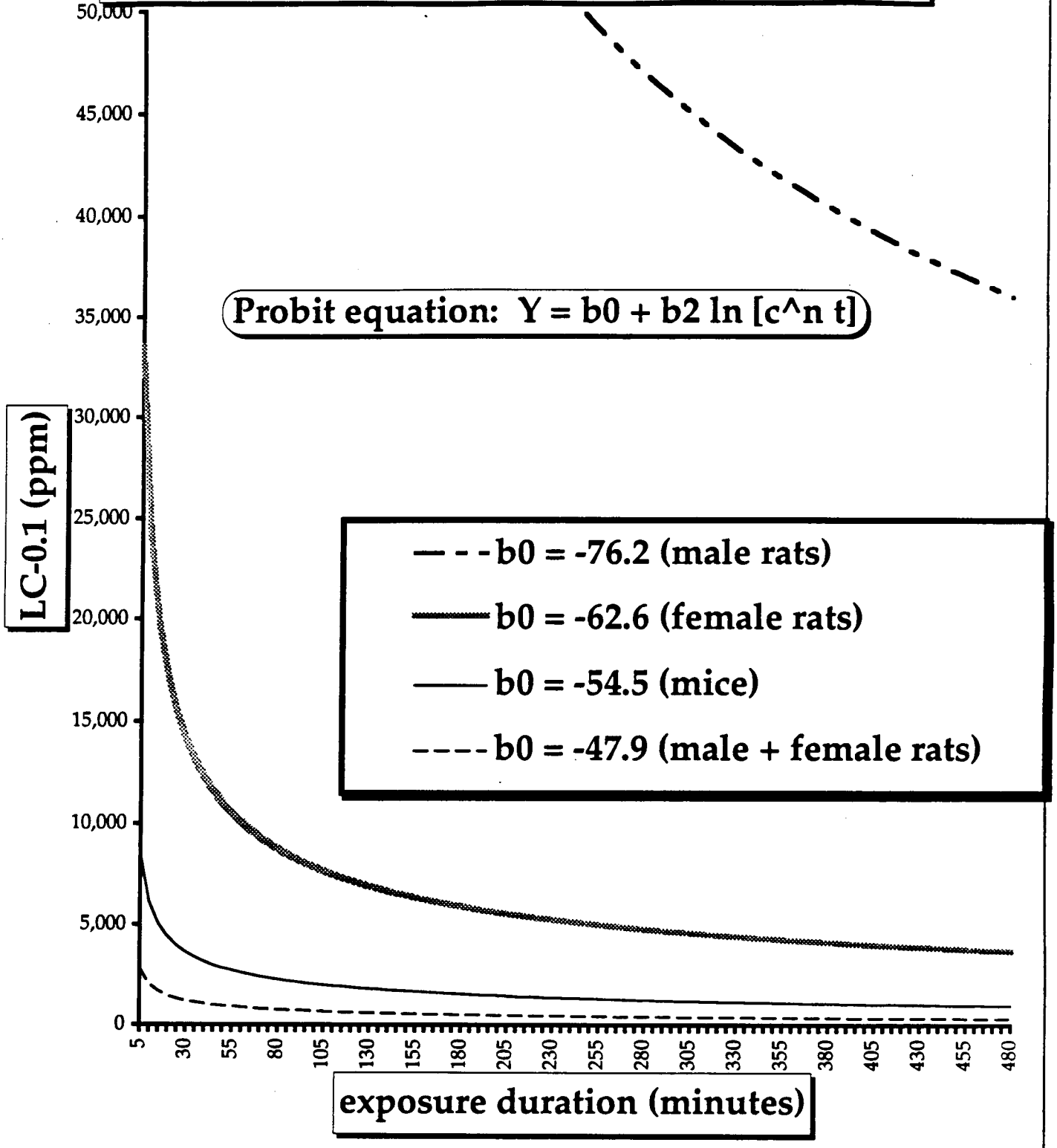


Figure 3 illustrates the potent effect of b_0 variation. This variability in b_0 could multiply or divide the $LC_{0.1}$ value by over an order of magnitude (factor of 10). Clearly, the exponential rather than linear dependence of the human $LC_{0.1}$ value upon the undetermined b_0 parameter places the rat and mouse data in exactly the same uncertainty class as the ammonia accident reconstruction data. Given the high degree of uncertainty associated with extrapolating dose-response curves when they are exponential or logarithmic rather than arithmetic and linear, *all data sources must be used fully. Those not used are a squandered information resource.*

Recommended Action on AEGL-3

Use accident data on an equal footing with animal bioassay data in meta-analysis. ORNL and NAC AEGL should reject ORNL's draft conclusion (ORNL, page 38) that uncertainty about exposure levels in accident reconstructions requires preference of animal data to derive AEGL-3 values. ORNL could have just as well pointed to uncertainties about animal data to conclude–equally incorrectly–that accident reconstruction data should be used.[3] The fact is, no source of data appears to be adequate by itself. The purpose, and premise, of EPA's standard weight-of-evidence analysis is to combine available data sources to exploit the strengths of each source in a *meta-analysis*, and thereby overcome weaknesses in other sources evident when considered individually. Accident reconstruction data are uniquely valuable in providing information about short-term exposures to high concentrations of ammonia, which is highly relevant to emergency exposure scenarios. The accident reconstruction data also pertain directly to humans. Such data may be flawed, but no more so (and perhaps less so) than the widely divergent animal bioassay database. Thus, accident reconstruction data are appropriate for use on an equal footing with animal bioassay data, and should be so incorporated into ORNL's analysis.

[3] ORNL does point to uncertainty about extrapolating animal data to humans. However, this source of uncertainty is not the one which bedevils interpretation of the ammonia database. Rather, mice and rats are unequally sensitive, so the more important source of uncertainty is, which species to extrapolate to humans. ORNL originally supported use of rat data because of the technical superiority of the rat bioassays, which used multiple ammonia concentrations and exposure durations, but has retreated from that position after upward correction to ORNL's analysis suggested higher ammonia lethality values for humans based upon the rat data. ORNL has not provided technical justification for now preferring the mouse data, though the source of the mouse data explicitly concludes that *"[t]hese findings suggest that experiments using mice do not provide an appropriate basis for predicting quantitatively the mortality response of humans"* (Ten Berge, *et al.*, 1986; page 308). Despite this conclusion, ORNL has attempted to reconcile the rat and mouse data by showing that they can both be made to yield similar human lethality values, though the suite of necessary assumptions is unreasonable, as documented in earlier RAM TRAC comments (see citations in *Literature Cited* section).

Use Rat Data Instead of Mouse Data. Both the RD_{50} and accident reconstruction data, though imperfect, should send a strong message that the equation, *humans = mice,* is incorrect. Like RAM TRAC, neither ORNL nor NAC AEGL may judge the Potchefstroom accident reconstruction alone to be adequate for AEGL-3 derivation.[4] However, ORNL and NAC AEGL should heed the message, and recognize the important contribution of accident reconstruction data to the conclusion that the mouse data over-predict the lethality of ammonia to humans. Consistent with the Ten Berge, et al. (1986) conclusion, ORNL and NAC AEGL should prefer rat data over mouse data for deriving AEGL-3 values.

If mouse data are to be used, convert to HEC values. The mouse data could be more reasonably used if converted to human equivalent concentrations, as discussed in detail in earlier RAM TRAC comments. Indeed, Larry Gephart of NAC AEGL orally indicated at the September meeting that ORNL also prefers this approach. Use of HECs would multiply the AEGL-3 values by a factor of approximately 2.6.

[4] RAM TRAC derived an AEGL as the Potchefstroom LC_0 divided in half. However, this was based upon multiple independent sources of data, from which the Potchefstroom data produced the lowest, most conservative AEGL-3 value. Had a different data source produced a lower value, that source might have been used. Indeed, one approach to consider would be the geometric mean value of multiple sources of data, including mouse and rat data, accident data, and other data sources cited in previous RAM TRAC comment documents (see citations in *Literature Cited* section).

AEGL-2

Regarding the Silverman, *et al.* (1949) study involving exposure of seven individuals to ammonia at 500 ppm, ORNL states that *"[o]nly two subjects were able to continue nasal breathing for the full 30 minutes"* (ORNL, page 10). However, this statement is misleading in implying that the volunteers may have terminated their exposure to ammonia when they terminated their nasal breathing pattern. However, Silverman, *et al.* stated that the volunteers switched to mouth breathing because of dryness of their nasal passages. This should be acknowledged by ORNL.

The Silverman, *et al.* (1949) study provides the most relevant data available for deriving AEGL-2 values because it shows that all seven individuals exposed to 500 ppm of ammonia for 30 minutes tolerated the exposure voluntarily and without adverse effect, and certainly without becoming disabled. Indeed, the exposures were voluntary, and presumably far from levels which would be clinically significant. However, ORNL omits the Silverman *et al.* study from its section on *"Human Data Relevant to AEGL-2."* Whether or not one agrees on the significance of the Silverman *et al.* study, clearly it is relevant to AEGL-2, and should not have been omitted from consideration in that context.

On page 42, ORNL includes the RD_{50} study among *"Animal Data Relevant to AEGL-2."* This study shows that ammonia depressed the respiratory rates of mice exposed to 330 ppm. However, ORNL excludes from the preceding section on *"Human Data Relevant to AEGL-2"* the Silverman, *et al.* (1949) data on the effect of ammonia on human respiratory rates. The data show that, far from depressing the human respiratory rate, ammonia elevated the respiratory rates of human volunteers. Thus, like the accident reconstruction data, the mouse RD_{50} data illustrate that mouse data is a poor quantifier of human response to ammonia. This issue should be addressed by ORNL.

NAC AEGL *tentatively* decided to define the AEGL-2 to include both irreversible injury and impairment of escape. However, the traditionally assumed time for escape is 30 minutes, as specified by the NIOSH IDLH. Extrapolating a concentration which is disabling within 30 minutes to one, four, or eight hours; as was done for ammonia; is illogical. What is the meaning of being unable to escape an ammonia release within 30 minutes as a result of being exposed to ammonia for one, four, or eight hours? At the 17-September NAC meeting, the definition of the AEGL-2 parameter was reexamined. The committee agreed that AEGL-2 values should not be downwardly adjusted beyond 30 minutes (except to preclude irreversible toxic effects from materializing at the longer exposure durations). This change of definition should be reflected in a commensurate change in *ammonia* AEGL-2 values beyond 30 minutes.

Contrary to the AEGL-2 definition, ammonia AEGL-2 values were based on *"nondisabling and reversible irritant effects."* The AEGL-2 was defined primarily to preclude Bhopal-type irreversible injuries. To implement this purpose, NAC AEGL included inability to escape within 30 minutes as an AEGL-2 criterion. However, ORNL and NAC AEGL have experienced difficulty quantifying this parameter, and have settled for a further degradation of the irreversible injury criterion. Specifically, ORNL and NAC AEGL have suggested that lacrimation might impair vision, precluding escape within 30 minutes. However, lacrimation is an adaptive response, not an adverse health effect. The American Thoracic Society (1985) and U. S. EPA (1993) published identical definitions of adverse health effects for Clean Air Act Standard setting, and nuisance irritation does not qualify. Indeed, peeling onions causes eye irritation and lacrimation, but is unregulated under the Clean Air Act, and onion juice is excluded from NAC AEGL's list of chemicals for AEGL development. The fact is, eye irritation and lacrimation can and do run the gamut from nuisance phenomena to clinically significant effects. However, ORNL has failed to address the potential clinical significance of the lacrimation and upper respiratory irritation associated with ammonia at exposure concentrations proposed for irreversible injury or impairment of escape. This issue must be addressed, especially in light of the voluntary nature of exposures of human subjects giving rise to ORNL's and NAC AEGL's perception of these issues.

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Attachment 9

REVIEW AND TECHNICAL CRITIQUE OF ACUTE EXPOSURE GUIDELINE LEVELS (AEGLs) PROPOSED FOR AMMONIA

Prepared for the

The Fertilizer Institute
Washington, DC

Prepared by

ENVIRON Corporation
Arlington, Virginia
Irvine, California

December 1996

NAC/AEGL MEETING, DECEMBER 1996
Scope of ENVIRON's Presentation

- Present and describe the technical basis for ENVIRON's proposals regarding AEGL values for ammonia.

- Offer some observations and principles regarding the development of AEGL values generally.

AEGL VALUES
Highlights of NAS/NRC Guidance

- The first choice for data is *"well documented description of the clinical effects seen in a representative sample of the general population exposed to accurately measured concentrations of the substance under consideration for relevant exposure periods."*

- *"CEELs* [community emergency exposure levels] *should be established for each toxic effect for a number of exposure periods, up to 1-8 hr, when the data allow it...."*

- *"In selecting UFs* [uncertainty factors] *for deriving CEELs, it is important to recognize that the intent is to avoid unnecessary conservatism that might result in exposure levels with little or nor biological plausibility."*

AEGL-3 VALUES
Current Definition

- .. the airborne concentration of a substance (ppmv) at or above which the general population, including susceptible but not hypersusceptible individuals, could experience ***life-threatening effects or death***.

AEGL-3 VALUES FOR AMMONIA
General Observations

- Human dose response data from accidents are relevant to AEGL-3 values and should be strongly considered.

- We agree with ORNL that, among the animal data, the data generated from the rat studies are more appropriate for extrapolating lethal doses in humans.

- At best, the ten Berge equation is applicable to a limited range of exposure durations, concentrations, and species. There is no basis for its application by ORNL to humans for exposure durations greater than one hour.

- There is not a sound scientific basis for AEGL-3 values for exposure durations greater than one hour.

AEGL-3 VALUES FOR AMMONIA
ENVIRON's Proposals

- If animal data are to be used in developing AEGL-3 values, they should be based upon the rat data of Appleman et al. (1982).

- Differences in dose delivered to the target tissue in humans versus rats (for a given exposure concentration) should be taken into account (i.e., human equivalent concentrations). The regional gas dose ratio (RGDR) approach outlined by the USEPA can be used to account for these differences.

- Based upon mechanistic considerations, an interspecies adjustment factor of approximately 3 (to account for any differences in respiratory tract physiology) should be health protective.

- Based upon Pedersen and Selig's (1989) probit equations for the general population and "vulnerable individuals", an intraspecies adjustment factor of approximately 3 should be health protective for sensitive individuals.

AEGL-3 VALUES FOR AMMONIA
ENVIRON's Proposals (continued)

- When $LC_{0.1}$ estimates are used to approximate a "no effects" threshold (or a "low incidence of effects") concentration, the resulting AEGL-3 values are
  - 8,100 ppmv for 5 minutes
  - 3,300 ppmv for 30 minutes and
  - 2,400 ppmv for 60 minutes.

- For comparison, the proposed AEGL-3 values are approximately 25% lower than the $LC_{0.1}$ estimates that can be calculated from Pedersen and Selig's (1989) probit equation for "vulnerable individuals" (Pedersen and Selig 1989). Alternative $LC_{0.1}$ estimates, based upon revised exposure (dose reconstruction) modeling for the South African accident (Michaels 1996), exceed the proposed AEGL-3 values by even greater amounts.

- There is not a sound scientific basis for AEGL-3 values for exposure durations greater than one hour. Consistent with NRC guidance, the NAC should not propose AEGL-3 values when there is not a sound scientific basis to do so.

AEGL-2 VALUES
Current NAC Definition

- .. the airborne concentration of a substance (ppmv) at or above which the general population, including susceptible but excluding hypersusceptible individuals, could experience ***irreversible or other serious, long-lasting effects or impaired ability to escape***.

AEGL-2 VALUES FOR AMMONIA
General Observations

- According to NRC guidance, the first choice for data is *"well documented description of the clinical effects seen in a representative sample of the general population exposed to accurately measured concentrations of the substance under consideration for relevant exposure periods."*

- *"The data set was very deficient in exposure estimates for disabling effects in humans. In addition, the data set is deficient in well-conducted animal studies on disabling effects."* (ORNL 1996b)

- ORNL's recommendations are based upon one study (Verberk 1977) regarding exposure levels for reversible temporary effects in humans.

- There is no technical basis for ORNL's application of the ten Berge equation to non-lethal responses in any species.

- Consistent with NRC guidance, the NAC should not propose AEGL-2 values when there is not a sound scientific basis to do so.

AEGL-2 VALUES FOR AMMONIA
ENVIRON's Proposals for 30 Minutes

- Silverman et al. (1949) exposed 7 adult males to 500 ppmv ammonia through a half-face respirator for 30 minutes. Slight increases in respiratory rate were observed and upper respiratory irritation was reported, but these effects were temporary. This study suggests that inhalation exposures to 500 ppmv ammonia, the only exposure concentration tested, should not cause irreversible or long-lasting effects in humans.

- Lehmann (1886) exposed himself to either 200 or 330 ppmv ammonia for 30 minutes and two other subjects to 300 ppmv for 20 minutes. Upper respiratory irritation was reported, but was not long lasting. This study, at best, suggests that the 30-minute AEGL-2 value should be greater than 300 ppmv.

- ENVIRON, therefore, recommends that the 30-minute AEGL-2 value for ammonia be set at a concentration greater than 300 ppmv and up to 500 ppmv.

AEGL-2 VALUES FOR AMMONIA
ENVIRON's Proposals for Two Hours

- Verberk (1977) exposed 16 subjects to 140 ppmv for up to two hours. No subjects had any long-lasting effects after 2 hours at 140 ppmv. This study, at best, established that the two-hour AEGL-2 value for ammonia should be greater than 140 ppmv, the highest exposure level tested.

- ENVIRON, therefore, recommends that a two-hour AEGL-2 value for ammonia be set at a concentration greater than 140 ppmv.

AEGL-2 VALUES FOR AMMONIA
ENVIRON's Proposals for Six Hours

- Ferguson et al. (1988) exposed 6 human subjects to 100 ppmv ammonia for 6 hours daily for six days. There were no significant changes in vital functions or performance tests. This study, at best, established that the six-hour AEGL-2 value for ammonia should be greater than 100 ppmv, the highest exposure level tested.

- ENVIRON, therefore, recommends that a six-hour AEGL-2 value for ammonia be set at a concentration greater than 100 ppmv.

AEGL-1 VALUES
Current NAC Definition

- .. the airborne concentration of a substance (ppmv) at or above which the general population, including susceptible, but excluding hypersusceptible individuals, could experience ***notable discomfort***.

AEGL-1 VALUES FOR AMMONIA
General Observations

- AEGL-1 levels should not be based upon odor threshold concentrations. They should be based upon thresholds for notable discomfort.

- In the case of ammonia, airborne concentrations associated with discomfort are greater than odor threshold concentrations.

- According to the AEGL-1 definition, airborne concentrations less than AEGL-1 values represent exposure concentrations that could produce mild odor, taste or other sensory responses.

- According to NRC guidance, the first choice for data is *"well documented description of the clinical effects seen in a representative sample of the general population exposed to accurately measured concentrations of the substance under consideration for relevant exposure periods."*

AEGL-1 VALUES FOR AMMONIA
ENVIRON's Proposals

- Based upon the weight of evidence from relevant studies with human subjects, the AEGL-1 values should be 50 ppmv for all time periods from 5 minutes to 8 hours.

AEGL-1 VALUES FOR AMMONIA
Summary of Key Studies

- Industrial Biotest Labs (1973) reported that a 5-minute exposure to 50 ppmv caused no lacrimation or eye, nose or chest irritation.

- MacEwen et al. (1970) reported that 50 ppmv caused moderate irritation in 4 of 6 subjects exposed for 10 minutes.

- In the Cole et al. (1977) study, no material discomfort (only dryness of the mouth and a prickling sensation) was reported by 48 subjects exposed to 101, 151, 205, and 335 ppmv for 20 minutes, while exercising for 8 to 11 minutes.

- In the Verberk (1977) study, no subjects exposed to 50 ppmv reported any symptoms worse than "nuisance" for exposure durations between 30 minutes and two hours.

- Ferguson et al. (1988) reported that exposure to 50 ppmv for 30 minutes up to six hours caused no effects other than mild irritation.

DR. JOSEPH V. RODRICKS: Dr. Rodricks is one of the founding Principals of ENVIRON Corporation, with internationally recognized expertise in assessing the risks to human health of exposure to toxic substances. Dr. Rodricks received his B.S. from M.I.T. in 1960, and his Ph.D. in biochemistry from the University of Maryland in 1968. In 1969-1970, he was a postdoctoral scholar at the University of California, Berkeley. Dr. Rodricks is Certified as a Diplomate of the American Board of Toxicology. Since becoming a consultant, Dr. Rodricks has conducted and directed numerous risk assessments for private clients, trade associations, and government agencies. He has provided such analyses for a large number of pesticides, occupational agents, environmental pollutants, food additives, and consumer and medical products.

Before working as a consultant, Dr. Rodricks spent fifteen years at the Food and Drug Administration. In his final two years of service, he was Deputy Associate Commissioner for Science (1978-1980), with special responsibility for risk assessment. Dr. Rodricks was a member of the National Academy of Sciences Board on Toxicology and Environmental Health Hazards, and has also served on and chaired ten other Academy Committees. He was recently a member of the National Research Council's Committee on Risk Assessment of Hazardous Air Pollutants. Dr. Rodricks has nearly 100 scientific publications on food safety and risk assessment and has lectured nationally and internationally on these subjects. He has also provided expert testimony before U.S. Congress, in administrative proceedings, and in court, and has served as a consultant to the World Health Organization. He is the author of *Calculated Risks*, a non-technical work on toxicology and risk assessment published in 1992 by Cambridge University Press.

DR. BARRY H. HOOBERMAN: Dr. Hooberman is a Senior Associate at ENVIRON Corporation with expertise in genetic toxicology, structure-activity relationships, and mechanistic risk assessment. He received his B.S. in Microbiology from The University of Michigan in 1978, his M.P.H. in Environmental and Industrial Health from the School of Public Health, The University of Michigan in 1980, and his Ph.D. in Toxicology in 1992, also from The University of Michigan. Dr. Hooberman conducted his thesis research on quantitative structure-activity relationships in the mutagenicity and biotransformation of aliphatic epoxides. He also worked on several other research projects examining the mutagenicity of chemicals from occupational and environmental exposures. In addition, Dr.

Hooberman was employed by the R.P. Scherer Corporation as an analytical chemist, developing HPLC methods for drug stability studies and for the analysis of new drug delivery systems. At ENVIRON, he has been involved in analyzing epidemiologic data, writing toxicity profiles for both technical and non-technical audiences, evaluating the biodegradation of medical implant materials, developing and critiquing safe exposure levels, examining structure-activity relationships in the mechanisms of halocarbon carcinogenicity, and using mechanistic studies to determine underlying mechanisms of toxicity.

DR. JILL RYER-POWDER, Ph.D, DABT: Dr. Powder is a Manager at ENVIRON Corporation. She has over nine years of experience in toxicology, occupational health, and product safety. She has managed or performed health risk assessments for over several hazardous waste sites, including major Superfund sites, town gas sites in southern California, and other industrial waste disposal or spill sites. She has extensive experience performing critical evaluations of toxicology and epidemiology literature for setting exposure limits, characterizing dose-response relationships, performing product safety reviews, or evaluating evidence for a causal relationship between the substance and given health effects. She spent five years at Unocal Corporation overseeing the health effects related sections of Material Safety Data Sheets for all of Unocal's products, including petroleum products, agricultural products, and solvents. Dr. Powder received her B.S. in Nutrition from Cornell University and her Ph.D. in Toxicology from Rutgers University / University of Medicine and Dentistry of New Jersey.

RICHARD B. KAPUSCINSKI, Ph.D., P.E.: Dr. Kapuscinski is a Manager at ENVIRON Corporation. He has a broad background in environmental engineering with substantial experience in evaluating the need for and approaches to site remediation and applying mathematical models to evaluate chemical fate and transport and to estimate chemical exposures. His work at ENVIRON has included directing the development of a cleanup plan for a former chemical manufacturing facility with extensive VOC and arsenic contamination in soil and ground water; conducting multi-media environmental risk assessments under CERCLA, RCRA, FIFRA, and TSCA; using risk assessments to evaluate alternative remedial action plans; assisting clients in negotiating site cleanup plans and cleanup goals, developing

site investigation strategies, and interpreting chemical risk assessments; and providing litigation support in the areas of chemical exposure assessment, cost allocation and recovery, and the environmental impacts of waste management practices. Prior to joining ENVIRON, Dr. Kapuscinski served on the civil engineering faculties at the University of Michigan and the University of Vermont. He has a Ph.D. and an M.S. in Engineering (Environmental) from Harvard University, and a B.S. in Civil and Environmental Engineering from Cornell University. He is licensed as a Professional Engineer in the Commonwealth of Virginia.

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INHERENT UNCERTAINTIES IN DOSE RECONSTRUCTIONS USING DISPERSION MODELS

OVERVIEW

All dose reconstructions are unable to overcome inherent multiple levels of uncertainties associated with the analytical process, such as:

- *Dispersion models have inherent uncertainties under idealized conditions.*
- *Highly complex circumstances, beyond model capabilities, introduce uncertainties.*
- *Choice of appropriate dispersion model is crucial to obtaining meaningful results.*
- *Limited measured data introduces further uncertainties into modeled results.*
- *Source term/meteorological characterization from observations increases uncertainties.*
- *Inappropriate interpretation of model results introduces additional uncertainties.*

As the final level of uncertainty accumulates and becomes too large, the confidence in the final results diminishes. Therefore, the dose reconstruction must become more comprehensive, so as to eliminate as many of the uncertainties as possible.

This peer review examines the level of uncertainties that are applicable to the Potchefstroom dose reconstruction. Some of the conclusions that are reached are as follows:

- *The absence of key real-time meteorological data (i.e., stability class) to accurately describe the temporally variant meteorological conditions during the ammonia release significantly limits the confidence in using the HGSYSTEM modeling results.*

- *HGSYSTEM may be unable to address multiple source releases, such as occurred at Potchefstroom.*

- *HGSYSTEM is unable to address indoor concentrations. Indoor concentrations should be modelled with an appropriate code to provide a complete ammonia exposure evaluation for both onsite and offsite receptors.*

- *HGSYSTEM is unable to model a delayed transport scenario of puff expansion in calm winds followed by wind transport, as existed during the Potchefstroom incident.*

- *HGSYSTEM, although a reasonably capable model, is limited by the complex meteorological conditions and multiple release circumstances. Many other public domain models are available for dose reconstruction applications.*

- *The Benign Bubble hypothesis is impossible to prove with the absence of 3-dimensional wind field data.*

March 1996 Four Elements Inc. Report on the
Dose Reconstruction of the 1973 Potchefstroom S.A. Ammonia Incident
Uncertainties in Dispersion Model Analyses

I) Inherent Uncertainties in Dose Reconstructions Using Dispersion Models

A) All Dispersion Models Provide Less than Certain Results

- *Dispersion models are accurate to a factor of 2 under idealized conditions of a singular gaseous release point in flat terrain without building obstacles with invariant meteorological conditions.*

- *Dispersion model accuracy decreases significantly when modeling complex circumstances inclusive of:*

  * *terrain features;*
  * *building obstacles;*
  * *chemical phase changes;*
  * *multiple sources and/or multiple non-point sources;*
  * *temporally variant meteorological conditions; and,*
  * *many other circumstances.*

B) Dispersion Model Selection Process: THE APPROPRIATE MODEL

- *Not all dispersion models were created equal. Selection of an inappropriate dispersion model that can not address the physics and thermodynamics of the event will increase uncertainty.*

- *Appropriate dispersion models need to undergo a stringent Verification & Validation (V & V) model surety process to reduce their uncertainty.*

C) Establishing Dispersion Model Input from Real-time Observations and Measurements: THE APPROPRIATE INPUT

- *Dispersion models do not think; they only do what they are told to do. Therefore, incorrect input streams will yield uncertain results.*

- *The accuracy in describing dispersion model inputs is dependent on the availability of real-time data to base source term definition, and transport and dispersion estimates. Errors in describing the input parameters may increase the uncertainty of the results, perhaps by as much as one or two orders of magnitude.*

D) Dispersion Model Output Examination: THE APPROPRIATE INTERPRETATION

March 1996 Four Elements Inc. Report on the
Dose Reconstruction of the 1973 Potchefstroom S.A. Ammonia Incident
Uncertainties in Dispersion Model Analyses

- *Dispersion model output streams require effective interpretation. Incorrect interpretation results in additional uncertainties.*

II) Multiple Uncertainties Exist in the Potchefstroom Dose Reconstruction

A) The Potchefstroom dose reconstruction exposure estimates are highly dependent upon the model output. The model output is highly dependent on the accuracy its inputs (i.e., source term and meteorology). The model input is dependent upon the precision with which they describe the actual circumstances. ***Thus, there are multiple levels of uncertainty which need to be examined to establish a level of confidence in the modeled results.***

B) The authors of the "Report on the Potchefstroom South Africa Ammonia Incident" recognized these uncertainties by the following statement on page 3 of this report:

"There is ***always a level of uncertainty in conducting gas dispersion modeling.*** *One type of uncertainty is attributable to our* ***lack of complete understanding of the complex mass and heat transport phenomena*** *which take place during the atmospheric dispersion process. Uncertainty also arises when we are* ***unable to accurately characterize all the necessary input parameters required by a physical model.*** *This "parameter" uncertainty is particularly evident when reconstructing the consequences of a historical accident as* ***relatively few variables are known.*** *Consequently, both an upper and lower bound have been placed on the* ***concentration estimates*** *provided herein, in order to minimize the* ***effect that parameter uncertainty plays in making decisions based on the results.*** *(Emphases added)*

C) A peer review evaluation of the various uncertainties used in the estimation of airborne ammonia exposures, is merited to ensure that good science is being applied throughout.

D) Since the Four Elements Inc. report did not comprehensively describe all of the necessary information for evaluation of the uncertainties:

- *Various interrogatories have been prepared to identify the unknowns which limit further evaluation.*
- *Various statements of fact have been prepared from what has been established.*

III) Peer Review of the Potchefstroom Dose Reconstruction Approach

A) Description of Observations/Measurements

- *Accident: Catastrophic failure of tank and railcar of pressurized (90 psig) liquid non-cryogenic (@ 59 deg F) anhydrous ammonia on a winter afternoon.*

- *Source Term: 38 tons of liquid non-cryogenic ammonia was released within 30 sec through a greater than 6"ft^2 opening. Ammonia cloud observed to measure 150 meters in diameter (almost 20 meters depth) shortly after failure.*

- *Meteorological Conditions: Temperature approximately 66 deg F and the low relative humidity was between 30 and 35%. No wind initially, within a few minutes a slight breeze.* ***Stability class not identified****. Cloud reached 300 meters in width at about 450 meters downwind.*

B) Model Selection

- *HGSYSTEM, since it is capable of treating dense gas and instantaneous release behavior, and subject to extensive testing and validation.*

C) Probable HGSYSTEM Input Parameters and Accident Type

- *Instantaneous (Puff) Release: 76,000 # of NH_3 from 6 ft^2 opening*
- *Ammonia storage parameters: 90 psig @ 59 deg F (non-cryogenic liquid)*
- *Ambient temperature: 66 deg F*
- *Relative humidity: 30-35% (e.g., dry day with few clouds)*
- *Wind Speed: 1 m/sec (upper bound); 2 m/second (lower bound)*
- *Stability Class:* ***unknown*** *(Likely Pasquill-Gifford Class B)*

- *Reconstruction suggests initial huge 150-meter diameter, 20-meter high oblate hemispheroid Gaussian puff expanding 3-dimensionally. At an unidentified time later, the expanding puff slowly transported downwind. It is uncertain when calm wind (i.e., no puff transport) transitioned to a light breeze (puff transport).*

D) HGSYSTEM Model Output and Interpretation for Dose Reconstruction

Ammonia concentrations at 50-meter increments both downwind and ***upwind*** *from the point of failure for both the upper and lower bound wind speeds. Table of ammonia concentration vs time from 5 - 600 sec for receptors from 50 m - 400 m for upper and* ***lower bound*** *winds. For receptors of interest (i.e., 50 m, 100 m, 150 m, and 250 m),*

concentration versus time curves were likely constructed from model output. Integration under curve approximates airborne dose exposure for each receptor.

IV Statements of Fact and Interrogatories

A) Validity of HGSYSTEM Model to Address Potchefstroom Dose Reconstruction

- *HGSYSTEM unable to address indoor concentrations using building air exchange (i.e., 1-e^{-at}) algorithm. Therefore it could **not** be applied to the survivors in the control room within the initial puff. (ALOHA can model indoor concentrations).*

- *HGSYSTEM may not be able to address multiple source releases.*

- *HGSYSTEM unable to model a delayed transport scenario of puff expansion in calm winds followed by wind transport of expanded puff.*

- *HGSYSTEM, although a reasonably capable model, is limited by the complex meteorological conditions, complex chemistry of ammonia phase change, and multiple release circumstances.*

- *Many other public domain models are available for dose reconstruction applications.*

- *EPA uses ALOHA and SLAB for its 40 CFR 68 Risk Management Plan look-up tables, for neutral and dense gases, respectively.*

IV Statements of Fact and Interrogatories (continued)

B) Validity of Establishing Source Term/Meteorological Model Input Parameters from Observations/Measurements?

- *Source Term*
  - *Since HGSYSTEM was selected for its dense gas capabilities, was the non-cryogenic ammonia release modeled as a dense gas or a neutrally buoyant gas?*
  - *Were both releases (i.e., tank and railroad car) modelled separately or combined into one release?*
  - *Were the observed cloud dimensions compared to HGSYSTEM-modeled puff size to validate ammonia release input assumptions?*
- *Meteorological Conditions*
  - *How were the non-measured meteorological inputs (i.e., stability class, wind speed/wind direction history with time) inferred from the observations?*
  - *Were actual wind speed/wind direction time histories (initial calm and then slight breeze) adequately characterized in the HGSYSTEM input stream?*
  - *Was the atmospheric stability class representative of actual meteorological conditions used as HGSYSTEM input?*

NOTE: HGSYSTEM input/output streams need to be examined to satisfy these interrogatories.

V Potential Issues

A) Uncertainties in Establishing the Dimensions of the Ammonia Cloud

- *It is uncertain whether estimated ammonia cloud dimensions have been accurately described by the HGSYSTEM model since the dimensions of the observed ammonia cloud have not been compared to the dimensions of the HGSYSTEM-modeled cloud.*

- *The ammonia storage and ambient conditions do not support a dense gas scenario, yet HGSYSTEM was chosen for its dense gas properties. If the incident resulted in a dense gas release, the resultant transport and dispersion of the cloud would be significantly different than if it was a neutrally buoyant gas (i.e., dense gas would result in a more concentrated cloud near the ground). Initial cloud height of 20 meters (70 ft) suggest the release was neutrally buoyant, which would rise vertically and consequently reduce downwind ground-level concentrations.*

B) Uncertainties Due to Absence of Key Real-time Meteorological Data

- *The absence of key real-time meteorological data to accurately describe the temporally variant meteorological conditions during the ammonia release significantly limits the confidence in using the HGSYSTEM modeling results since the validity of the results are very sensitive to matching inputs to actual meteorological conditions.*

    * *HGSYSTEM is very sensitive to stability class, a very important input parameter affecting 3-dimensional puff growth. Incorrect assessment of stability class, even as close as 50 meters downwind, can affect model results by 1 to 2 orders of magnitude.*

    * *HGSYSTEM is also sensitive to changes in wind speed. The exact timing of the slight breeze, and therefore subsequent transport offsite, will have a major impact on the exposure times to all receptors, especially for far-field receptors.*

V Potential Issues (continued)

- *The dose reconstruction should be in two stages. Stage I models the expanding ammonia puff with no transport wind, while Stage II models the puff transported to offsite receptors. A range of post-accident light breeze onset times should be used to bound this unknown variable.*

- *For the Stage II light breeze transport calculation, the upper and lower bounds need to be described not only by a wind speed range (e.g., 1-2 m/sec), but by a stability class/wind speed couplet range. For sunny to partly cloudy daytime situations, an upper bound of C stabilty @ 2.0-2.5 m/sec and a lower bound of A stability @ 1.0-1.5 m/sec may be applicable to the Potchefstroom incident* ***after the slight breeze sprang up****. Under these likely conditions, the ammonia concentrations would decrease rapidly during the transport phase.*

- *In 40 CFR 68 EPA Risk Management Plan guidance, F-stabilty @ 1.5 m/sec [worst case scenario and D-stability @ 4.5 m/sec [average meteorology] are used as bounding cases.*

C) Inability to Model Indoor Concentrations

- *The Potchefstroom workers in the control room and other near-field locations were not killed (as their less fortunate colleagues were that did not benefit from the shielding the building offered). Indoor concentrations should be modeled by ALOHA and/or another appropriate model to determine what exposures the control room individuals experienced. This analysis will provide a more complete evaluation of ammonia exposures for both onsite and offsite receptors, as well as additional insights to the LC_0 concentrations.*

D) Uncertainty of Benign Bubble Hypothesis

- *The Benign Bubble hypothesis is impossible to prove with the absence of 3-dimensional wind field data. Numerous tracer studies, conducted over the past 40 years, have not confirmed that such a phenomenon exists in nature. Therefore, the factor of 2 ascribed to account for this uncertainty does not appear to have scientific merit.*

VII) Recommendations to Reduce Uncertainty in the Dose Reconstruction Results

A) Verify and Validate Model Input Data Assumptions

- *Carefully compare HGSYSTEM input data and model assumptions to observed/measured information to establish source term and meteorological input data integrity.*

B) Obtain More Precise Source Term and Meteorological Information for Use in Appropriate Dispersion Model

- *Obtain more precise information, if available, on cloud size to calibrate source term element of the dispersion model. Establish if release is a dense gas or a neutrally buoyant gas.*

- *Obtain more precise information on key meteorological input parameters (especially stability class), if available, to calibrate transport and dispersion elements of the dispersion model.*

C) Suggested Modeling to Decrease Dose Reconstruction Uncertainties

- *Perform dose reconstruction modelling in two stages;* ***puff expansion without transport, puff transport and dispersion*** *to obtain more realistic dose reconstruction results.*

- *ALOHA is one of the few chemical dispersion models that is capable of providing* ***indoor concentrations.*** *It should be considered for this application to augment the dose reconstruction.*

- *Input more precise source term and meteorological data (e.g., upper and lower bound wind speed-stability class couplet) into the above analyses.*

- *Note: The Department of Energy (DOE) Accident Phenomenology And Consequences (APAC) Methodology Evaluation Chemical Dispersion and Consequence Assessment Working Group is studying 25 chemical dispersion models in detail, inclusive of HGSYSTEM. Draft report to be issued January 8, 1997. Other appropriate chemical dispersion models can be selected on the basis of the recommendations of this upcoming report.*

VI) Recommendations to Reduce Uncertainty in the Dose Reconstruction Results (continued)

D) Establish Caveats if More Precise Information Can not be Obtained

- *If more precise data is not available, and/or other modeling is not contemplated, establish appropriate caveats in the use of the less than certain dispersion model results that impact the veracity of the Potchefstroom dose reconstruction.*

E) Recognition of Inherent Dispersion Model Uncertainties

- *Under the most optimum circumstances of real-time data availability, a simple point release under invariant meteorological conditions, and utilizing a well-constructed and applied dispersion model, an uncertainty of a factor of 2 is inherent in any dose reconstruction. Confounding factors, as enumerated in the above discussion, serve to broaden the uncertainty further.*

Attachment 12

METHYLHYDRAZINE AEGL

NAC/AEGL MEETING NO. 4
DECEMBER 16-18, 1996
WASHINGTON, D.C.

PROPOSED AEGL VALUES FOR METHYLHYDRAZINE					
Classification	30-min	1-hour	4-hour	8-hour	Endpoint(Reference)
AEGL-1	2 ppm	1 ppm	0.5 ppm	0.5 ppm	Irritation of eye, nose, and throat with no changes in clinical chemistry parameters; human exposure to 90 ppm for 1 hr (MacEwen et al., 1970)[a]; adjusted to 9 ppm to account for steep exposure-response relationship; temporal scaling followed $C^2 \times t = k$
AEGL-2	3 ppm	2 ppm	1 ppm	0.5 ppm	Notable hemolytic response (decreased Hct, Hb, RBC) with no mortality in rhesus monkeys exposed to 160 ppm[b], 1 hr (Haun et al., 1970); 160 ppm adjusted to 53 ppm to account for steep exposure-response relationship; temporal scaling followed $C^2 \times t = k$
AEGL-3	3 ppm	2 ppm	1 ppm	1 ppm	1-hr LC_{50} of 162 ppm for rhesus monkeys (Haun et al., 1970) adjusted to an estimated LC_0 of 54 ppm[c]; temporal scaling followed $C^2 \times t = k$

[a] Uncertainty factor of 3 applied to account for susceptible but not hypersusceptible individuals; the 90-ppm exposure was reduced by an order of magnitude to account for the exposure-response relationship affirmed by data from multiple laboratory species.

[b] Mean exposure of 160 ppm reduced 3-fold (53 ppm) to assure nonlethal concentration; uncertainty factor of 10 for interspecies variability and 3 for protection of susceptible but not hypersusceptible individuals.

[c] Uncertainty factor of 30 applied to account for interspecies variability (UF=10) and susceptible but not hypersusceptible individuals (UF=3); 1-hr exposure to 160 ppm resulted in notable but reversible hemolytic responses and no deaths.

AEGL-1 FOR METHYLHYDRAZINE (ppm)				
AEGL Level	30-min	1-hr	4-hr	8-hr
AEGL-1	2 ppm	1 ppm	0.5 ppm	0.5 ppm

- Seven human volunteers exposed for 10 minutes to methylhydrazine (90 ppm [169 mg/m^3]) (MacEwen et al., 1970).
- Irritation of the eyes, nose, and throat but no excessive lacrimation or coughing.
- Clinical chemistry parameters at 60 days were not significantly affected; a 3-5% increase in Heinz body formation at day 7 that declined after two weeks.
- Spirometry tests revealed no exposure-related effects.
- Exposure-response data not available for humans.
- For AEGL-1 derivation, the 90-ppm exposure was reduced by an order of magnitude (i.e., to 9 ppm) to account for the very steep exposure-response relationship affirmed by data from multiple laboratory species.
- A factor of 3 was applied to account for individual variability in the irritation response to methylhydrazine exposure.

AEGL-2 FOR METHYLHYDRAZINE (ppm)				
AEGL Level	30-min	1-hr	4-hr	8-hr
AEGL-2	3 ppm	2 ppm	1 ppm	0.5 ppm

- AEGL-2 was derived based upon a measurable hemolytic response observed in rhesus monkeys following a 1-hr exposure to 160 ppm methylhydrazine (Haun et al., 1970).

- Although this exposure produced a hemolytic response with no mortality, it appears to be very close to the lethality threshold for other laboratory and is nearly identical to the estimated 1-hr LC_{50} of 162 ppm for this species.

- Because the animal data suggest a very narrow threshold between lethality and nonlethal, reversible effects, the 160 ppm exposure was reduced threefold to 53 ppm. This appears to be an exposure that is below any lethality thresholds for any species.

- Uncertainty factors for interspecies variability (UF=10) and intraspecies variability (UF=3) were applied.

AEGL-3 FOR METHYLHYDRAZINE (ppm)				
AEGL Level	30-min	1-hr	4-hr	8-hr
AEGL-3	3 ppm	2 ppm	1 ppm	1 ppm

- Lethality data are available for several laboratory species (Jacobson et al., 1955; Haun et al., 1969; Haun et al., 1970; MacEwen and Vernot, 1975).

- One-hour LC_{50} values of 162, 82, 96, 244, 122, and 991 ppm have been reported for rhesus monkeys, squirrel monkeys, beagle dogs, rats, mice, and hamsters, respectively.

- AEGL-3 values were derived based upon the 1-hr LC_{50} value of 162 ppm reported for rhesus monkeys (Haun et al., 1970).

- Because there appears to be very little margin between exposures causing minor effects and those causing lethality, the 1-hr LC_{50} of 162 ppm reported by Haun et al. (1970) was reduced by one third to estimate a lethality threshold (i.e., 54 ppm).

- A total uncertainty factor adjustment of 30 was applied to account for interspecies variability (UF=10) and protection of sensitive but not hypersusceptible individuals (UF=3).

DERIVATION OF AEGL-2 VALUES FROM DIFFERENT DATA SETS				
Time Point	Rhesus monkeys; 160 ppm for 1 hr; no deaths, notable hemolytic response (Haun et al., 1970)[a]*	Squirrel monkeys; 75 ppm, 1 hr; no deaths (Haun et al., 1970)[b]	Beagle dogs; 15 ppm, 4 hrs.; no deaths, hyperactivity, retching, tremors and convulsions, vomiting, hemolysis; recovery after 8 days (Jacobson et al., 1955)[c]	Beagle dogs; 92 ppm, 1 hr or 180 ppm, 30 min.; no deaths, notable hemolytic response (Haun et al., 1970)[d]
30 min	2 ppm	4 ppm	1 ppm	6 ppm
1 hr	1 ppm	3 ppm	1 ppm	3 ppm
4 hr	0.5 ppm	1 ppm	0.5 ppm	3 ppm
8 hr	0.5 ppm	1 ppm	0.5 ppm	2 ppm

Values rounded to nearest 0.5 ppm

* Data set used for AEGL-1

[a] Mean exposure of 160 ppm reduced 3-fold to assure nonlethal concentration; uncertainty factor of 10 for interspecies variability and 3 for protection of susceptible but not hypersusceptible individuals.

[b] Uncertainty factor of 10 for interspecies variability and 3 for protection of susceptible but not hypersusceptible individuals; 75 ppm exposure is only slightly below the estimated LC_{50} of 82 ppm for this species.

[c] Uncertainty factor of 10 for interspecies variability and 3 for protection of susceptible but not hypersusceptible individuals.

[d] Uncertainty factor of 10 for interspecies variability and 3 for protection of susceptible but not hypersusceptible individuals; 92 ppm exposure is only slightly below the estimated LC_{50} of 96 ppm for this species.

DERIVATION OF AEGL-3 VALUES FROM DIFFERENT DATA SETS					
Time Point	Rhesus monkey; 1-hr LC_{50} of 162 ppm, adjusted to est. LC_0 of 54 ppm[a] (Haun et al., 1970)*	Squirrel monkey; 1-hr LC_{50} of 82 ppm adjusted to est. 1-hr LC_0 of 27 ppm[b] (Haun et al., 1970)	Beagle dog: 1-hr LC_{50} of 96 ppm adjusted to est. 1-hr LC_0 of 32 ppm[c] (Haun et al., 1970)	Rat: 1-hr LC of 244 ppm adjusted to est. 1-hr LC_0 of 81 ppm[d] (Haun et al., 1970)	Mouse: 4-hr LC_{01}[e] (Haun et al., 1970)
30 min	3 ppm	1 ppm	2 ppm	4 ppm	2 ppm
1 hr	2 ppm	1 ppm	1 ppm	3 ppm	2 ppm
4 hr	1 ppm	0.5 ppm	0.5 ppm	1.5 ppm	1 ppm
8 hr	1 ppm	0.5 ppm	0.5 ppm	1 ppm	0.5 ppm

Values rounded to nearest 0.5 ppm

* Data set used for AEGL-2

[a] Uncertainty factor of 30 applied to account for interspecies variability (UF=10) and susceptible but not hypersusceptible individuals (UF=3); 1-hr exposure to 160 ppm resulted in notable but reversible hemolytic responses and no deaths.

[b] Uncertainty factor of 30 applied to account for interspecies variability (UF=10) and susceptible but not hypersusceptible individuals (UF=3); 1-hr exposure to 75 ppm was not lethal.

[c] Uncertainty factor of 30 applied to account for interspecies variability (UF=10) and susceptible but not hypersusceptible individuals (UF=3); 1-hr exposure to 92 ppm was not lethal.

[d] Uncertainty factor of 30 applied to account for interspecies variability (UF=10) and susceptible but not hypersusceptible individuals (UF=3)

[e] Uncertainty factor of 30 applied to account for interspecies variability (UF=10) and susceptible but not hypersusceptible individuals (UF=3)

CANCER ASSESSMENT OF METHYLHYDRAZINE

- Neither an inhalation nor an oral slope factor are currently available for methylhydrazine.
- Slope factors for 1,1-dimethylhydrazine and 1,2-dimethylhydrazine were available but have been withdrawn from the U.S. EPA Integrated Risk Information System (IRIS). For a preliminary carcinogenicity assessment, the withdrawn inhalation slope factor for 1,1-dimethylhydrazine (cited in ATSDR, 1994) will be used as a surrogate for methylhydrazine.

- The withdrawn slope factor for 1,1-dimethylhydrazine was 3.5 $(mg/kg\text{-}day)^{-1}$ which, based upon a human inhalation rate of 20 m^3/day and a body weight of 70 Kg, is equivalent to 1 $(mg/m^3)^{-1}$.

- The assessment follows previously described methodologies (NRC, 1985; Henderson, 1992).

To convert to a level of methylhydrazine that would cause an excess cancer risk of 10^{-4}:

Risk of 1×10^{-4}	=	$(1 \times 10^{-4}/1) \times 1$ mg/m^3 =	1×10^{-4} mg/m^3 (virtually safe dose)

To convert a 70-year exposure to a 24-hour exposure:

24-hr exposure	=	d x 25,600		
	=	(1×10^{-4} mg/m^3)	x	25,600 days
	=	2.56 mg/m^3		

To account for uncertainty regarding the variability in the stage of the cancer process at which methylhydrazine or its metabolites may act, a multistage factor of 2.8 is applied (Crump and Howe, 1984):

(2.56 mg/m^3)/2.8	=	0.9 mg/m^3 (0.5 ppm)

Therefore, based upon the potential carcinogenicity of methylhydrazine, an acceptable 24-hr exposure would be 0.9 mg/m^3 (0.5 ppm).

If the exposure is limited to a fraction (f) of a 24-hr period, the fractional exposure becomes 1/f x 24 hrs (NRC, 1985).

24-hr exposure	=	0.9 mg/m^3 (0.5 ppm)
8-hr	=	2.7 mg/m^3 (2 ppm)
4-hr	=	5.4 mg/m^3 (3 ppm)
1-hr	=	21.6 mg/m^3 (11 ppm)
0.5 hr	=	43.2 mg/m^3 (23 ppm)

Because the AEGLs based upon acute toxicity were equivalent to or lower than the values derived based on potential carcinogenicity, the acute toxicity data were used for the proposed AEGLs for methylhydrazine.

Attachment 13

DIMETHYLHYDRAZINE AEGL

NAC/AEGL MEETING NO. 4
DECEMBER 16-18, 1996
WASHINGTON, D.C.

PROPOSED AEGL VALUES FOR DIMETHYLHYDRAZINE					
Classification	30-min	1-hour	4-hour	8-hour	Endpoint(Reference)
AEGL-1	5 ppm	3 ppm	2 ppm	1 ppm	No significant signs of toxicity in dogs exposed to 96 ppm for 1 hr. (Weeks et al., 1963)
AEGL-2	9 ppm	7 ppm	3 ppm	2 ppm	Behavioral changes and muscle fasciculations in dogs exposed to 400 ppm for 15 minutes (Weeks et al., 1963)
AEGL-3	15 ppm	11 ppm	6 ppm	4 ppm	Lethality threshold of 327 ppm for 1 hr estimated from 1-hr LC_{50} in dogs (Weeks et al., 1963)

Values are rounded to nearest whole integer.

AEGL-1 FOR DIMETHYLHYDRAZINE (ppm)				
EGL Level	30-min	1-hr	4-hr	8-hr
EGL-1	5 ppm	3 ppm	2 ppm	1 ppm

Four-hour exposure of dogs to 24 ppm (Jacobson et al., 1955) and the 1-hour exposure of dogs to 96 ppm 1,1-dimethylhydrazine (Weeks et al., 1963) resulted in cumulative exposures of 96 ppm·hr that produced no significant toxic effects.

Total uncertainty factor of 30 (10 for interspecies variability and 3 for individual variability [protection of susceptible but not hypersuceptible individuals]) was applied to scaled values.

AEGL-2 FOR DIMETHYLHYDRAZINE (ppm)				
AEGL Level	30-min	1-hr	4-hr	8-hr
AEGL-2	9 ppm	7 ppm	3 ppm	2 ppm

- Dogs exposed to 400 ppm for 15 minutes (Ct = 100 ppm·hr) exhibited behavioral changes and mild muscle fasciculations in dogs (Weeks et al., 1963).

- Although an equivalent exposure (1,550 ppm for 5 minutes; Ct= 129 ppm'hr) produced similar effects, the 15-minute, 400-ppm exposure was considered more appropriate for AEGL derivation because it would be somewhat more valid for extrapolating to AEGL-specific time frames.

- A total uncertainty factor of 30 (10 for interspecies variability and 3 for individual variability [protection of susceptible but not hypersuceptible individuals]) was applied to the scaled values.

AEGL-3 FOR DIMETHYLHYDRAZINE (ppm)				
AEGL Level	30-min	1-hr	4-hr	8-hr
AEGL-3	15 ppm	11 ppm	6 ppm	4 ppm

- The lethality threshold for dogs exposed to 1,1-dimethylhydrazine was estimated from the 1-hr LC_{50} of 981 ppm reported by Weeks et al. (1963) by reducing this value three-fold to 327 ppm.
- This results in an exposure concentration three times greater than the 1-hr concentration (i.e., 96 ppm, Weeks et al., 1963) associated with a no-effect level in dogs.
- A total uncertainty factor of 30 (10 for interspecies variability and 3 for individual variability [protection of susceptible but not hypersuceptible individuals]) was applied to the scaled values.

CANCER ASSESSMENT OF DIMETHYLHYDRAZINE

Neither an inhalation nor an oral slope factor are currently available for methylhydrazine. Slope factors for 1,1-dimethylhydrazine and 1,2-dimethylhydrazine were available but have been withdrawn from the U.S. EPA Integrated Risk Information System (IRIS). For a preliminary carcinogenicity assessment, the withdrawn inhalation slope factor for 1,1-dimethylhydrazine (cited in ATSDR, 1994) will be used. The assessment follows previously described methodologies (NRC, 1985; Henderson, 1992).

The withdrawn slope factor for 1,1-dimethylhydrazine was 3.5 $(mg/kg\text{-}day)^{-1}$ which, based upon a human inhalation rate of 20 m^3/day and a body weight of 70 Kg, is equivalent to 1 $(mg/m^3)^{-1}$.

To convert to a level of methylhydrazine that would cause an excess cancer risk of 10^{-4}:

$$\text{Risk of } 1 \times 10^{-4} = (1 \times 10^{-4}/1) \times 1\ mg/m^3 = 1 \times 10^{-4}\ mg/m^3 \text{ (virtually safe dose)}$$

To convert a 70-year exposure to a 24-hour exposure:

$$\text{24-hr exposure} = d \times 25{,}600$$
$$= (1 \times 10^{-4}\ mg/m^3) \times 25{,}600 \text{ days}$$
$$= 2.56\ mg/m^3$$

To account for uncertainty regarding the variability in the stage of the cancer process at which methylhydrazine or its metabolites may act, a multistage factor of 2.8 is applied (Crump and Howe, 1984):

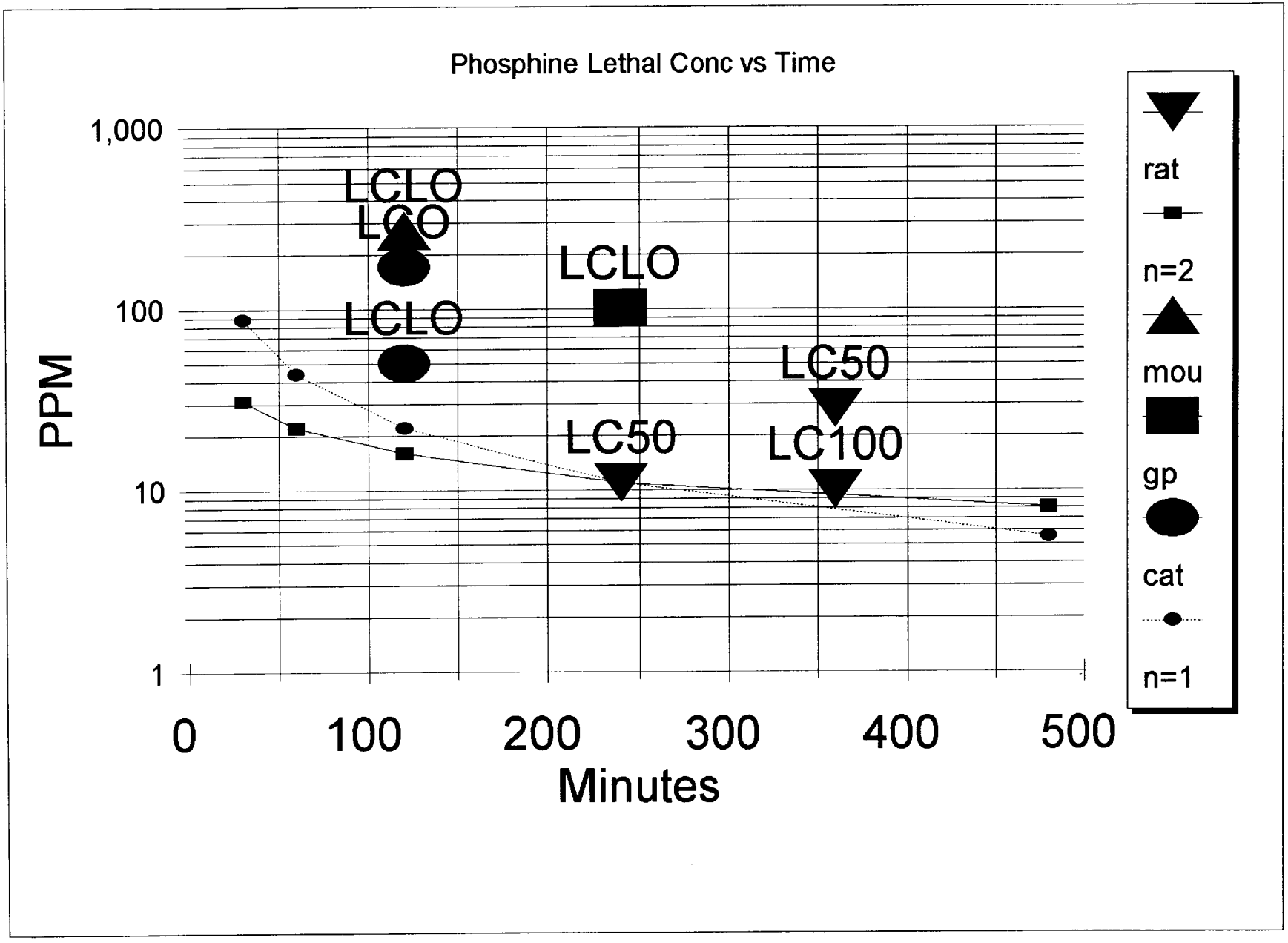
$$(2.56\ mg/m^3)/2.8 = 0.9\ mg/m^3\ (0.5\ ppm)$$

Therefore, based upon the potential carcinogenicity of methylhydrazine, an acceptable 24-hr exposure would be 0.9 mg/m^3 (0.5 ppm).

If the exposure is limited to a fraction (f) of a 24-hr period, the fractional exposure becomes 1/f x 24 hrs (NRC, 1985).

24-hr exposure	=	0.9 mg/m^3 (0.5 ppm)
8-hr	=	2.7 mg/m^3 (2 ppm)
4-hr	=	5.4 mg/m^3 (3 ppm)
1-hr	=	21.6 mg/m^3 (11 ppm)
0.5 hr	=	43.2 mg/m^3 (23 ppm)

Because the AEGLs based upon acute toxicity were equivalent to or lower than the values derived based on potential carcinogenicity, the acute toxicity data were used for the proposed AEGLs for dimethylhydrazine.



Attachment 14

Attachment 15

PROPOSED AEGL VALUES FOR PHOSPHINE

NAC/AEGL MEETING 4

DECEMBER 17, 1996

CHERYL B. BAST, ORNL
ERNEST V. FALKE, US E.P.A.

PROPOSED AEGL VALUES FOR PHOSPHINE					
Classification	**30-min**	**1-hour**	**4-hour**	**8-hour**	**Endpoint (Reference)**
AEGL-1 (Nondisabling)	-	-	-	-	**Appropriate data not available**
AEGL-2 (Disabling)	-	-	-	-	**Appropriate data not available**
AEGL-3 (Lethality)	**1.3 ppm (1.83 mg/m^3)**	**0.9 ppm (1.27 mg/m^3)**	**0.44 ppm (0.62 mg/m^3)**	**0.31 ppm (0.44 mg/m^3)**	**1/3 of 4-hour rat LC_{50} (Waritz and Brown, 1975)**

It is inappropriate to derive an AEGL-1 for phosphine

Human Data Relevant to AEGL-1

- No human data are available for the derivation of AEGL-1 for phosphine.
- Nonlethal effects observed were more severe than those defined by AEGL-1
- No reliable exposure parameters were available.

Animal Data Relevant to AEGL-1

- No Animal data are available for the derivation of AEGL-1 for phosphine.
- Rats exposed to 2.5, 5, or 10 ppm phosphine (Newton, 1991) survived and exhibited only red or mucoid nasal discharge.

- Signs of irritation were also reported by Waritz and Brown (1975), however, the concentrations at which irritation was observed were not reported, and it is not clear if these animals also died as a result of exposure. (LC_{50} = 11 ppm)

- Lethality has been observed in animals exposed to phosphine concentrations below the odor threshold (1.5- 200 ppm, dependent on impurities).

It is inappropriate to derive an AEGL-2 for phosphine

Human Data Relevant to AEGL-2

- No human data are available for the derivation of AEGL-2 for phosphine.
- Although effects such as headache, nausea, vomiting, coughing, shortness of breath, weakness, and paresthesia have been observed, the studies are not appropriate for the derivation since the descriptions of concentration, exposure time, and effects are not well defined.

Animal Data Relevant to AEGL-2

- No animal data are available for the derivation of AEGL-2 for phosphine.
- Newton (1991) observed statistically significant increases in hematological parameters; however, these effects were within historical control ranges and are not considered biologically significant. Chromosomal aberrations were also observed in this study, but statistical significance was not reached and there was no concentration response.

Children appear to be more sensitive than adults.

MMWR, 1994.

Four males were exposed to an undetermined concentration of phosphine in a boxcar containing loose bulk lima beans fumigated with aluminum phosphide.

Subjects were ages 12, 35, 39, and 52 years.

The 12 year old was found dead.

The adults survived. Effects included nausea, vomiting, headache, and abdominal discomfort.

Wilson et al., 1980

Aluminum phosphide fumigation aboard a grain freighter resulted in acute illness in two female children (ages 2 and 4) and 29 of 31 crew members.

The 2 year old died.

All others survived.

Phosphine concentrations measured four days after illness onset were:

2-30 ppm in void space above main deck
7.5-10 ppm around hatch on main deck
0.5 ppm in living quarters.

No exposure times were reported.

PROPOSED AEGL-3 VALUES FOR PHOSPHINE				
	30-min	1-hour	4-hour	8-hour
AEGL-3 (Lethality)	1.3 ppm (1.83 mg/m^3)	0.9 ppm (1.27 mg/m^3)	0.44 ppm (0.62 mg/m^3)	0.31 ppm (0.44 mg/m^3)

Species: Rat
Concentration: 11 ppm phosphine
Time: 4 hours
Endpoint: LC_{50}

$LC_{50} \div 3$ = estimate of LC_0

3: Due to the steepness of the concentration-response curve

n= 2

Uncertainty Factors: Total = 30

3: Rat to human (LC_{50} is most conservative value from most sensitive strain of most sensitive species)

10: Sensitive human subpopulations
(Children appear to be more sensitive than adults)

Body Weight to Minute Volume Correction:

$(V)_A / (V)_H \times (BW)_H / (BW)_A$

1.87×10^{-4} (m^3)/ 1.38×10^{-2} (m^3) x 70 kg/ 0.262 kg = 3.62

PROPOSED AEGL VALUES FOR PHOSPHINE					
Classification	30-min	1-hour	4-hour	8-hour	Endpoint (Reference)
AEGL-1 (Nondisabling)	-	-	-	-	Appropriate data not available
AEGL-2 (Disabling)	-	-	-	-	Appropriate data not available
AEGL-3 (Lethality)	1.3 ppm (1.83 mg/m^3)	0.9 ppm (1.27 mg/m^3)	0.44 ppm (0.62 mg/m^3)	0.31 ppm (0.44 mg/m^3)	1/3 of 4-hour rat LC_{50} (Waritz and Brown, 1975)

TWA PEL: 0.28 ppm

TLV TWA: 0.3 ppm

TLV STEL: 1 ppm

CHLORINE AEGLs

L.A. Gephart
S.S. Talmage

Attachment 16

CHLORINE

- PROPERTIES: Highly reactive greenish-yellow gas with moderate water solubility
- PRODUCTION: 24 billion pounds (1994)
- USES: Manufacture of nonagricultural chemicals such as vinyl chloride and ethylene dichloride; Commercial and household bleaching agent; Biocide in water purification
- TOXICITY CONCERNS:
  Lower concentrations scrubbed in nasal passages, upper respiratory tract
  Higher concentrations reach lungs producing necrosis, pulmonary edema
- AVAILABLE DATA
  Sensory irritation studies with human volunteers
  Nonlethal and lethal studies in variety of animal species

HUMAN DATA

- LETHAL EFFECTS: No measured concentrations
- SUBLETHAL EFFECTS:

  Accidents: Most had no measured exposure concentrations or exposure times
  66 ppm (no exposure time), dyspnea, chest pain, congestion
  30 ppm (estimated), irritation of eyes, sneezing, cough, retrostenal burning, dyspnea, apprehension, and vomiting; asymptomatic by 2 weeks postexposure

- NO EFFECTS/IRRITATION

  Epidemiology studies: no effects, concentrations < 1 ppm
  Human volunteers - 3 studies

TABLE 2
SUMMARY OF IRRITANT EFFECTS IN HUMANS

Concentration (ppm)	Exposure Time*	Effect	Reference
0.5	8 hours	perception of odor, no discomfort, no effects, no changes in pulmonary function measurements	Anglen 1981, Rotman et al. 1983
1.0	2 hours	no noticeable effects	Joosting and Verberk 1974
1.0	4 hours	discomfort for some sensations; no changes in pulmonary function measurements	Anglen 1981
1.0	4 hours	transient changes in pulmonary function measurements (airways resistance)	Rotman et al. 1983
1.0	8 hours	irritation (itchy eyes, runny nose, mild burning in throat); transient changes in pulmonary function measurements	Anglen 1981, Rotman et al. 1983
2.0	15 minutes	perception of odor; no significant irritation effects	Anglen 1981
2.0	30 minutes	not significantly different from control group for irritant effects, irritancy indices	Anglen 1981
2.0	1 hour	itching or burning of throat, urge to cough at ≥ nuisance level	Anglen 1981
2.0	2 hours	very slight irritation of eyes, nose, and throat; no changes in pulmonary function	Joosting and Verberk 1974
2.0	2 hours	no significant changes in pulmonary function	Anglen 1981
2.0	4 hours	≥ 50% response of subjects to sensations characterized as ≥ nuisance: itching or burning of nose or throat, urge to cough, runny nose, general discomfort; transient changes in pulmonary function	Anglen 1981
2.0	8 hours	not immediately irritating, objectional after several hours; increased mucous; transient changes in pulmonary function	Anglen 1981
4.0	2 hours	nuisance level of throat irritation, perceptible to nuisance level of nose irritation and cough	Joosting and Verberk 1974

* 8-hour studies were composed of two segments with a 30-minute or 1-hour break after 4 hours.

SUMMARY OF STUDIES WITH HUMAN VOLUNTEERS

- Joosting and Verberk (1974)

  Eight subjects, ages 28-52
  Two hour studies
  Concentrations of 0.5, 1, 2, 4 ppm
  Description of subjective sensory irritation:

0 = no sensation	3 = nuisance
1 = just perceptible	4 = offensive
2 = distinctly perceptible	5 = unbearable

  Heart rate, respiration rate, some pulmonary measurements
  Limited details reported

- Anglen (1981)

  Male and female subjects, ages 20-32
  Measurements at 1, 2, 4, 8 hours
  Concentrations of 0, 0.5, 1.0, 2.0 ppm
  Subjects were exercising (15 min/hour; heart rate 100 beats/min)
  14 sensory sensations; same scale as Joosting and Verberk
  Some pulmonary function measurements (FVC, FEV_1, EFR)
  Analyses: complicated by grouping sensations

- Rotman et al. (1983)

  Eight non-smoking males, ages 19-33
  Exposures for up to 8 hours (with break)
  Concentrations of 0, 0.5, 1.0 ppm
  15 pulmonary function measurements (measured at 4 hours)
  Subjects were exercising (15 minutes/hour; 100 beats/min)

SUMMARY OF IRRITANT EFFECTS IN HUMANS (CON'T)

- 2 HOURS
  - 1 ppm: Mild sensory irritation
  - 2 ppm: "Nuisance" irritation, no changes in pulmonary function measurements
  - 4 ppm: "Nuisance" level of throat and nose irritation, urge to cough
- 4 HOURS
  - 1 ppm: Mild sensory irritation
    Transient changes in pulmonary function measurements (1 of 2 studies)
  - 2 ppm: "Nuisance" irritation (itching or burning of nose or throat, urge to cough) runny nose, general discomfort; transient changes in pulmonary function

ANIMAL DATA

• ACUTE LETHALITY DATA (TABLE 4)

Good data base for rat for durations of 10-60 minutes
Mouse data questionable due to delayed deaths
Pre-1970 data not in agreement with later data (analytical methods?)
Lethality data tend to follow $C^{\vec{n}} \times t = K$ (ten Berge; data, this paper)

• ACUTE SERIOUS EFFECTS DATA (TABLE 3)

Information on rat, mouse, and rabbit: RD_{50} and LC_0 values
Some histological descriptions

TABLE 4
SUMMARY OF ACUTE LETHAL INHALATION DATA IN LABORATORY ANIMALS

Species	Concentration (ppm)	Exposure Time	Effect[a]	Reference
Dog	650	30 minutes	LC_{50}	Underhill 1920, Withers and Lees 1985a
Rat	700	30 minutes	LC_{50}	Zwart and Woutersen 1988
Rat	1000	53 minutes	LC_{50}	Weedon et al. 1940
Rat	455	1 hour	LC_{50}	Zwart and Woutersen 1988
Rat	288[b]	1 hour	LC_{01}	Zwart and Woutersen 1988
Rat	293[c]	1 hour	LC_{50}	MacEwen and Vernot 1972
Rat	250	7.3 hours	LC_{50}	Weedon et al. 1940
Rat	63	>16 hours	LC_{50}	Weedon et al. 1940
Mouse	290	25 minutes	100% mortality	Bitron and Aharonson 1978
Mouse	1000	28 minutes	LC_{50}	Weedon et al. 1940
Mouse	504	30 minutes	LC_{50}	Zwart and Woutersen 1988
Mouse	127	30 minutes	LC_{50}	Schlagbauer and Henschler 1967
Mouse	170	55 minutes	LC_{50}	Bitron and Aharonson 1978
Mouse	137[c]	1 hour	LC_{50}	MacEwen and Vernot 1972
Mouse	250	1 hour	LC_{50}	O'Neil 1991
Mouse	200	1 hour	LC_{50}	O'Neil 1991
Mouse	170	2 hours	~80% mortality	Bitron and Aharonson 1978
Mouse	10	3 hours	80% mortality	Schlagbauer and Henschler 1967
Mouse	250	7.3 hours	LC_{50}	Weedon et al. 1940
Mouse	63	>16 hours	LC_{50}	Weedon et al. 1940
Rabbit	500	30 minutes	LC_{100}	Barrow and Smith 1975

TABLE 3. SUMMARY OF SUBLETHAL EFFECTS IN LABORATORY ANIMALS

Species	Concentration (ppm)	Exposure Time	Effect[a]	Reference
Rat	2841	5 minutes	LC_0	Zwart and Woutersen 1988
Rat	1500	2 minutes	mild perivascular edema, leucocytic infiltration	Dematti et al. 1995
Rat	200, 500	2, 5 minutes	slight perivascular edema	Dematti et al. 1995
Rat	50, 100	2 minutes	no effect	Dematti et al. 1995
Rat	1500	10 minutes	epithelial hyperplasia, goblet cell metaplasia	Dematti et al. 1995
Rat	25	10 minutes[b]	RD_{50}	Barrow and Steinhagen 1982
Rat	547	30 minutes	LC_0	Zwart and Woutersen 1988
Rat	322	1 hour	LC_0	Zwart and Woutersen 1988
Rat	213	1 hour	LC_0	MacEwen and Vernot 1972
Rat	10.9	6 hours	RD_{50}	Chang and Barrow 1984
Rat	9.1	6 hours	lesions in nasal passages; less severe changes in nasopharynx, larynx, trachea, and lungs	Jiang et al. 1983
Mouse	290	6 minutes	LC_0	Bitron and Aharonson 1978
Mouse	754	10 minutes	LC_0	Zwart and Woutersen 1988
Mouse	9.3	10 minutes	RD_{50}	Barrow et al. 1977
Mouse	55	30 minutes	LC_0	Schlagbauer and Henschler 1967
Mouse	150	1 hour	LC_0	O'Neil 1991
Mouse	3.5	1 hour	RD_{50}	Gagnaire et al. 1994
Mouse	9.1	6 hours	lesions in nasal passages; less severe changes in nasopharynx, larynx, trachea, and lungs	Jiang et al. 1983
Rabbit	50	30 minutes	no gross or microscopic lung changes	Barrow and Smith 1975
Rabbit	100, 200	30 minutes	initial changes in lung function; hemorrhage, pneumonitis, bronchitis; recovery at 60 days except pulmonary compliance	Barrow and Smith 1975

[a] Observed immediately after exposure (Jiang et al. 1983), 72 hours post exposure (Dematti et al. 1995), 5 days post exposure (O'Neil 1991), 14 days post exposure (MacEwen and Vernot 1972, Barrow and Smith 1975, Zwart and Woutersen 1988), 30 days post exposure (Bitron and Aharonson 1978).

[b] The RD_{50} test is a 10-minute test.

SELECTION OF ANIMAL DATA

- Mouse data complicated by delayed deaths attributed to pneumonia

- Good data base for rats; most comprehensive data: Zwart and Woutersen (1988)
  - 4 exposure periods (5, 10, 30, and 60 minutes)
  - 4-7 concentrations/exposure period
  - 14-day post-exposure observation period
  - Respiratory and histological descriptions
  - Analysis method: colorimetric

- 60-minute LC data (determined by probit analysis); (experimental LC_0 is 322 ppm)

LC_{50}	455 ppm
LC_{01}	288 ppm
$LC_{0.1}$	258 ppm

AEGL-1

- USED MILD SENSORY IRRITATION, SLIGHT TRANSIENT CHANGES IN PULMONARY FUNCTION IN HUMANS EXPOSED TO Cl_2 AT 1 PPM FOR 4 HOURS (Anglen 1981, Rotman et al. 1983)

  No uncertainty factor for differences in human sensitivity:
  Below effects level of AEGL-1
  Both sexes were tested
  Subjects were exercising and performing pulmonary function tests

  Scale to 30 minute and 1 and 8 hours using $C^2 \times t = k$

Time	30 Minute	1 Hour	4-Hour	8-Hour
AEGL-1	3	2	1	1

AEGL-2

- USED "NUISANCE" LEVEL OF SUBJECTIVE SENSORY IRRITATION (Joosting and Verberk 1974)

  No uncertainty factor for differences in human sensitivity:
  Below effects level of AEGL-2

  Scale to 30 minute and 1 and 8 hours using $C^2 \times t = k$

Time	30 Minute	1 Hour	4-Hour	8-Hour
AEGL-2	8	6	3	2

- Used 60-minute LC_{01} of 288 ppm for rats (Zwart and Woutersen 1988)

Modifying and uncertainty factors
- 2 to ensure no deaths (SPF rats)
- 3 for interspecies (species LC_{50} values by same author differed by 2)
- 3 for differences in human sensitivity
  (used for other corrosive gases; lethality is a function of the concentration of chlorine in the air, i.e. direct-acting agent)

Scale to 30 minute and 4 and 8 hours using $C^2 \times t = k$

Time	30 Minute	1 Hour	4-Hour	8-Hour
AEGL-3	23	16	8	6

PROPOSED CHLORINE AEGLs

Classification	Exposure Duration			
	30-Minute	**1-Hour**	**4-Hour**	**8-Hour**
AEGL-1 (Nondisabling)	3 ppm (9 mg/m^3)	2 ppm (6 mg/m^3)	1 ppm (3 mg/m^3)	1 ppm (3 mg/m^3)
AEGL-2 (Disabling)	8 ppm (23 mg/m^3)	6 ppm (17 mg/m^3)	3 ppm (9 mg/m^3)	2 ppm (6 mg/m^3)
AEGL-3 (Lethal)	23 ppm (67 mg/m^3)	16 ppm (46 mg/m^3)	8 ppm (23 mg/m^3)	6 ppm (17 mg/m^3)

ACUTE EXPOSURE GUIDELINE LELELS (AEGLs) FOR ETHYLENE OXIDE

PRELIMINARY REPORT

PREPARED BY

KOWETHA A. DAVIDSON, Ph.D., D.A.B.T.
OAK RIDGE NATIONAL LABORATORY
OAK RIDGE, TENNESSEE

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Attachment 17

SUMMARY OF LETHAL EFFECTS OF ETHYLENE OXIDE IN EXPERIMENTAL ANIMALS

Species/sex	LC_{50}[a]		Exposure time (min)	Comments	Reference
	ppm	mg/m^3			
Rat/male	1,460	2,630	240	lowest experimental concentration causing lethality was 882 ppm (20%)	Jacobson et al., 1956
Rat/male	1,972	3,550	240	lowest experimental concentration causing mortality was 2,026 ppm (80%); no mortality at 1,850 ppm	Nachreiner, 1991
Rat/female	1,537	2,767	240	lowest experimental concentration causing mortality was 1,443 ppm (20%); no mortality at 1,021 ppm	Nachreiner, 1991
Rat/male & female	1,741	3,134	240	No comments	Nachreiner, 1991
Rat/male	5,748	10,346	60	lowest experimental concentration causing mortality was 5,546 ppm (20%); no mortality at 4,827 ppm	Nachreiner, 1992
Rat/female	4,439	7,990	60	lowest experimental concentration causing mortality was 3,966 ppm (40%); no mortality at 3,609 ppm	Nachreiner, 1992
Rat/male & female	5,029	9,052	60	no comments	Nachreiner, 1992
Rat/sex not specified	ND	ND	30	1:100 (10,679 ppm) was fatal to rats; no additional information; 1:150 (7,119 ppm) was not fatal	Walker and Greeson, 1932
Mouse/female	835	1,504	240	lowest experimental concentration causing mortality was 533 ppm (20%); lowest concentration tested	Jacobson et al., 1956
Mouse/male	ND	ND	240	LC_{50} was not calculated; 100% mortality at 800 ppm; no deaths at 400 ppm	NTP, 1987

SUMMARY OF LETHAL EFFECTS OF ETHYLENE OXIDE IN EXPERIMENTAL ANIMALS (CONTINUED)

Species/sex	LC_{50}[a]		Exposure time (min)	Comments	Reference
	ppm	mg/m^3			
Mouse/female	660	1,188	240	lowest experimental concentration causing mortality was 800 ppm (80%); no mortality at 400 ppm	NTP, 1987
Mouse	ND	ND	30	1:150 (7119 ppm) was fatal to mice	Walker and Greeson, 1932
Dog/male	960	1,730	240	no deaths occurred at 710 pm	Jacobson et al., 1956
Guinea pig	ND	ND	480	1,300 ppm caused death	Waite et al., 1930
Guinea pig	ND	ND	330	3,000 ppm caused death	Waite et al., 1930
Guinea pig	ND	ND	190	3,000 ppm caused death	Waite et al., 1930
Guinea pig	ND	ND	150	7,000 ppm caused death	Waite et al., 1930
Guinea pig	ND	ND	60	25,000 ppm caused death	Waite et al., 1930
Guinea pig	ND	ND	10	63,000 ppm caused death	Waite et al, 1930

[a]LC_{50} or the percent mortality at the lowest experimental concentration causing mortality.

SUMMARY OF NONLETHAL EFFECTS OF ETHYLENE OXIDE IN HUMANS

Concentration		Exposure duration	Effects	Reference
ppm	mg/m^3			
13349	24028	10 sec	definitely irritating to nasal passages	Walker and Greeson, 1932
2670	4806	not reported	slightly irritating to nasal passages, acetic acid-like odor	Walker and Greeson, 1932
≥700	1260	30 min	odor, headache, gastrointestinal effects, eye and upper respiratory tract irritation, pruritus, muscle weakness, dizziness, hemolysis	Deleixhe et al., 1986; Laurent, 1988
≥700	≥1260	4 h/day for 4 days	coughing, shortness of breath, wheezing, slight peripheral neuropathy, immunological asthma	Deschamps et al., 1992
excursions ≥700	≥1260	2 weeks to 2 months	eye and mucous membrane irritation, difficult swallowing, headache, gastrointestinal effects, lethargy, fatigue, problems with memory and thinking, major motor seizures, peripheral neuropathy	Gross e al., 1979
≤500	900	2 to 5 min	gastrointestinal effects, unconsciousness, apnea, muscle twitching, malaise, incoordination for up to 1 week	Salinas et al., 1981
not reported	not reported	4 months to 1½ years	eye irritation, headaches, smelling of fumes, distal axonal neuropathy	Finelli et al., 1983
0.23 to 0.56 ppm (TWA); excursions of 11 or 77 ppm	0.4 to $1mg/m^3$; 19.8 to 139.6 mg/m^3	chronic	sweet-like odor, headache, dizziness, irritation of mucous membranes, gastrointestinal effects, fatigue, nervousness	Zey et al., 1994

SUMMARY OF NONLETHAL EFFECTS OF ETHYLENE OXIDE IN HUMANS (CONTINUED)

Concentration		Exposure duration	Effects	Reference
ppm	mg/m^3			
peak = 23.5 total up to 10.7 average 3.4	42.3 19.3 6.1	up to 1 min up to 11.75 min not reported	odor, headache, skin and eye irritation, dry mouth, sore throat, runny nose, shortness or breath, nausea, numbness in fingers, drowsiness	Bryant et al., 1989
0.1 to 0.5 ppm (8-h TWA); peak 250 ppm; 5 to 10 ppm (20 min daily)	0.18 to 0.9 (TWA); 450 9 to 18	during pregnancy	increased risk of spontaneous abortion	Hemminki et al., 1982
not reported	not reported	any duration during pregnancy	increased risk of spontaneous abortion, preterm birth, or postterm birth	Rowland et al., 1996

GENOTOXIC EFFECTS OF INHALED ETHYLENE OXIDE ON GERM CELLS IN MALE RODENTS

Species/Strain	Assay	Experimental Protocol	c × t	Results	Reference
Rat/Long-Evans	Dominant lethality[a]	1,000 ppm for 4 h; mated with females weekly for 10 weeks	4,000 ppm•h	Positive: increase in dead implants per pregnancy (wks 2, 3, 5) and dead implants per total implants (wks 1, 2, 3, 5)	Embree et al., 1977
Mouse/ $(C3H \times B110)F_1$	DNA strand breaks and UDS	450 ppm for 4 h, 900 ppm for 2 h, or 1,800 ppm for 1 h	1,800 ppm•h	Positive: DNA strand breaks and UDS; exposure-rate effect: 1800 ppm>900 ppm>450 ppm	Sega et al., 1988
Mouse/ $(C3H \times B110)F_1$	DNA alkylation of sperm and hemoglobin	75 ppm for 4 h, 150 ppm for 2 h, or 300 ppm for 1 h	300 ppm•h	DNA alkylation of epididymal and vas sperm and hemoglobin	Sega et al., 1991
Mouse/ $(101 \times C3HF_1)$	Dominant lethality[b]	255 ppm, 6 h/day, 5 d/wk for 2 or 11 wks	15,300 ppm•h or 84,150 ppm•h	Positive: dominant lethals produced after 2 (39%) and 11 weeks (55%)	Generoso et al., 1983
Mouse/($C3H \times 101)F_1$	Dominant lethality	control, 300, 400, or 500 ppm, 6 h/d for 4 d	7,200 ppm•h, 9,600 ppm•h, 12,000 ppm•h	Positive: exposure-related increase; 4, 27, and 62% dominant lethals	Generoso et al., 1986

GENOTOXIC EFFECTS OF INHALED ETHYLENE OXIDE ON GERM CELLS IN MALE RODENTS (CONTINUED)

Species/Strain	Assay	Experimental Protocol	c × t	Results	Reference
Mouse/ $(C3H \times 101)F_1$	Dominant lethality	control, 300 ppm for 6 h/d, 600 ppm for 3 h/d, or 1,200 ppm for 1.5 h/d for 4 d	1,800 ppm•h	Positive: exposure-rate increase; 11, 32, and 64% dominant lethals	Generoso et al., 1986
Mouse/ $(C3H \times 101)F_1$	Dominant lethality	control, 165, 204, 250, or 300 ppm 6 h/d, 5 d/wk for 6 wks, then 7 d/wk for 2.5 wks.	47,025 - 85,500 ppm•h	Positive: dose-related increase; 6-8, 13-14, 23-24, and 45-60% dominant lethals	Generoso et al., 1990
Mouse/ $(C3H \times 101)F_1$	Heritable translocation	control, 165, 204, 250, or 300 ppm 6 h/d, 5 d/wk for 6 wks, then 7 d/wk for 2.5 wks.	47,025 - 85,500 ppm•h	Positive: dose-related increase; 0.05, 2.80, 5.09, 10.84, and 25.53% translocation carriers in combined female strains	Generoso et al., 1990

[a]Defined as the number of dead implants per total implants.
[b]Defined as the average no. living embryos in experimental group/average no. for controls.
UDS = unscheduled DNA synthesis

DEVELOPMENTAL AND REPRODUCTIVE EFFECTS OF ETHYLENE OXIDE VAPOR

Species	Exposure	Effect	Reference
Rat	0, 10, 33, 100 ppm, 6 h/day, gd 6-15	33 ppm – NOEL 100 ppm – mild retarded growth of fetus	Snellings et al., 1982a
Rat	0, 50, 125, 250 ppm, 6 h/day, gd 6-15	50 ppm – NOEL 125 ppm – growth retardation of fetus 250 – more severe growth retardation	BRRC, 1993
Rat	0, 150 ppm, 7 h/day, 5 d/wk, premating, gd 7-16, or 1-16	growth retardation of fetus regardless of stage of exposure	Hackett, 1982
Mouse	0, 1200 ppm, 1½ h, gd 1	fetal deaths, hydrops, and other malformations	Rutledge and Generoso, 1989
Mouse	0, 200, 400 ppm, 6 h/day, 5, 15, or 25 exposures	200 ppm: abnormal spermatozoa 400 ppm: abnormal spermatozoa	Ribeiro et al., 1987
Rat	0, 10, 33, 100 ppm, 6 h/day, 1-generation reproduction	33 ppm – NOEL 100 ppm – reproductive and fetal effects	Snellings et al., 1982b
Rat, males	0, 50, 100, 250 ppm, 6 h/day, subchronic	50 ppm – abnormal sperm, teratic type 100 ppm – abnormal sperm, teratic type 250 ppm – abnormal sperm, testicular degeneration	Mori et al., 1991
Rabbits	0, 150 ppm, 7 h/day, gd 7-19 or 1-19	no developmental effects	Hackett et al., 1982

ESTIMATES OF LETHAL CONCENTRATIONS OF ETHYLENE OXIDE BASED ON ANIMAL DATA									
Species	Duration of Exp. (hours)	LC_{50}		LC_{01} (ppm)	AEGL Values[a] (ppm)				Reference
		(ppm)	mg/m^3		30 min	1 hour	4 hours	8 hours	
Rat	4	1460	2628	628	1672	836	209	105	Jacobson et al., 1956
		1741	3134	922	2456	1228	307	154	Nachreiner, 1991
Mouse		835	1503	406	1080	540	135	68	Jacobson et al., 1956
		623	1121	264	**704**	**352**	**88**	**44**	NTP, 1987
Dog		960	1728	120	~~1280~~ 320	~~640~~ 160	~~160~~ 40	~~80~~ 20	Jacobson et al., 1956
Rat	1	5029	9052	2494	1662	831	208	104	Nachreiner, 1992
Mouse	1.5	1200	2160	NA	~~1662~~ 1200	~~831~~ 600	~~208~~ 150	~~104~~ 75	Rutledge and Generoso, 1989
Mouse	1.5 × 4 days[a]	1200	2160	NA	~~1662~~ 1200	~~831~~ 600	~~208~~ 150	~~104~~ 75	Generoso et al., 1987
	6 × 10 days[a]	300	540	NA	**1200**	**600**	**150**	**75**	Generoso et al., 1987

[a]Rhomberg et al. (1990) showed that the relationship between concentration of ethylene oxide in air and hemoglobin adduct formation is linear for several species (mouse, rat, rabbit, human); therefore, UF = 3 (intraspecies sensitivity) is selected for exposure adjustment; no uncertainty factor for interspecies extrapolation.
[b]Late fetal deaths, severe defects (82% induced loss of conceptuses, 39.2% abnormal fetuses)

ESTIMATES OF AEGL-2 VALUES BASED ON ANIMAL DATA

NONLETHAL TOXICITY

- Rat – 1000 ppm, 4 h (4000 ppm•h), CNS toxicity, eye and respiratory irritation (Embree et al., 1977)
  AEGL-2 = 333 ppm (1332 ppm•h) (UF = 3) for a 4-h exposure

  AEGL-2 = **2664 ppm** (30-min); **1332 ppm** (1-h); **333 ppm** (4-h); **167 ppm** (8-h)

DEVELOPMENTAL TOXICITY

- Rat – *100 ppm, 6 h (600 ppm•h), fetal growth retardation (Snellings et al., 1982a)
  33 ppm, 6 h (198 ppm•h), NOEL
  *AEGL-2 = 33 ppm (198 ppm•h) (UF = 3) for a 6-h exposure

  *AEGL-2 = **396 ppm** (30-min); **198 ppm** (1-h); **50 ppm** (4 h); **25 ppm** (8-h)

- Rat – 225 ppm, 6 h (1350 ppm•h), fetal growth retardation (BRRC, 1993)
  125 ppm, 6 h (750 ppm•h), fetal growth retardation
  *50 ppm, 6 h (300 ppm•h), fetal growth retardation
  *AEGL-2 = 17 ppm (102 ppm•h) (UF = 3) for a 6-h exposure

  *AEGL-2 = **204 ppm** (30-min); **102 ppm** (1 h); **26 ppm** (4-h); **13 ppm** (8 h)

ESTIMATES OF AEGL-2 VALUES BASED ON HUMAN DATA

- ≥700 ppm, 4 h (2800 ppm•h), respiratory irritation, peripheral neuropathy (Deschamps et al., 1992)
  AEGL-2 = 233 ppm (932 ppm•) (UF = 3) for a 4-h exposure

  AEGL-2 = **1864 ppm** (30-min); **932 ppm** (1-h); 233 ppm (4-h); **117 ppm** (8-h)

- ≥700 ppm, 30 min (1400 ppm•h), CNS toxicity, muscle weakness, hemolysis (Deleixhe et al., 1986; Laurent, 1988)
  AEGL-2 = 233 ppm (117 ppm•h) (UF = 3) for a 30-min exposure

  AEGL-2 = **233 ppm** (30-min); **117 ppm** (1-h); **29 ppm** (4 h); **15 ppm** (8 h)

ESTIMATES OF AEGL-1 VALUES BASED ON ANIMAL DATA

- Rat – 100 ppm, 6 h (600 ppm•h), fetal growth retardation (Snellings et al., 1982a)
  33 ppm, 6 h (198 ppm•h), NOEL
  AEGL-1 = 11 ppm (66 ppm•h) (UF = 3) for a 6-h exposure

  *AEGL-1 = ~~33~~ 132 **ppm** (30-min); **66 ppm** (1-h); **16.5 ppm** (4 h); **8 ppm** (8-h)

Attachment 18

ETHYLENE OXIDE LC50 VALUES

FROM B RRC LABORATORY

Exposure Time	LC50(ppm) ♂	LC50(ppm) ♀	(Factor)
4 hr	1972	1537	1.3x
1 hr	5748	4439	1.3x
(factor)	2.9x	2.9x	
30 min	~10000	~8000	(guess)

SOLVAY SOLKATRONIC CHEMICALS

Attachment 19

solkatronic®

September 23, 1996

Dr. George Rusch, DABT
Allied Signal, Inc.
P.O. Box 1139R
Columbia Road
Morristown, NJ 07962

Dear Dr. Rusch:

At the recent AEGL meeting of September 17, 1996, the Committee agreed to develop AEGLs for ten minute exposures recognizing that accidental releases could peak and dissipate in this amount of time. As I mentioned at the meeting, this would be true if the release of the Hydrogen Fluoride was in the vapor phase and its heat of evaporation would then cool the remaining liquid. In large releases of liquefied gases, this would have a significant affect on the pressure and would lower it to atmospheric pressure in a very short time period. Attached please find some ideal calculations of releases and temperatures the liquefied gas such as Ammonia or Chlorine would reach in this event.

Since the Committee accepts this for Hydrogen Fluoride, it should also accept this for the other liquefied compressed gases in order to be consistent. These would include:

- Ammonia
- Arsine
- Boron Trichloride
- Chlorine
- Hydrogen Chloride
- Hydrogen Selenide
- Phosphine

This would be very helpful for us in developing our preplans for our facilities. If you or the Committee should require any other information regarding this, I would be more than happy to address them.

I look forward to seeing you at the next meeting.

Sincerely,

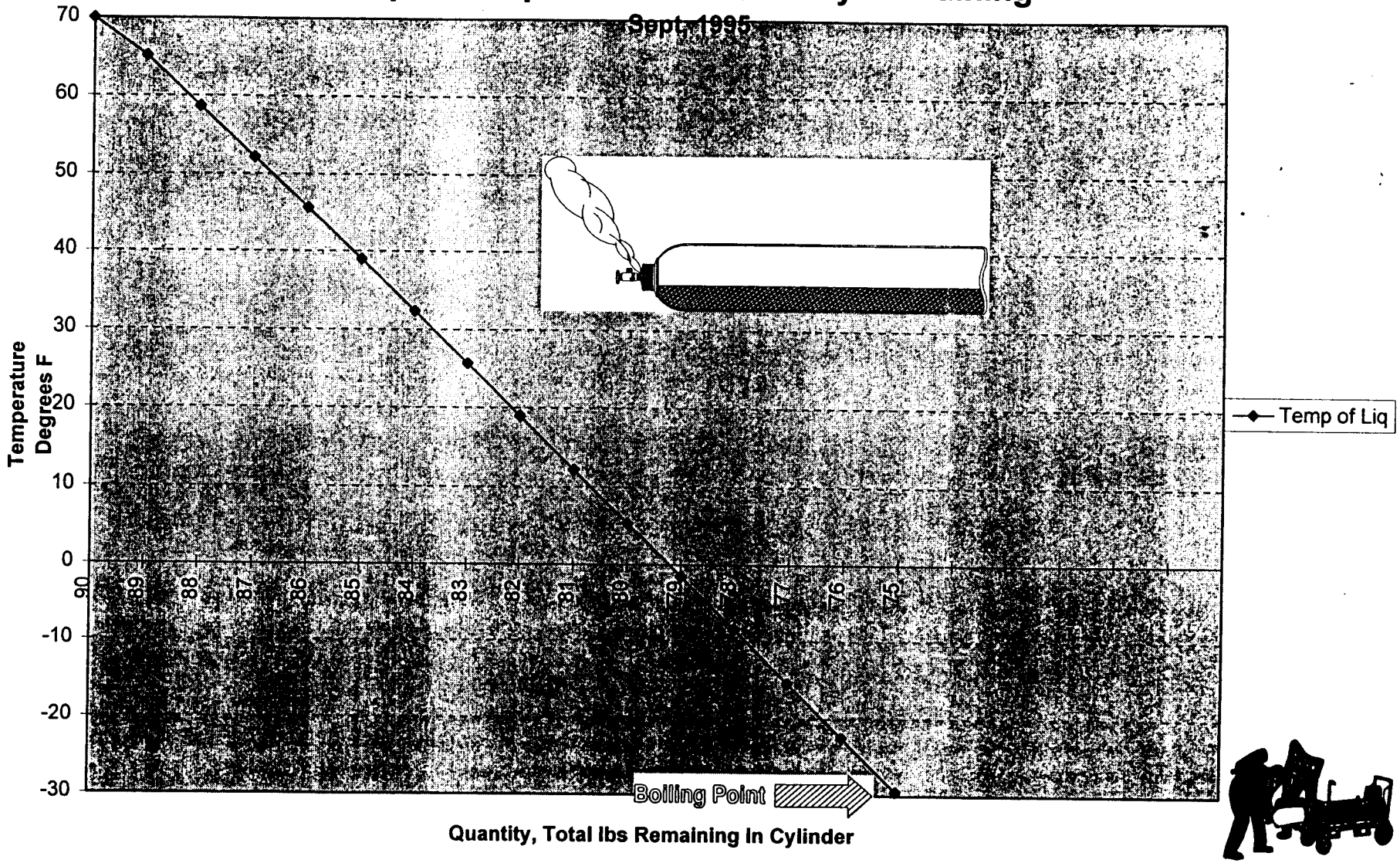
Eugene Y. Ngai
Vice President
Corporate Development & Technology

EYN/ss
Att.
cc: J-L Anspach
J. A. Swanciger
J. R. Hannis
J. McDermott
Wolfe Wagner

Solkatronic Chemicals, 99 Two Bridges Road, Fairfield, New Jersey 07004-1530, 1-800-521-3981, 201 882-7900, Fax 201 882-7967

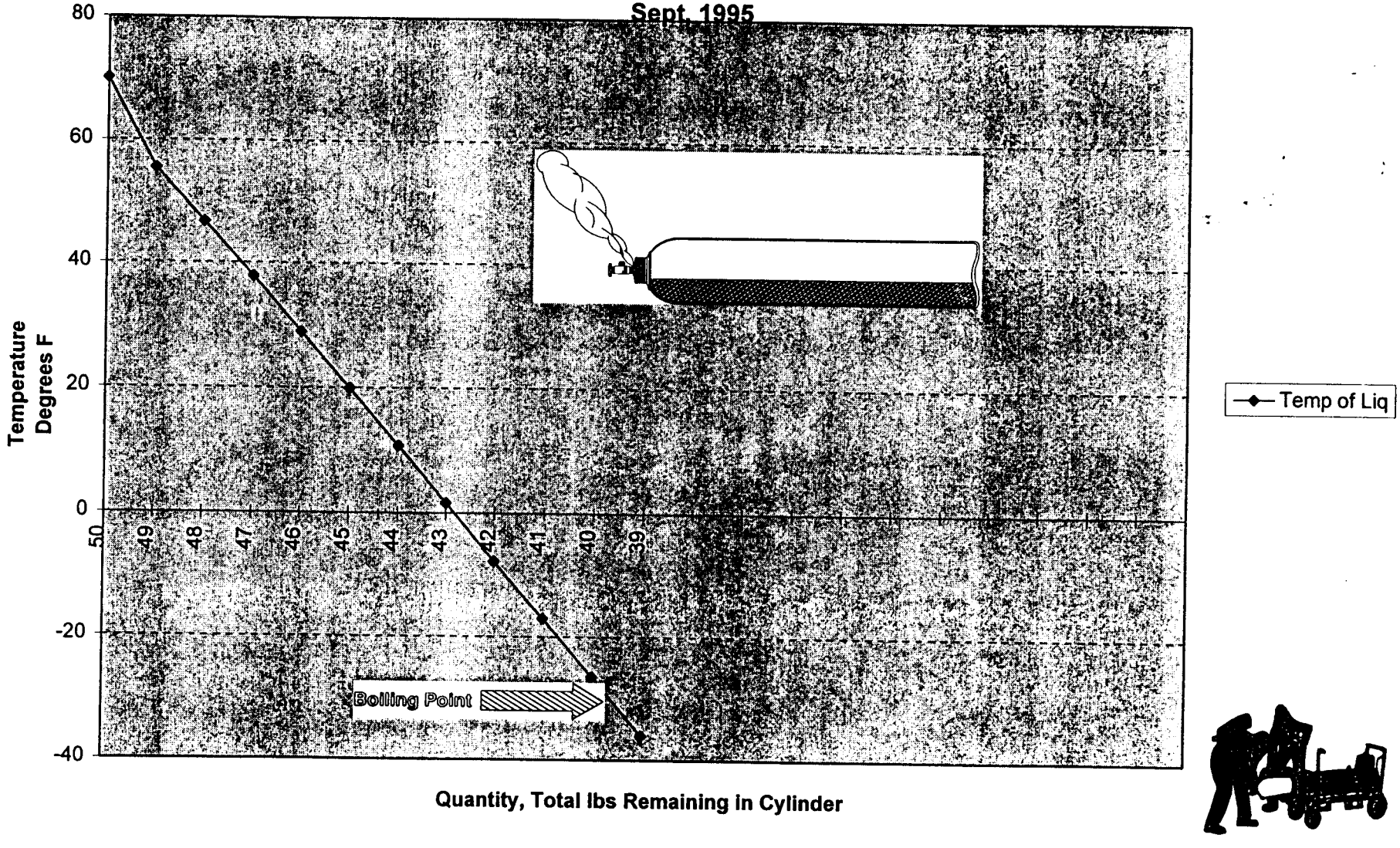
solkatronic

Chlorine RELEASE, Theoretical, 90 lbs
Liquid Temperature vs. Quantity Remaining
Sept. 1995



solkatronic®

AMMONIA RELEASE, Theoretical, 50 lbs
Liquid Temperature vs. Quantity Remaining
Sept. 1995



AlliedSignal
ENGINEERED
MATERIALS

AlliedSignal Inc.
P.O. Box 1139
Morristown, NJ 07962-1139

October 8, 1996

Mr. Eugene Y. Ngai
Vice President
Corporate Development & Technology
SOLVAY - Solkatronic Chemicals
30 Two Bridges Road
Fairfield, N.J. 07004

Dear Mr. Ngai:

I thank you for your recent letter regarding the question of short-term exposure limits for the series of additional materials. By copy of this letter, I am sending your letter to Dr. Po-Yung Lu that he may include it in the agenda for our December meeting. I will then discuss this request with the other members of the Committee.

Sincerely,

GMR:rb

Dr. George M. Rusch, Ph.D., DABT
Director of Toxicology

cc: Dr. Po-Yung Lu ✓

q:\erp\10-8-96a

FEDERAL AGENCIES

Agency for Toxic Substances and Disease Registry*
Centers for Disease Control
Department of Defense
(Army*/Navy/Air Force)
Department of Energy
Department of Transportation
Environmental Protection Agency
(OPPT/Superfund/ORD)
Federal Emergency Management Agency
Food and Drug Administration
National Institute for Occupational Safety and Health

INDUSTRY

AlliedSignal

Exxon Biomedicals

Olin Corporation

ORGANIZATIONS

AFL-CIO*

American Association of Poison Control Centers

American Association of State and Territorial Health Officials

American Industrial Hygiene Association (represented by Olin Chemical Co. rep.)

American College of Occupational and Environomental Medicine

Environmmental Group*

ICEH

National Fire Protection Agency

STAPPA/ALAPCO

National Advisory Committee for the Development of Acute Exposure Guideline Levels for Hazardous Substances (NAC/AEGL)
*** = not yet a member**

STATES

California

Minnesota

New Jersey

New York

Texas

ACADEMIA

Oregon State

Rutgers University

University of Idaho

Virginia Polytechnical Institute

Attachment 20

THE FERTILIZER INSTITUTE
501 Second Street, N.E., Washington, D.C. 20002
TEL: 202/675-8250
FAX: 202/544-8123

Attachment 21

JIM M. SKILLEN
Director
Environmental Programs

January 24, 1997

Po-Yung Lu, Ph.D.
Biomedical and Environmental Information Analysis
Oak Ridge National Laboratory
1060 Commerce Park, MS 6480
Oak Ridge, TN 37830

RE: Additional Comments to the National Advisory Committee on Acute Exposure Guideline Levels (AEGLs)

Dear Dr. Lu:

Attached are thirty (30) copies of additional comments prepared by ENVIRON on behalf of TFI. These comments were prepared to address three comments or questions that were raised by members of the National Advisory Committee on Acute Exposure Guideline Levels (AEGLs). The questions were raised during the discussion about proposed AEGL values for ammonia after Dr. Joseph V. Rodricks' presentation on December 16, 1996.

Please distribute these additional comments from TFI to the members of the NAC/AEGL Committee.

Sincerely,

James M. Skillen

James M. Skillen

JMS/gcm
Attachments a/s

ENVIRON

January 23, 1997

Mr. Jim M. Skillen
Director, Environmental Programs
The Fertilizer Institute
501 Second Street, N.E.
Washington, D.C. 20002

Re: AEGL Values for Ammonia

Dear Mr. Skillen:

Three comments or questions posed by members of the National Advisory Committee on Acute Exposure Guideline Levels (AEGLs) during the December 16, 1996 meeting pertained to ENVIRON's report entitled *Review and Technical Critique of Acute Exposure Guideline Levels (AEGLs) Proposed for Ammonia* ("ENVIRON Report") and my presentation. With this letter, I provide our thoughts and responses to these three issues.

Pedersen and Selig's Probit Equations

ENVIRON was asked to summarize the basis for Pedersen and Selig's (1989)[1] probit equations for healthy and vulnerable human populations and explain how we used those equations in our analysis.

Pedersen and Selig relied upon the work of Withers et al. (1988) who compiled and combined available animal data regarding lethality and generated a probit equation, as follows:

$$Probit = 1.85 \times \ln D - 35.9 \quad \textbf{(1)}$$

where D, referred to as the "dosement" by Withers and Lees (1985a), is a dose term given by $C^2 \times t$, where C is the constant exposure concentration (ppmv ammonia) and t is the duration of exposure (minutes). Withers et al. (1988) concluded that (1) ammonia was a respiratory irritant in both animals and humans, representing a local rather than a systemic effect; (2) the spectrum of effects in animals and man suggest a common mechanism of action; and (3) although there are major differences between animals and man in their respiratory anatomy and physiology, the differences in susceptibility to ammonia "between man and rodents must be relatively small." As a result, they chose to make no adjustments to the data for mice and rats and suggested that the probit equation obtained using animal data "should be applicable to man."

[1] References cited herein are provided on the list at the end of this letter.

The probit equation developed by Withers et al. (1988) was used by Pedersen and Selig (1989) to identify a set of concentrations which they expected could cause lethality in the general (healthy) population. Pedersen and Selig (1989) used the probit equation shown above to predict the "distance to zero fatality" for two accidents for which they reconstructed exposure concentrations: an accident in Houston, Texas (United States) and an accident in Potchefstroom (South Africa). They reported that the areas in which deaths actually occurred "at Houston and Potchefstroom were relatively small compared with calculated predictions." They concluded "that the distance to zero fatality [predicted using the above probit equation for the general population] provides a fairly realistic estimate of the limit of the high risk area."

Pedersen and Selig (1989) recognized that a proportion of the general population, including children, older people, individuals with respiratory or heart disorders, might be more vulnerable to ammonia. They, therefore, derived a modified probit equation for vulnerable individuals, based upon an approach outlined by Eisenberg et al. (1975) in a report to the U.S. Coast Guard. Eisenberg et al. (1975) proposed and used the following relationship between the lethal concentrations of ammonia and chlorine for the general population and the vulnerable population:

Proposed Relationship Between Susceptibility of Vulnerable Individuals versus the General Population (Eisenberg et al. 1975)

Toxic Effect	Incidence (% of Individuals Exposed) Expected in the General Population	Incidence (% of Individuals Exposed) Expected in the Vulnerable Population
Lethality	3	50
Lethality	50	100

Dosements associated with 3% lethality (LD_3) and 50% lethality (LD_{50}) in the general population were obtained by Pedersen and Selig (1989) from the probit equation #1 shown above. If these dosements are assigned, respectively, to the LD_{50} and LD_{100} (approximated by the $LD_{99.9}$) for the vulnerable population, as proposed by Eisenberg et al. (1975), then the resulting probit equation for the vulnerable population can be determined algebraically to be:

$$Probit = 3.04 \times \ln D - 59.1 \qquad (2)$$

When these two probit equations are employed to estimate the "zero lethality" concentrations, the following values are obtained (see, for example, ORNL 1996a, p. 31 and ORNL 1996b, p. 33):

Estimates of Lethal Concentrations of Ammonia to Humans Based Upon the Probit Equations Used by Pedersen and Selig (1989)			
Exposure Duration	**Probability of Mortality**	**Lethal Concentration (LC) of Ammonia (ppmv) for Stated Duration and Probability**	
		General Population (Equation 1)	**Vulnerable Population (Equation 2)**
5 minutes	0.01 (1%)	15,199	11,620
	0.001 (0.1%)	12,363	10,246
30 minutes	0.01(1%)	6,205	4,744
	0.001 (0.1%)	5,047	4,183
60 minutes	0.01 (1%)	4,388	3,356
	0.001 (0.1%)	3,569	2,958
240 minutes	0.01 (1%)	2,194	1,677
	0.001 (0.1%)	1,784	1,479
480 minutes	0.01 (1%)	1,551	1,186
	0.001 (0.1%)	1,262	1,046

These data show that the LC_{01} (1% mortality probability) and the $LC_{0.1}$ (0.1% mortality probability) values (ppmv ammonia) provide similar estimates ($\pm$ 20% approximately) of the "zero lethality" concentrations. For example, the 5-minute LC_{01} value for the "vulnerable" population is 11,620 ppmv compared to 10,246 ppmv for the 5-minute $LC_{0.1}$ value. The LC values for the vulnerable population are lower than those for the general population by similar fractions (i.e., $\pm$ 20% approximately). For example, the 5-minute $LC_{0.1}$ value for the "vulnerable population" is 10,246 ppmv compared to 12,363 ppmv for the general population. Conceptually, the shape of the probit equation (i.e., relationship between mortality and dose) for the general population in the lower range of doses (e.g., $LC_{0.1}$ and LC_{01} values) would be heavily influenced by the susceptibility of the vulnerable subset within the general population. On this basis, it should be expected that the $LC_{0.1}$ or LC_{01} values might be similar for the general human population and the vulnerable subset of the general population.

In the initial (April 1996) report by Oak Ridge National Laboratory (ORNL), their recommended AEGL-3 values, based upon data for rats (Appleman et al. 1982), were compared to the results (shown in the preceding table) from the probit equation by Pedersen and Selig (1989). For example, ORNL recommended a 30-minute AEGL-3 value of 1,700

ppmv ammonia compared to a 30-minute $LC_{0.1}$ of 5,047 to 6,205 ppmv for the general population and 4,183 to 4,744 ppmv for the "vulnerable population" (see below). ORNL concluded that their recommended "values are supported by the results from the probit equation reported by Pedersen and Selig (1989)."

In the ENVIRON Report (p. 9), we compared our recommended AEGL-3 value for one-hour (2,400 ppmv) and the "zero lethality" concentration predicted by the Pedersen and Selig probit equation (#2 above) for vulnerable individuals (2,950 ppmv for using the $LC_{0.1}$ value). As shown in the preceding table, the $LC_{0.1}$ value for the general population predicted by Pedersen and Selig (1989) is 3,600 ppmv. Because Pedersen and Selig (1989) found that their probit equations over-predicted the extent of the areas with mortality due to two ammonia accidents, we conclude that our recommended AEGL-3 values, which are lower than the $LC_{0.1}$ values predicted by Pedersen and Selig's probit equations, should be protective.

HEC Adjustment

Our recommendations regarding AEGL-3 values for ammonia are based upon probit equations developed for rats (Appleman et al. 1982), an adjustment of the external exposure concentration of the rats to a human equivalent concentration (HEC) (USEPA 1994), and the use of a ten-fold overall uncertainty factor. The default value of the regional gas dose ratio (RGDR) for the pulmonary region for Type I gases (USEPA 1994) was used to make the HEC adjustment, which accounts for interspecies differences in delivered dose.

As noted in the USEPA's 1994 report entitled *Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry,* "[t]he various species used in inhalation toxicology studies do not receive identical doses in comparable respiratory tract regions when exposed to the same external particle or gas concentration." (p. 3-1) This is principally because "[t]he respiratory systems of humans and various experimental animals differ in anatomy and physiology in many quantitative ways." (p. 3-3) "In general, laboratory animals have much more convoluted nasal turbinate systems than do humans, and the length of the nasopharynx in relation to the entire length of the nasal passage also differs between species. This greater complexity of the nasal passages, coupled with the obligate nasal breathing of rodents, is generally thought to result in greater deposition in the upper respiratory tract (or [extra thoracic] region) of rodents than in human beings breathing orally or even nasally." (p. 3-4) "It should be recognized that the respiratory tract contains a variety of different cells types that possess different metabolizing potential and are distributed in a manner that varies among species." (p. 3-26) "In addition... the regional thickness and composition of the airway epithelium (a function of cell types and distributions) is an important factor in gas absorption and contributes to the solubility and extent of reaction of the gas." (pp. 3-16 to 3-17) "The biologic endpoint or health effect, therefore, may be more directly related to the quantitative pattern of mass deposited within the respiratory tract than to external exposure concentration." (p. 3-1) Likewise, the Subcommittee of the National Academy of Sciences on Guidelines for Developing Community Emergency Exposure Levels

for Hazardous Substances has stated that "[i]f the effect [of a chemical agent] is directly on the surfaces of the lung [as is the case with ammonia], then the effect might well depend on [external] concentration, although the effect also will depend upon breathing rate and the geometry of the airways and lungs of each species." (NRC 1993, pp. 91-92) Given the above, there should be no doubt that an adjustment of exposure concentrations experienced by laboratory animals to HECs is justified if a realistic interspecies extrapolation of inhalation data is sought.

The regional gas dose ratio (RGDR) for the pulmonary region for Type I gases was employed by ENVIRON because "[t]he pulmonary region is the region of concern for lethality in humans exposed to ammonia" (ORNL 1996b, p. 36) and ammonia exhibits the characteristics of a Type I gas, as defined by USEPA (1994) (i.e., highly water soluble and/or rapidly reactive in the surface-liquid tissue of the respiratory tract). The RGDR model for highly reactive and highly soluble gases (such as ammonia) ".. takes into account the loss of chemical in the airstream to the upper respiratory tract as it progresses to the lower respiratory tract and separate equations are provided to calculate the dose in each region." (USEPA 1994, pp. 4-46 to 4-47). The fraction of inhaled chemical concentration penetrating the upper (extra thoracic and tracheobronchial) regions (fp_{ET} and fp_{TB}, respectively) and available for absorption in the pulmonary region depends upon the minute volume of the species (V_E), the surface areas of the extrathoracic and tracheobronchial regions (SA_{ET} and SA_{TB}, respectively), and the overall mass transport coefficient in these two regions (Kg_{ET} and Kg_{TB}, respectively) (USEPA 1994). The delivered dose to the pulmonary region also depends upon the alveolar ventilation rate (Q_{alv}), the surface area of the pulmonary region (SA_{PU}), and the overall mass transport coefficient in this region (Kg_{PU}). According to this USEPA model, the fraction absorbed in each region can be expressed in terms of these anatomic and physiologic factors of the respiratory tract. The RGDR ratio is simply the ratio of predicted absorption (fraction absorbed) in a given region in the animal species to the predicted absorption (fraction absorbed) in the same region in humans. Given the above, the USEPA-derived RGDR model for the pulmonary region provides a rational approach to calculating HECs from exposure concentrations in animal studies, when a realistic interspecies extrapolation of inhalation data is sought.

Consistent with recommendations made by ORNL (1996a,b), the default value of the RGDR for the pulmonary region was used to derive ENVIRON's recommended AEGL-3 values. One committee member suggested that the default RGDR value is not valid because ammonia absorption may be less than 100% at lethal exposure concentrations.

The model for the default value represents a simplified expression that is valid for cases where the penetration fractions for the upper (extra thoracic and tracheobronchial) regions (fp_{ET} and fp_{TB}, respectively) are comparable for the animal and human species (see footnotes 1 and 2, p. I-24 and I-26, in Appendix I of USEPA (1994)). Some of these cases will occur at relatively low exposure concentrations for which the penetration fraction from the upper regions is negligible (i.e., practically 100% absorption). Other valid cases, however, can entail higher

concentrations where the penetration fractions from the upper regions are comparable, but closer to 100% penetration. Calculations we have performed using the generic ("non-default") versions of the RGDR model confirm that the default value of the USEPA-derived RGDR model for the pulmonary region is appropriate for calculating HECs for ammonia from exposure concentrations in lethality studies involving animals.

Silverman et al. Study

In a study by Silverman et al. (1949), seven adult males were exposed to 500 ppmv for up to 30 minutes by means of a half-face respirator. There were small changes in respiratory physiology, however these changes returned to pre-exposure levels within 5 minutes after exposure ceased.

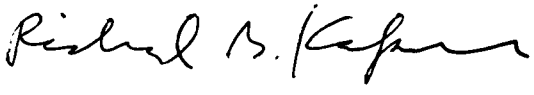
One commenter questioned whether the hyperventilation in the seven male subjects that was reported by Silverman et al. (1949) was expected and had been confirmed in other studies. Our review of the toxicological literature regarding ammonia indicates that there are limited data on human subjects. Most studies tested ammonia exposure concentrations less than 500 ppmv (as summarized in the ENVIRON report, as well as ORNL 1996a and ORNL 1996b), which would not provide for a direct confirmation or contradiction of Silverman et al.'s results.

Moreover, ENVIRON's use of the Silverman study does not rely upon the finding, or any confirmation, of hyperventilation, but rather the temporary nature of all effects observed and reported. As noted in the ENVIRON report, the Silverman et al. study suggests that inhalation exposures to 500 ppmv ammonia, the only exposure concentration tested, should not cause irreversible or long-lasting effects in humans. On the basis of this study and one reported by Lehmann (1886), ENVIRON continues to recommend that the 30-minute AEGL-2 value for ammonia be set at a concentration greater than 300 ppmv and up to 500 ppmv.

We hope that you and members of the National Advisory Committee on AEGLs will find this information useful.

Please give me a call if you have any questions regarding any of these issues. I can be reached at 703-516-2315.

Very truly yours,



for Joseph V. Rodricks, Ph.D.
Principal

Enclosure

CITED REFERENCES

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National Advisory Committee (NAC)
for Acute Exposure Guideline Levels (AEGL) for Hazardous Substances
Final Meeting 3 Highlights
Green Room, 3rd Floor, Ariel Rios Building
1200 Pennsylvania Avenue, NW
Washington, D.C.
September 17-19, 1996

INTRODUCTION

Dr. George Rusch, Chair, opened the meeting and welcomed the new members and participants including observers from the private sector to NAC AEGL meeting 3. The highlights of the meeting are noted below, and the meeting agenda (Attachment 1) and attendee list (Attachment 2) are attached.

The highlights of meeting 2 (August 5-7, 1996) were reviewed and approved with a minor change (Appendix A).

Dr. Roger Garrett welcomed the committee members and provided a brief overview of the NAC/AEGL program.

DISCUSSION OF TECHNICAL ISSUES

Single Exposure and Tumorigenic Responses

Dr. Edward Calabrese (University of Massachusetts School of Public Health) gave a presentation on a database that he has been compiling regarding increased tumorigenic responses following single exposures to chemicals. He noted that there are data showing tumorigenic responses to single low-dose exposures (e.g., 1/50, 1/75, 1/100 of the LD_{50}) (see Attachment 3). Several generic topics were mentioned, including the $B6C3F_1$ mouse issue and the importance of dose-rate vs cumulative dose and the timing of this with an endogenous promotion process. The database (developed in FoxPro) is a multiple field query format for single-exposure protocol data. Dr. Calabrese noted that: (1) only peer-reviewed data are used, (2) approximately 80 to 100 data sets per month are currently being entered, (3) only genuine single-exposure protocol (with no confounders) are selected, and (4) weight-of-evidence judgements are evaluated. He further noted that other factors are also critical (e.g., concurrent controls, descriptive vs hypothesis-testing statistics, and dosing protocol) in evaluating the data sets. In response to Committee questions, Dr. Calabrese noted that chemicals that were positive for single exposure tumor response were also positive in genotoxicity assays, and that the database includes therapeutic agents and not just chemicals of environmental importance. Dr. Calabrese emphasized that only a small percentage of the entries were for the inhalation exposure route, but that route-specific queries can be made in the database. He claimed not to have formulated any risk assessment strategies based on his data base. Dr. Calabrese offered the Committee access to the database.

Sensitive and Susceptible Subgroups

Dr. Jonathan Borak provided an overview (Attachment 4) on sensitive populations, including definitions of sensitivity and susceptibility for various groups (NRC Guidelines, AEGL definitions, NRC Science and Judgement, Commission on Risk Assessment). He also provided examples of such susceptible subgroups as infants, elderly, and individuals with coronary heart disease, liver disease, or asthma (Attachment 4). In summary Dr. Borak provided a list of seven recommendations upon which the Committee could base its considerations. Regarding the susceptibility of asthmatics, Dr. Borak noted that responses would likely be chemical specific and difficult to quantify. Additionally, he noted that exposure to levels of substances (e.g., nickel) that may sensitize should be within the purview of AEGLs but that hypersensitive responses (e.g., anaphylaxis) should not. There was a discussion followed by the Committee with agreement to establish a subcommittee to address the issue related to the susceptible and hypersusceptible populations. The subcommitte will include Drs. Borak (Chair), Koller, and Rodgers. A preliminary report will be presented in the December meeting.

AEGL Definitions

The AEGL definitions were reworded to be more "user friendly". Several issues arose including: (1) inclusion of a generic statement in the technical support documents preceding the definitions noting that AEGLs are derived for 30 min, 1 h, 4 h, and 8 h; (2) the relevance of "impaired escape", especially for 4- and 8-h time frames; (3) concern regarding the use of "susceptible"; (4) "overlap" of AEGL values (e.g., for HF, a 30-min AEGL-2 effect might be present at the 4-h time period for AEGL-3); and, (5) it was suggested that quotes might be placed around susceptible and hypersusceptible to emphasize that these terms are concepts defined in context. The final version of the AEGL definitions (Appendix B) was approved.

Time Frame for NAC/AEGL Processes and Products

A time line for document review was distributed by Dr. Rusch and reviewed by the Committee. Comments focused on the need for adequate review time. There were also comments regarding the need for adequate time to prepare the draft technical support documents. A need for a master list of chemicals was noted for inclusion in the *Federal Register*. It was also noted that priority chemicals (determined by storage or use) could be likely candidates for emergency-response potential (Attachment 5).

Uncertainty Factors (UFs)

Some considerations regarding uncertainty factor application were distributed by Dr. Rusch to the Committee. In the ensuing discussions, it was noted that the Committee should, as chartered, follow NAS guidelines. Several issues identified include: (1) what are the key judgments that justify the use of a UF less than the default of 10; (2) the Committee should track its use of UFs in a "living" document; and, (3) a subcommittee was formed to address UF issues (Attachment 6) and report the progress in the December meeting. The subcommittee includes Drs. Thomas (Chair), Alexeeff, Belluck, Falke, and Gephart.

Acute Inhalation Toxicity Study Protocol

Dr. Rusch requested comments about the distributed memo (Attachment 7) regarding the need for study protocol development for acute inhalation toxicity studies to fill data gaps identified by the NAC/AEGL.

REVIEW OF AEGL PRIORITY CHEMICALS

Hydrogen Fluoride, CAS Reg. No. 7664-39-3

Chemical Manager: Mr. Larry Gephart, Exxon Biomedical Sciences
Author: Dr. Sylvia Talmage, ORNL
Discussion focused on the need for a 10-min AEGL for HF. It was noted that this time frame (especially for compressed gases) would be appropriate for this chemical, especially for emergency planning purposes. Petroleum Environmental Research Forum will have an opportunity to comment when the proposed HF values are published in the *Federal Register*. It was the consensus of the Committee that a 10-min AEGL be derived for HF at the next meeting.

Ammonia, CAS Reg. No. 7664-41-7

Chemical Manager: Mr. Larry Gephart, Exxon Biomedical Sciences
Author: Dr. Kowetha Davidson, ORNL
Mr. Larry Gephart provided a summary of the revised ammonia AEGL document. Comments were received from International Institute of Ammonia Refrigeration indicating that they had not provided a response to the Committee because of time constraints and recent litigation. Dr. Robert Michaels of RamTrac indicated that he had requested that the ammonia industry submit data to the Committee; he also summarized alternate views regarding AEGLs for ammonia (Attachment 8). Some discussion focused on data-set selection for the ammonia AEGL. Ammonia was deferred to the December meeting. Mr. Gephart provided additional information and interpretations (Attachment 9) in response to Dr. Michaels.

Cyanogen Chloride (CK), CAS Reg. No. 506-77-4

Chemical Manager: Dr. Mark McClanahan, CDC
Author: Dr. Carol Forsyth, ORNL
Dr. Forsyth noted the acquisition of an additional reference as well as the difficulty in obtaining DoD data but noted cursory examination of some DoD data suggested that it would be of limited and questionable use for AEGL derivation. Dr. Forsyth explained that the AEGL-1 values were based on a 10-min LOAEL of 1 ppm and that 0.33 ppm be used for all time points. The proposed AEGL-2 values were based on tolerable irritation at 2 ppm and 0.66 ppm was initially proposed for all time points. No data were available for deriving AEGL-3 values (Attachment 10). Initially, concern was expressed that the conversion of CK to cyanide may require some type of pharmacokinetic analysis. However, the critical effect (pulmonary edema-induced lethality) did not support this concern. Furthermore, it was noted that additional data were not available. The Committee unanimously agreed that no AEGL-3 values be derived for CK until new information was available. For AEGL-1 and AEGL-2, the Committee decided (with one opposing vote) that consideration of these values be deferred until additional data become available. Actions recommended for cyanogen chloride were: (1) determine rationale for cyanogen chloride inclusion as an AEGL priority chemical; (2) attempt to retrieve DoD data; and (3) attempt to develop required data (via NAC/AEGL program or via manufacturers/industry). Derivation of AEGLs for cyanogen chloride was tabled indefinitely until additional data become available (Appendix C).

Nitric Acid, CAS Reg. No. 7697-37-2

Chemical Manager: Dr. Loren Koller, Orgeon State University
Author: Dr. Carol Forsyth, ORNL

Dr. Forsyth provided clarifications regarding the allergy and asthma studies in the technical support document and their categorization as hypersuceptible or susceptible. The limited human exposure data were also briefly reviewed (Attachment 11). For AEGL-1, it was noted that 0.25 ppm NO_2 was a NOAEL for exercising asthmatics. Discussion ensued regarding the possible relevance of NO_2 in deriving AEGLs for nitric acid. It was unanimously decided to accept 0.5 ppm as the AEGL-1 for nitric acid for all time points. Dr. Alexeeff noted that additional human exposure data were available in which a 1-h exposure of two individuals to 12 ppm resulted in notable irritation. Based on these data, NAC members suggested that the AEGL-2 values be 5, 4, 2.7, and 2.2 ppm for the 30-min, 1-h, 4-h, and 8-h periods, respectively (original draft document values were 30, 25, 17, and 14 ppm for these time frames). It was proposed that AEGL-2 values of 5, 4, 3, and 2 ppm be considered. Although the values were based on old data from only two exposed subjects, the data are consistent with more recent anecdotal, unpublished information, and the European MAK for nitric acid is based on these data. The Committee voted unanimously to adopt the proposed values but recommended that the data for NO_2 be evaluated to determine, in the December meeting, if it supports the AEGL-2 values for nitric acid. For AEGL-3, Dr. Koller suggested using the values based on red fuming nitric acid (15, 13, 8, and 7 ppm for 30-min, l-h, 4-h , and 8-h), respectively. These values were accepted by the Committee (Appendix D).

SUMMARY OF PROPOSED AEGL VALUES FOR NITRIC ACID

Classification	30-min	1-hour	4-hour	8-hour	Endpoint
AEGL-1	0.5 ppm 1.3 mg/m^3	0.5 ppm 1.3 mg/m^3	0.5 ppm 1.3 mg/m^3	0.5 ppm 1.3 mg/m^3	Minor irritation in humans
AEGL-2	5 ppm 12.9 mg/m^3	4 ppm 10.3 mg/m^3	3 ppm 7.7 mg/m^3	2 ppm 5.2 mg/m^3	Notable irritation, respiratory effects in humans
AEGL-3	15 ppm 38.7 mg/m^3	13 ppm 33.5 mg/m^3	8 ppm 20.6 mg/m^3	7 ppm 18.1 mg/m^3	Approximate LD_0 in rats

Hydrogen Cyanide, CAS Reg. No. 74-90-8

Chemical Manager: Dr. George Rodgers, AAPCC
Author: Dr. James Norris, ORNL

A data overview was presented by Dr. Rodgers (Attachment 12). It was noted that the steep dose-response curve may impact the validity of defining AEGLs for all three levels of concern. Dr. Norris presented specifics regarding data and derivation of AEGLs for hydrogen cyanide. He noted that for AEGL-3, data from a study using monkeys was used to validate a probit analysis equation originally derived by ten Berge et al. (1986) for scaling HCN exposures (Attachment 13). Dr. Neill Krivanek (DuPont/Haskell Laboratory) noted that the probit equation may not be valid beyond 1-h durations and that the AEGL-3 should be re-evaluated (Attachment 14). He agreed that an AEGL-1 may not be appropriate and that data are available for deriving an AEGL-2. It was Committee consensus that insufficient data were available for deriving AEGL-1 values. For AEGL-

3, Dr. Krivanek recommended 30, 25, 20, and 10 ppm for the 30-min, l-h, 4-h, and 8-h time points. He noted that the AEGL-2 may be based upon the i.v. study data of Wexler et al. (1947). Dr. Alexeeff stated that the Purser study noted EKG alterations at 60 ppm and that the above values should be reduced by a UF of 3. Dr. Barbee suggested that the Wexler data could be used and proposed AEGL-3 values of 20, 10, 6, and 3 ppm, respectively. Discussions ensued regarding intra- and interspecific variability in rhodanese activity and the robustness of the data sets. A polling of the Committee indicated that there was no consensus on the above values. Mr. Gephart felt that the original ORNL values were defensible because they were based on human experience but that the 4- and 8-h values should be similar because occupational exposures to 10 ppm have been shown to be nonlethal. Based on the Wexler i.v. data and several assumptions, Dr. Barbee proposed AEGL-3 values of 20, 14, 7, and 5 ppm for the 30-min, l-h, 4-h, and 8-hr time points. These proposed values were accepted by a majority vote. There was Committee consensus to attempt to derive AEGL-2 values for HCN. It was suggested that the AEGL-3 values be used as a reference point for this derivation. Dr. Alexeeff suggested that the original ORNL values adjusted by a UF of 3 be used (i.e., 9, 6, 3, and 2 ppm). Dr. Rodgers, in turn, suggested that the Wexler i.v. data adjusted by a UF of 3 be used for the 30-min AEGL-3 (i.e., 7 ppm). Dr. Alexeeff suggested that the AEGL-3 values, reduced three-fold to adjust for nonlethal effect, be used in conjunction with Dr. Rodgers proposal of 7 ppm for 30-min (i.e., 7, 5, 2, and 2 ppm, respectively). Dr. Krivanek cautioned that AEGLs should not be equivalent to normal CN^- blood levels. Dr. Borak suggested that for this AEGL determination, the Committee should err on the less conservative side because HCN releases will not be pressurized releases and that safety planning will have built-in safety factors. A divisor of 3 could then be used to reduce the AEGL-3 values to AEGL-2 values. A vote on the 7, 5, 2, and 2 ppm AEGL-2 values indicated majority disapproval. Dr. Thomas proposed that the AEGL-3 values divided by 2 be used as AEGL-2 (i.e., 10, 7, 4, and 3 ppm). The Committee accepted the proposed values (with 3 negative votes) (Appendix E).

SUMMARY OF PROPOSED AEGL VALUES FOR HYDROGEN CYANIDE					
Classification	**30-min**	**1-hour**	**4-hour**	**8-hour**	**Endpoint**
AEGL-1	-	-	-	-	Not verifiable, insufficient data
AEGL-2*	10 ppm 11 mg/m^3	7 ppm 8 mg/m^3	4 ppm 4 mg/m^3	3 ppm 3 mg/m^3	Cardiac effects in humans (adjusted from AEGL-3)
AEGL-3*	20 ppm 22 mg/m^3	14 ppm 15 mg/m^3	7 ppm 8 mg/m^3	5 ppm 6 mg/m^3	Cardiac effects in humans

*Regarding the AEGL values for hydrogen cyanide, Dr. Steve Barbee noted that the Wexler et al. (1974) data should have been used to derive the AEGL-2 values instead of the AEGL-3 values. This change will not affect the selected concentrations and will be reflected in the issuance of the final draft report to be circulated for public comment.

1,2-Dichloroethylene, CAS Reg. No. 540-59-0 (mixture); 156-59-2 (*cis*), 156-60-5 (*trans*)

Chemical Manager: Dr. Ernest Falke, U.S. EPA
Author: Dr. Cheryl Bast, ORNL

Dr. Falke presented an overview of the title chemical (Attachment 15), and Dr. Bast presented the AEGL values and their respective derivation rationale (Attachment 16). The values as presented were accepted by the Committee with two dissenting votes (one regarding inadequate accounting of uncertainty and the other indicating that improper linking of UFs resulted in overly conservative values) (Appendix F).

SUMMARY OF PROPOSED AEGL VALUES FOR 1,2 DICHLOROETHYLENE					
Classification	**30-min**	**1-hour**	**4-hour**	**8-hour**	**Endpoint**
AEGL-1	19 ppm 75 mg/m^3	13 ppm 53 mg/m^3	7 ppm 26 mg/m^3	5 ppm 19 mg/m^3	No effect level - human exposure
AEGL-2	56 ppm 224 mg/m^3	40 ppm 160 mg/m^3	20 ppm 80 mg/m^3	14 ppm 56 mg/m^3	Slight dizziness - human
AEGL-3	200 ppm 800 mg/m^3	141 ppm 564 mg/m^3	71 ppm 284 mg/m^3	50 ppm 200 mg/m^3	Fibrous swelling and hyperemia of cardiac muscle with poorly maintained striation - rat

Methyl Mercaptan, CAS Reg. No. 7783-06-4

Chemical Manager: Dr. Doan Hansen, Brookhaven National Laboratory
Author: Dr. James Norris, ORNL

In a revisit of methyl mercaptan, Dr. Norris provided a recap of the status of AEGL-3 values from the August 5-7, 1996, meeting (Attachment 17). The AEGL-2 values were based on shallow breathing/hypoactivity in mice. Alternatively, the AEGL-2 could also be based upon shallow breathing only. The Committee decided that the shallow-breathing/hypoactivity data should drive the AEGL-2. Dr. Hansen proposed that 0.5 ppm be considered for all AEGL-1 time points

(Attachment 18). The proposal was accepted by the Committee. The AEGL-2 and AEGL-3 proposed values were accepted in the previous (August 5-7, 1996) meeting. However, Mr. Gephart noted the AEGL-2 values may be overly conservative because there were no effects in the Tansy reports in rodents subjected to repeated exposures to 50 ppm. Following some discussion, it was suggested to change the AEGL-2 values from 3, 2, 1, and 1 (for 30-min, 1-h, 4-h, and 8-h, respectively) to 7, 5, 3, and 2 ppm. The Committee agreed to accept these values (Appendix G).

SUMMARY OF PROPOSED AEGL VALUES FOR METHYL MERCAPTAN

Classification	30-min	1-hour	4-hour	8-hour	Endpoint
AEGL-1	0.5 ppm 1 mg/m^3	0.5 ppm 1 mg/m^3	0.5 ppm 1 mg/m^3	0.5 ppm 1 mg/m^3	Based relative to TLV
AEGL-2	8 ppm 16 mg/m^3	6 ppm 12 mg/m^3	3 ppm 6 mg/m^3	2 ppm 4 mg/m^3	Shallow breathing and hypoactivity in mice (Elf Atochem, 1996)
AEGL-3	34 ppm 67 mg/m^3	25 ppm 49 mg/m^3	13 ppm 26 mg/m^3	10 ppm 20 mg/m^3	Highest non-lethality in rats (Tansy et al., 1981) (n=2.2)

Arsine, CAS Reg. No. 7784-42-1

Chemical Manager: Dr. Richard Thomas, I.C.E.H.
Author: Dr. Robert Young, ORNL

Dr. Thomas provided an overview of salient information regarding arsine and the effects of acute exposures to this chemical (Attachment 19). Dr. Young provided a summary of AEGL values and their respective key studies and effects (Attachment 20). Because of the extreme toxicity of arsine and the fact that toxic effects to arsine exposure have been known to occur in the absence of odor, Dr. Thomas proposed that all AEGL-1 values be 0.1 ppm. The proposal was accepted by the Committee. Dr. Young noted that AEGLs derived using human equivalent dosimetric adjustments gave values that were considerably higher than those derived without dosimetric adjustment. It was the consensus of the Committee that such an adjustment was not warranted. Because of the extremely steep exposure-response curve for arsine, it was suggested that the AEGL-3 values be further reduced and based on a concentration that was not lethal to rats. This resulted in AEGL values somewhat lower than those proposed in the draft technical support document; 0.7, 0.5, 0.25, 0.18 ppm vs 2, 1, 0.7, and 0.5 ppm for the 30-min 1-h, 4-h, and 8-h periods, respectively. The adjusted values were approved by the Committee. AEGL-2 values were similarly altered based on exposures that did not produce potentially serious effects in rats. The adjusted and approved values were 0.24, 0.17, 0.08, and 0.06 ppm vs 2, 1, 0.7, and 0.5 ppm for the 30-min, 1-h, 4-h, and 8-h time exposures, respectively (Appendix H).

SUMMARY OF PROPOSED AEGL VALUES FOR ARSINE					
Classification	**30-min**	**1-hour**	**4-hour**	**8-hour**	**Endpoint**
AEGL-1	0.1 ppm 0.3 mg/m^3	0.1 ppm 0.3 mg/m^3	0.1 ppm 0.3 mg/m^3	0.1 ppm 0.3 mg/m^3	No effect level for hematological alterations in mice (Blair et al., 1990)
AEGL-2	0.24 ppm 0.8 mg/m^3	0.17 ppm 0.5 mg/m^3	0.1 ppm 0.3 mg/m^3	0.1 ppm 0.3 mg/m^3	No effect level for physiologically relevant hematological changes in mice (Peterson and Bhattacharrya, 1985)
AEGL-3	0.7 ppm 2.2 mg/m^3	0.5 ppm 1.6 mg/m^3	0.25 ppm 0.8 mg/m^3	0.18 ppm 0.6 mg/m^3	No effect level for lethality in mice (Peterson and Bhattacharrya, 1985)

Dimethyldichlorosilane, CAS Reg. No. 75-78-5

Chemical Manager: Dr. Ernest Falke, U.S. EPA
Author: Dr. Cheryl Bast, ORNL

Dr. Falke presented an overview of the title chemical (Attachment 21), and Dr. Bast followed with a more detailed account of AEGL derivations and key data (Attachment 22). The use of the mouse RD_{50} was considered to be applicable for derivation of the AEGL-1 for dimethyldichlorosilane. The AEGL-1 proposed values based on 0.01 x RD_{50} (1 ppm, 0.75 ppm, 0.4 ppm, and 0.3 ppm for 30-min, 1-h, 4-h, and 8-h periods, respectively) were unanimously accepted by the Committee. Dr. Falke proposed that the AEGL-2 values (0.1 x RD_{50}) as derived in the draft technical support document be accepted. The Committee accepted the values following rounding of the values to 10, 7, 4, and 3 ppm. The Committee agreed that 1/3 of the rat LC_{50} would be an acceptable estimate of the rat lethality threshold for this chemical. Dr. Garrett mentioned that the NAC guidelines indicate that human data should be preferentially considered. AEGL-3 values of 37, 26, 13, and 9 ppm were proposed for 30-min, 1-h, 4-h, and 8-h periods, respectively. The proposed values were accepted unanimously (Appendix I).

SUMMARY OF PROPOSED AEGL VALUES FOR DIMETHYLDICHLOROSILANE					
Classification	**30-min**	**1-hour**	**4-hour**	**8-hour**	**Endpoint**
AEGL-1	1 ppm 6 mg/m^3	0.75 ppm 4 mg/m^3	0.4 ppm 2 mg/m^3	0.3 ppm 1 mg/m^3	0.01 RD_{50} - mouse
AEGL-2	10 ppm 55 mg/m^3	7 ppm 40 mg/m^3	4 ppm 19 mg/m^3	3 ppm 14 mg/m^3	0.1 RD_{50} - mouse
AEGL-3	37 ppm 195 mg/m^3	26 ppm 138 mg/m^3	13 ppm 69 mg/m^3	9 ppm 49 mg/m^3	0.33 x LC_{50} - rat

ADMINISTRATIVE MATTERS

Dr. Belluck distributed suggestions regarding format adjustments for data summarization in the technical support documents (Attachment 23). It was noted that the next list of priority chemicals will be made available within a few weeks. The high quality of the draft technical support documents and the need for adequate preparation time were noted.

Tentative schedules for the next three meetings were noted: December 16-18, 1996; March 11-13, 1997, or March 24-26, 1997; and June 9-11, 1997.

December Meeting
Agenda items include:

1. Report on sensitive-population issues
2. Uncertainty/safety factor report
3. Report on acute inhalation toxicity study protocol
4. 10-min AEGL for HF
5. Finalization of ammonia document
6. Discussions regarding:
   - -Dr. Belluck's document format suggestions
   - -Summary of NO_2 research
   - -Dr. Falke's "living" document - compilation of rationale for AEGL values
7. New chemicals for future meetings (Attachment 24)

Meeting minutes were prepared by Drs. Robert Young and Po-Yung Lu, ORNL.

Table of Contents of Attachments

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

Table of Contents of Appendices

Appendix B

Date of AEGL NAC meeting: 12/17/96 **Chemical:** ARSINE

NAC Member	AEGL1	AEGL2	AEGL3	NAC Member	AEGL1	AEGL2	AEGL3
George Alexeeff		A		Thomas C. Hornshaw		Y	
Steven Barbee		Y		Nancy K. Kim		Y	
Lynn Beasley		A		Loren Koller		Y	
David Belluck		Y		Mark A. McClanahan		Y	
Kyle Blackman		Y		John S. Morawetz		PASS*	
Jonathan Borak		PASS		Richard W. Niemeier		Y	
William Bress		Y		Zarena Post		Y	
Guy Colonna		Y		George Rodgers		Y	
George Cushmac		Y		George Rusch		Y	
Marion F. Ehrich		A		Bob Snyder		Y	
Ernest Falke		Y		Thomas J. Sobotka		A	
Larry Gephart		Y		Kenneth Still		A	
Robert E. Hazen		A		Patricia Ann Talcott		Y	
John Hinz		A		Richard Thomas		Y	
Jim Holler		Y*		~~Thomas Tuccinardi~~/ Doan Hansen		PASS*	
				TALLY		20/20	

A = ABSENT

* = NOT A VOTING MEMBER

PPM, (mg/m^3)	30 Min	60 Min	4 Hr	8Hr
AEGL 1	,( )	,( )	,( )	,( )
AEGL 2	~~A~~ ,( )	,( )	0.1 ,( )	0.1 ,( )
AEGL 3	,( )	,( )	,( )	,( )

AEGL 1 Motion: R. Thomas **Second:** R. Niemeier

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

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

Approved by Chair: _____ **DFO:** _____ **Date:** 12/17/96

Comments:

Appendix C

Date of AEGL NAC meeting: 12/16/96 **Chemical:** HF

NAC Member	AEGL1	AEGL2	AEGL3
George Alexeeff	A	A	A
Steven Barbee	Y	Y	Y
Lynn Beasley	A	A	A
David Belluck	Y	Y	Y
Kyle Blackman	Y	Y	Y
Jonathan Borak	Y	Y	Y
William Bress	Y	Y	Y
Guy Colonna	Y	Y	Y
George Cushmac	Y	Y	Y
Marion F. Ehrich	Y	Y	A
Ernest Falke	Y	Y	Y
Larry Gephart	Y	Y	Y
Robert E. Hazen	A	A	A
John Hinz	PASS	PASS	Y
Jim Holler	Y*	Y*	Y*

NAC Member	AEGL1	AEGL2	AEGL3
Thomas C. Hornshaw	Y	PASS	Y
Nancy K. Kim	PASS	PASS	Y
Loren Koller	Y	Y	Y
Mark A. McClanahan	Y	Y	Y
John S. Morawetz	Y*	N*	PASS*
Richard W. Niemeier	Y	Y	Y
Zarena Post	Y	PASS	Y
George Rodgers	Y	Y	Y
George Rusch	Y	Y	Y
Bob Snyder	Y	Y	Y
Thomas J. Sobotka	Y	Y	A
Kenneth Still	A	A	A
Patricia Ann Talcott	Y	PASS	Y
Richard Thomas	Y	Y	Y
~~Thomas Tuccinardi/~~ Doan Hansen	PASS*	PASS*	Y*
TALLY	21/21	18/18 3 PASS	21/21

A = ABSENT
Y* = NOT A MEMBER

PPM, (mg/m^3)	10 Min ~~30 Min~~	60 Min	4 Hr	8Hr
AEGL 1	2 ,( )	,( )	,( )	,( )
AEGL 2	130 ,( )	,( )	,( )	,( )
AEGL 3	170 ,( )	,( )	,( )	,( )

AEGL 1 Motion: L. GEPHART **Second:** L. KOLLER

AEGL 2 Motion: L. GEPHART **Second:** L. KOLLER

AEGL 3 Motion: L. GEPHART **Second:** G. RODGERS

Approved by Chair: 12/16 **DFO:** Paul S. Tobin **Date:** 12/16/96 AEGL 1,2

Comments: 12/17 Paul S. Tobin 12/17/96 AEGL 3

Appendix D

Date of AEGL NAC meeting: **Chemical:** METHYL HYDRAZINE

NAC Member	AEGL1	AEGL2	AEGL3
George Alexeeff	A	A	A
Steven Barbee	Y	Y	Y
Lynn Beasley	A	A	A
David Belluck	Y	Y	Y
Kyle Blackman	Y	Y	Y
Jonathan Borak	A	Y	Y
William Bress	Y	Y	Y
Guy Colonna	Y	Y	Y
George Cushmac	Y	Y	Y
Marion F. Ehrich	A	A	A
Ernest Falke	Y	Y	Y
Larry Gephart	Y	Y	Y
Robert E. Hazen	A	A	A
John Hinz	Y	Y	Y
Jim Holler	Y*	Y*	Y*

NAC Member	AEGL1	AEGL2	AEGL3
Thomas C. Hornshaw	Y	Y	Y
Nancy K. Kim	Y	Y	Y
Loren Koller	Y	Y	Y
Mark A. McClanahan	Y	Y	Y
John S. Morawetz	Y*	Y*	Y*
Richard W. Niemeier	Y	Y	Y
Zarena Post	Y	Y	Y
George Rodgers	Y	Y	Y
George Rusch	Y	Y	Y
Bob Snyder	Y	PASS	PASS
Thomas J. Sobotka	Y	A	A
Kenneth Still	A	A	A
Patricia Ann Talcott	Y	Y	Y
Richard Thomas	Y	Y	Y
~~Thomas Tuccinardi~~/ Doan Hansen	N*	Y*	Y*
TALLY	21/21	20/20	20/20

A = ABSENT

* = NOT A VOTING MEMBER

PPM, (mg/m^3)	30 Min	60 Min	4 Hr	8Hr
AEGL 1	NA* ,( )	NA ,( )	NA ,( )	NA ,( )
AEGL 2	2 ,( )	1 ,( )	0.2 ,( )	0.1 ,( )
AEGL 3	6 ,( )	3 ,( )	0.6 ,( )	0.3 ,( )

0.1 FOR HYDRAZINE, WHEN ~~HERE~~ ~~BE~~ PRESENT IN METHYL HYDRAZINE

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

AEGL 2 Motion: G. RODGERS **Second:** R. NIEMEIER

AEGL 3 Motion: G. RODGERS **Second:** R. NIEMEIER

Approved by Chair: _____ **DFO:** _____ **Date:** 12/17/96

Comments:

Date of AEGL NAC meeting: 12/17/96 **Chemical:** 1,2-DIMETHYLHYDRAZINE

NAC Member	AEGL1	AEGL2	AEGL3	NAC Member	AEGL1	AEGL2	AEGL3
George Alexeeff	A	A	A	Thomas C. Hornshaw	Y	Y	Y
Steven Barbee	Y	Y	Y	Nancy K. Kim	Y	Y	Y
Lynn Beasley	A	A	A	Loren Koller	Y	Y	Y
David Belluck	Y	Y	Y	Mark A. McClanahan	Y	Y	Y
Kyle Blackman	Y	Y	Y	John S. Morawetz	Y*	Y*	Y*
Jonathan Borak	Y	Y	Y	Richard W. Niemeier	Y	Y	Y
William Bress	Y	Y	Y	Zarena Post	Y	Y	Y
Guy Colonna	Y	Y	Y	George Rodgers	Y	Y	Y
George Cushmac	Y	Y	Y	George Rusch	Y	Y	Y
Marion F. Ehrich	A	A	A	Bob Snyder	Y	Y	Y
Ernest Falke	Y	Y	Y	Thomas J. Sobotka	Y	Y	Y
Larry Gephart	Y	Y	Y	Kenneth Still	A	A	A
Robert E. Hazen	A	A	A	Patricia Ann Talcott	Y	Y	Y
John Hinz	Y	Y	Y	Richard Thomas	Y	Y	Y
Jim Holler	Y*	Y*	Y*	~~Thomas Tucchiardi~~ Doan Hansen	PASS*	PASS*	PASS*
				TALLY	22/22	22/22	22/22

A = ABSENT

* = NOT A VOTING MEMBER

PPM, (mg/m^3)	30 Min	60 Min	4 Hr	8Hr
AEGL 1	NA ,( )	NA ,( )	NA ,( )	NA ,( )
AEGL 2	6 ,( )	3 ,( )	0.8 ,( )	0.4 ,( )
AEGL 3	22 ,( )	11 ,( )	3 ,( )	1.5 ,( )

= 0.1 ppm FOR HYDRAZINE WHEN PRESENT IN 1,2-DIMETHYLHYDRAZINE

AEGL 1 Motion: G. ROGERS **Second:** J. HINZ

AEGL 2 Motion: G. ROGERS **Second:** J. HINZ

AEGL 3 Motion: G. RODGERS **Second:** J. HINZ

Approved by Chair: [signature] **DFO:** Paul S. Tobin **Date:** 12/17/96

Comments:

Appendix F

Date of AEGL NAC meeting: 12/17/96 **Chemical:** 1,1- DIMETHYL HYDRAZINE

NAC Member	AEGL1	AEGL2	AEGL3	NAC Member	AEGL1	AEGL2	AEGL3
George Alexeeff	A	A	A	Thomas C. Hornshaw	Y	Y	Y
Steven Barbee	Y	Y	Y	Nancy K. Kim	Y	Y	Y
Lynn Beasley	A	A	A	Loren Koller	Y	Y	Y
David Belluck	Y	Y	Y	Mark A. McClanahan	Y	Y	Y
Kyle Blackman	Y	Y	Y	John S. Morawetz	Y*	Y*	Y*
Jonathan Borak	Y	Y	Y	Richard W. Niemeier	Y	Y	Y
William Bress	Y	Y	Y	Zarena Post	Y	Y	Y
Guy Colonna	Y	Y	Y	George Rodgers	Y	Y	Y
George Cushmac	Y	Y	Y	George Rusch	Y	Y	Y
Marion F. Ehrich	A	A	A	Bob Snyder	Y	Y	Y
Ernest Falke	Y	Y	Y	Thomas J. Sobotka	Y	Y	Y
Larry Gephart	Y	Y	Y	Kenneth Still	A	A	A
Robert E. Hazen	A	A	A	Patricia Ann Talcott	Y	Y	Y
John Hinz	Y	Y	Y	Richard Thomas	Y	Y	Y
Jim Holler	Y*	Y*	Y*	~~Thomas Tuccinardi/~~ Doan Hansen	PASS*	PASS*	PASS*
				TALLY	22/22	22/22	22/22

A = ABSENT

* = NOT A VOTING MEMBER

PPM, (mg/m^3)	30 Min	60 Min	4 Hr	8Hr
AEGL 1	*NA ,( )	NA ,( )	NA ,( )	NA ,( )
AEGL 2	6 ,( )	3 ,( )	0.8 ,( )	0.4 ,( )
AEGL 3	22 ,( )	11 ,( )	3 ,( )	1.5 ,( )

* = 0.1 ppm FOR HYDRAZINE WHEN PRESENT IN 1,1-DIMETHYLHYDRAZINE

AEGL 1 Motion: G. RODGERS **Second:** ~~G. RODGERS~~ JOHN HINZ

AEGL 2 Motion: G. RODGERS **Second:** JOHN HINZ

AEGL 3 Motion: G. RODGERS **Second:** JOHN HINZ

Approved by Chair: George M. Rusch **DFO:** Paul S. Tobin **Date:** 12/17/96

Comments:

Appendix G

Date of AEGL NAC meeting: 12/17/96 **Chemical:** PHOSPHINE

NAC Member	AEGL1	AEGL2	AEGL3	NAC Member	AEGL1	AEGL2	AEGL3
George Alexeeff	A	A	A	Thomas C. Hornshaw	Y	Y	Y
Steven Barbee	Y	Y	Y	Nancy K. Kim	Y	Y	Y
Lynn Beasley	A	A	A	Loren Koller	Y	Y	Y
David Belluck	Y	Y	Y	Mark A. McClanahan	Y	Y	Y
Kyle Blackman	Y	Y	Y	John S. Morawetz	N *	N *	N *
Jonathan Borak	Y	Y	Y	Richard W. Niemeier	Y	Y	Y
William Bress	Y	Y	Y	Zarena Post	Y	Y	Y
Guy Colonna	Y	Y	Y	George Rodgers	Y	Y	Y
George Cushmac	Y	Y	Y	George Rusch	Y	Y	Y
Marion F. Ehrich	A	A	A	Bob Snyder	Y	Y	Y
Ernest Falke	Y	Y	Y	Thomas J. Sobotka	Y	Y	Y
Larry Gephart	Y	Y	Y	Kenneth Still	A	A	A
Robert E. Hazen	A	A	A	Patricia Ann Talcott	Y	Y	Y
John Hinz	Y	Y	Y	Richard Thomas	A	A	A
Jim Holler	Y *	Y *	Y *	~~Thomas Tuccinardi~~/ Doan Hansen	Y *	Y *	Y *
				TALLY	21/21	21/21	21/21

A = ABSENT
* = NOT A VOTING MEMBER

PPM, (mg/m^3)	30 Min	60 Min	4 Hr	8Hr
AEGL 1	NA ,( )	NA ,( )	NA ,( )	NA ,( )
AEGL 2	0.4 ,( )	0.2 ,( )	0.1 ,( )	0.1 ,( )
AEGL 3	2 ,( )	1.5 ,( )	0.7 ,( )	0.5 ,( )

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

AEGL 2 Motion: G. RODGERS **Second:** S. BARBEE

AEGL 3 Motion: G. RODGERS **Second:** S. BARBEE

Approved by Chair: _____ **DFO:** Paul S. Tobin **Date:** 12/17/96

Comments:

Appendix H

Date of AEGL NAC meeting: 12/17/96 **Chemical:** CHLORINE

NAC Member	AEGL1	AEGL2	AEGL3	NAC Member	AEGL1	AEGL2	AEGL3
George Alexeeff	A	A	A	Thomas C. Hornshaw	Y	Y	Y
Steven Barbee	Y	Y	Y	Nancy K. Kim	Y	Y	Y
Lynn Beasley	A	A	A	Loren Koller	Y	Y	Y
David Belluck	Y	Y	Y	Mark A. McClanahan	Y	Y	Y
Kyle Blackman	Y	Y	Y	John S. Morawetz	Y *	Y *	Y *
Jonathan Borak	Y	Y	A	Richard W. Niemeier	Y	Y	Y
William Bress	Y	Y	Y	Zarena Post	Y	Y	Y
Guy Colonna	Y	Y	Y	George Rodgers	Y	Y	Y
George Cushmac	A	A	Y	George Rusch	Y	Y	Y
Marion F. Ehrich	A	A	A	Bob Snyder	Y	Y	Y
Ernest Falke	Y	Y	Y	Thomas J. Sobotka	Y	Y	A
Larry Gephart	Y	Y	Y	Kenneth Still	A	A	A
Robert E. Hazen	A	A	A	Patricia Ann Talcott	Y	Y	Y
John Hinz	Y	Y	Y	Richard Thomas	A	A	A
Jim Holler	Y *	Y *	Y *	~~Thomas Tuccinardi~~/ Doan Hansen	Y *	Y *	Y *
				TALLY	20/20	20/20	19/19

A = ABSENT
* = NOT A VOTING MEMBER

PPM, (mg/m^3)	30 Min	60 Min	4 Hr	8Hr
AEGL 1	1 ,( )	1 ,( )	0.5 ,( )	0.5 ,( )
AEGL 2	3 ,( )	2 ,( )	1 ,( )	~~1.0~~ 0.7 ,( )
AEGL 3	31 ,( )	22 ,( )	11 ,( )	8 ,( )

pgfsl/Tolan 4/28/97

AEGL 1 Motion: L. Koller **Second:** R. Niemeier

AEGL 2 Motion: R. Snyder **Second:** Zarena Post

AEGL 3 Motion: D. Hansen **Second:** S. Barbee

Approved by Chair: [signature] **DFO:** [signature] **Date:** 12/17/96

Comments: