NATIONAL ADVISORY COMMITTEE (NAC)
FOR ACUTE EXPOSURE GUIDELINE LEVELS (AEGLs)
FOR HAZARDOUS SUBSTANCES
Final Meeting 15 Highlights
Green Room, 3rd Floor, Ariel Rios Building
Washington, D.C.

September 14-15, 1999

INTRODUCTION

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

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

TECHNICAL DISCUSSIONS
Summary of Initiatives

International Involvement

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

AEGL/NAS Procedure

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

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

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

AEGLs in NAS/COT Review

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

Application of AEGLs

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

Benchmark Dose Methodology

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

AEGL PRIORITY CHEMICALS

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

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

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

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

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

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

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

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

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

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

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

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

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

SUMMARY OF PROPOSED AEGL VALUES FOR PROPYLENE GLYCOL DINITRATE

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

ADMINISTRATIVE ISSUES

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

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

LIST OF ATTACHMENTS

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

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

LIST OF APPENDICES

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

Attachment 1

National Advisory Committee for Acute Exposure Guideline Levels for Hazardous Substances

NAC/AEGL-15
September 14-16, 1999

Green Room, 1100 Pennsylvania Avenue, Washington, D.C.

AGENDA

Tuesday, September 14, 1999

10:00 AM	Introductory remarks and approval of NAC/AEGL-14 Highlights (George Rusch, Roger Garrett, and Paul Tobin)
10:15	Status Reports (Roger Garrett, George Rusch, and Ernest Falke) ✦International matters ✦NAS/COT AEGL Subcommittee Issues : • SOP Manual • Review of seven chemicals to be published by NAS
12:30 PM	Lunch
1:30	NAS/COT AEGL Subcommittee Issues (continued)
2:30	Presentation of Modeling and Applications of AEGL values (Bill Dunn, Argonne Nat. Lab.)
3:15	Break
3:30	Discussion of AEGL applications (including ceiling and time-weighted average issues)
4:30	Otto Fuel II (Bill Bress/Sylvia Talmage)
5:15	Adjourn for the day

Wednesday, September 15, 1999

8:30 AM	Otto Fuel II (continued)
10:15	Break
10:30	EPA Benchmark Dose Software Application to Ethylene Oxide (Judy Strickland, NCEA, EPA)
11:30	Lunch
12:30 PM	Bromine: AEGL-3 (Larry Gephart/Sylvia Talmage)
1:30	Phosphine (Ernie Falke/Cheryl Bast)
2:30	Break
2:45	Hydrogen sulfide (Steven Barbee/Cheryl Bast)
4:30	Furan (George Rodgers/Claudia Troxel)
4:45	Administrative issues, future meetings
5:00	Adjourn for the day

Thursday, September 16, 1999

8:30 AM	1,1,1-Trichloroethane (Mark McClanahan/Tessa Long)
10:15	Break
10:30	1,1,1-Trichloroethane (continued)
11:00	1,2-Dichloroethylene (Ernie Falke/Cheryl Bast)
1:00 PM	Adjourn meeting

Attachment 2

AEGL/NAC-15 Sept 14-16, 1999

Name	Affiliation	Phone No.
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Mark A McClanahan	CDC	770.488-~~3000~~ 7297
Jim Holler	ATSDR	404-639-6309
Dave Bellew	MnDOT	651-779-5354
Bill Pepelko	EPA/ORD	202-564-3309
Rick Niemeier	NIOSH	513-533-8388
George Rodgers	Univ of Louisville/APEC	502-852-8626
Lynn Beasley	USEPA/Superfund	703.603.9082
John Itinz	USAF	(210) 536-6136
Steve Barlas	Arch Chem/AIHA	203-229-2693
Nancy Kim	NYS DOH	518 402-7511
Bob Snyder	Rutgers Univ.	732-445-3720
Ernest Falke	US EPA	202-260-3433
Roger Lauver	US EPA	202-260-4302
George Rusch	Allied Signal	973-455-3672
Paul Tobin	US EPA	202 260-1736
Jorge Aldrett	Cal/EPA	(510) 622-3202
GEORGE CUSHMAC	USDOT	202-366-4493
Jonathan Borak	Yale (AOEM)	203-777-6611
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Loren Koller	Oregon State University	541 737 5547
Robert E. Dietz, Jr.	US DOE	301-903-6138

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NAC/AEGL-15 meeting

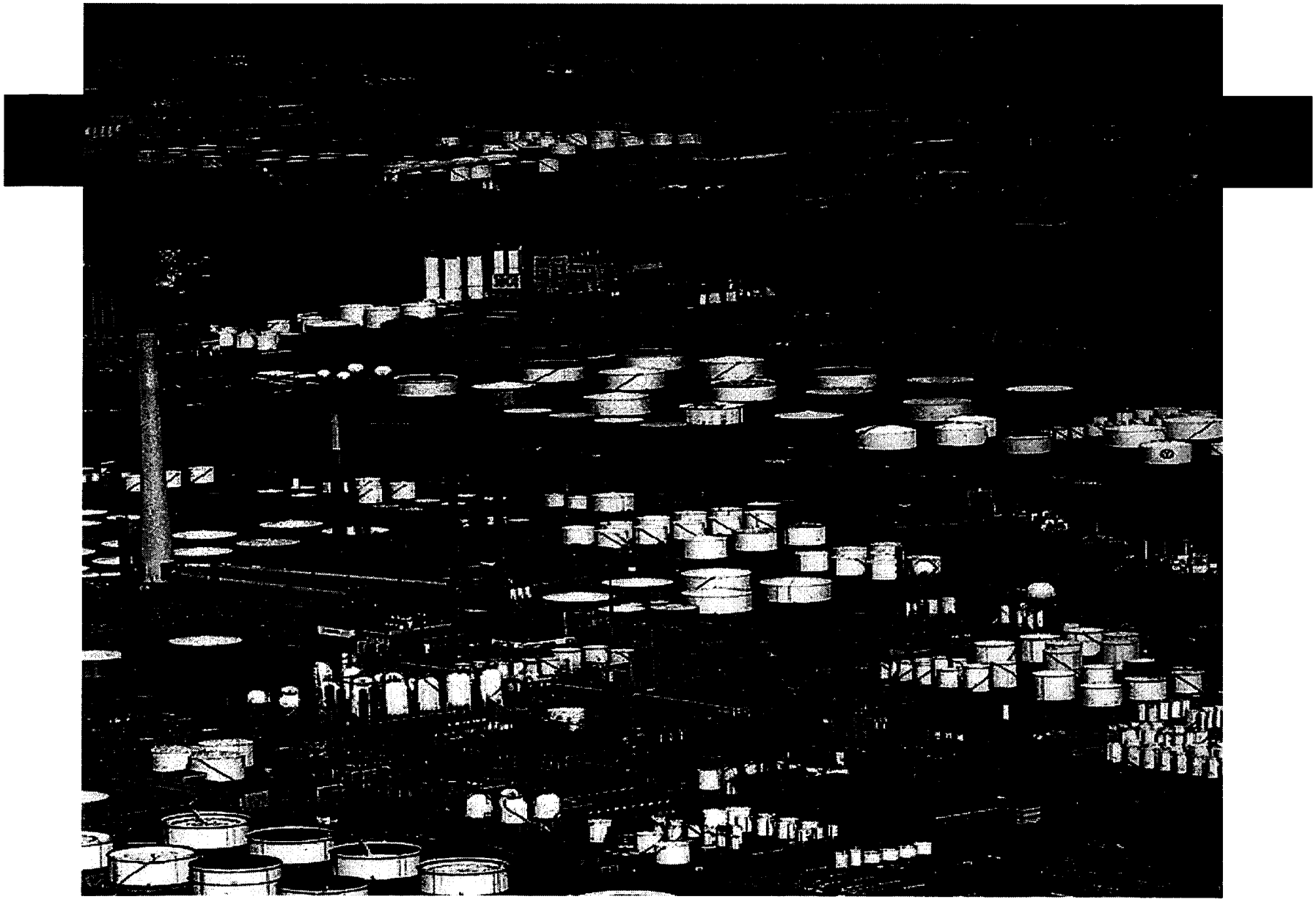
Name	Affiliation	Phone No
Po-Zhang Lu	ORNL	(423) 574-7587
Howard Grunin	NAVSEA	703 604-6132 x388
Bill Dunn	Univ. IL	217-333-3832
Sally L. Eagan	City of Mpls, Planning Dept	612-721-1809
Steve Hwang	DOT	202-366-4476
Veronique Hauschild	U.S. Army (CHPPM)	410-436-5213
Oda Hansen	DOE	516 344-7535
Bill Bress	Estho	802-863-7598
Larry Geyfant	Exxon Biomedical	732 873-6319
John S. Morawetz	ICWUC IUPAW	513-621-8882
Kenneth R. Still	US NAVY	937-255-6058 x202

Netherlands temporary emergency number program

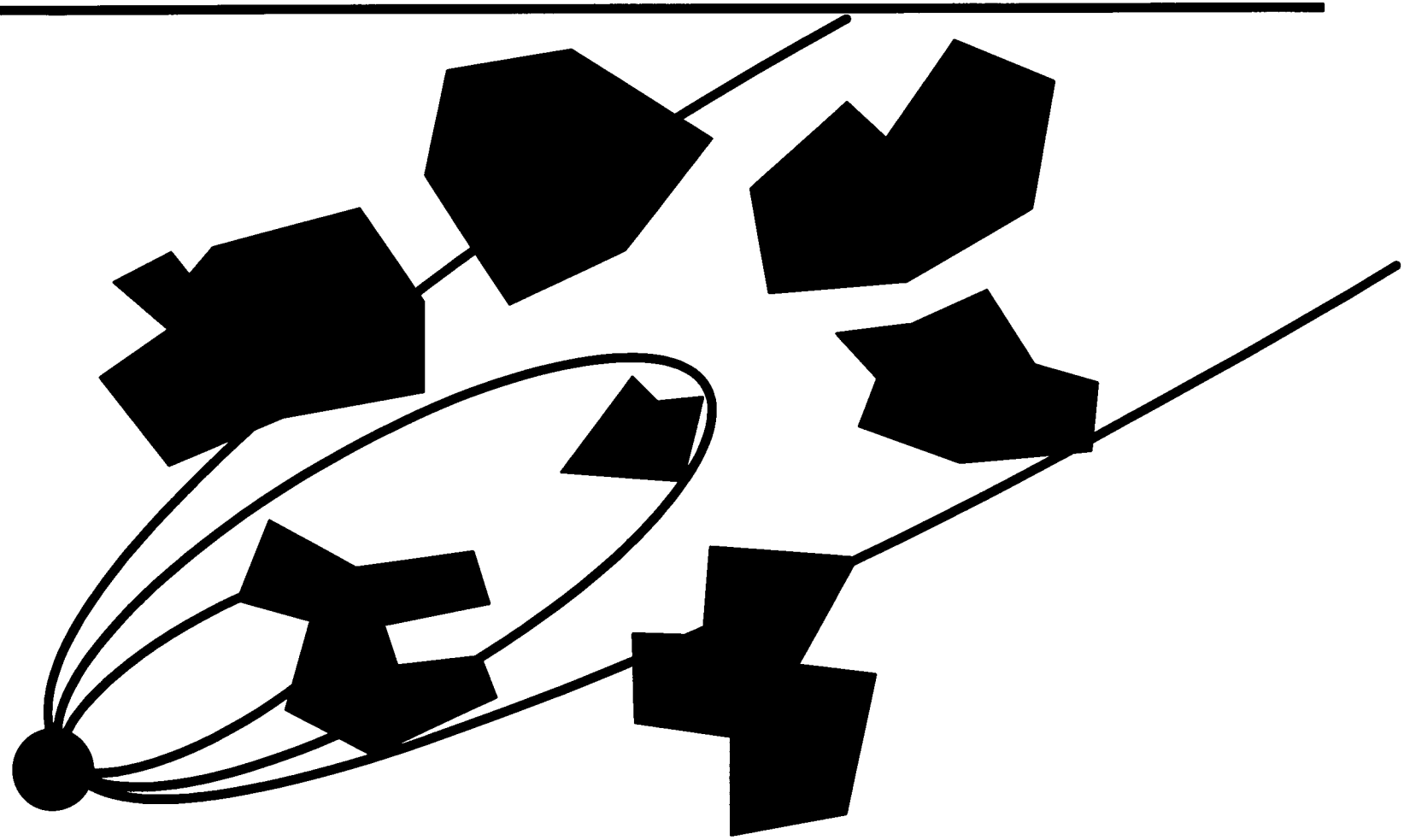
Marc Ruijten
Environmental Health Unit
Municipal Health Service Rotterdam

Attachment 3

Rotterdam area



Rapid health risk assessment



Local requirements

- Phase 1: identification of priority chemicals
  - ♦ production
  - ♦ storage
  - ♦ transportation
  - ♦ volatility
  - ♦ toxicity
- Result: 280 priority chemicals identified

Levels of ambition

- Level 1: generic methods
  - ♦ STEL - LC_{50}
- Level 2: quick and dirty evaluation of data
- Level 3: thorough evaluation of data
  - ♦ ERPG
  - ♦ AEGL
- Regardless of the level of ambition:

  Nationwide acceptance and application

The KISS principle

K Keep
I It
S Simple
S Stupid!

Local emergency response numbers

- ERPG methodology, but: secondary literature
- Choice of fixed levels (..- 1 - 2 - 5 - 10 - 20 -..)
  - ♦ limited precision of other input data
  - ♦ limited precision of analytical devices
  - ♦ limitations toxicological database
- All numbers in mg/m^3
- Nomenclature:
  - ♦ AEGL-1 = Communication Guidance Level
  - ♦ AEGL-2 = Alarm Threshold Level
  - ♦ AEGL-3 = Life-Threatening Level

Present developments

- Emergency numbers list is being updated
  - ♦ improve quality
  - ♦ add 30 chemicals
  - ♦ improve nationwide acceptance
- Draft S.O.P. available
- Problematic endpoints:
  - ♦ carcinogenicity
  - ♦ reproductive and developmental toxicity
- Participation in AEGL & ERPG programs

Co-oparation with NAC-AEGL

- Dutch government wants active participation in AEGL program
- Final emergency numbers
  - ♦ AEGLs will replace temporary numbers
  - ♦ ERPGs as backup
- This meeting:
  - ♦ listen
  - ♦ learn
  - ♦ report

PRINCIPAL ISSUES TO RESOLVE WITH NAS SUBCOMMITTEE FOR AEGLS

- Carcinogenic Substances
- AEGL-1 Values Not Developed
- Use of Non-Inhalation Routes of Exposure
- Primary vs. Secondary References
- AEGL-1 and AEGL-2 Definition Changes
- Use of NOELs in AEGL Development
- Benchmark Dose

Use of Primary vs. Secondary References in the Development of AEGL Values

- Primary references required for all "key" toxicological studies from which AEGL values are derived.

- Primary references required for all toxicological studies used to directly support the derivation of the AEGL value.

- Secondary references may be used to provide data and information on commercial uses, production volume, chemical and physical properties, background information on the toxicity of the chemical, and any other information not used directly in the derivation of the AEGL values.

Position of NAC/AEGL Committee on Alternate Routes of Exposure

- Because of the paucity of data and the complexities related to route-to-route extrapolations, the NAC/AEGL Committee to date has used only inhalation toxicity data to derive AEGL values.

- In accord with the 1993 NAS Guidance, the NAC/AEGL Committee will continue to consider all relevant data for the development of AEGL values.

- Toxicity data from alternate routes of exposure generally will not be used to derive AEGL values and will not be included in discussions in the TSDs unless it is considered important for supporting relevant pharmacokinetics or metabolism data or mechanisms and observed effects of toxicity.

- In the absence of inhalation data to derive an AEGL value, the NAC/AEGL Committee may decide to use toxicity data from other exposure routes if there is acceptable data to perform a credible route-to-route extrapolation. In the absence of acceptable data, the chemical will be referred for appropriate toxicity testing.

CARCINOGENIC SUBSTANCES

- Methodology for assessing risk
  - --- NAC/AEGL Committee follows 1993 NAS guidance
  - — NAS AEGL Subcommittee believes the adjustment factor of 2.8 currently used should be increased to 5 or 10 with appropriate justification
- Possible distinction between "genotoxic" and "cytotoxic" carcinogens
- Use of carcinogenicity data for deriving AEGL values
  - — NAC/AEGL Committee has not developed AEGLs based on carcinogenicity

ISSUES RELATED TO USING CANCER AS THE TOXIC END-POINT FOR DERIVING AEGL VALUES

- Little or no data are available on the relationship between carcinogenicity and a single short-term inhalation exposure.
- To date US federal regulatory agencies have not established regulatory standards based on, or applicable to, short-term exposures to carcinogenic substances.
- NAS SPEGLs were derived from carcinogenic data for 4 of 7 carcinogenic substances.
- Carcinogenic assessments for excess risk to exposures of less than 24 hours were conducted for only 1 of 10 carcinogenic substances in the development of SMACs.
- Considering a population-based risk range of 10^{-4} to 10^{-6} and a typical population of 1,000 to 5,000 at risk during most accidental chemical releases, the population-based risk approaches zero.
- Possibility that injury or death resulting from evacuation or other response measures exceeds the excess risk of cancer.

CURRENT APPROACH OF THE NAC/AEGL COMMITTEE TO SINGLE-EXPOSURE CARCINOGENIC RISKS

- Continue to identify and evaluate carcinogenic data on a chemical-by-chemical basis

- When appropriate, conduct assessments for excess risk in the range 10^{-4} to 10^{-6} following the 1993 NAS guideline

- Continue to provide carcinogenicity data and information on chemicals in the TSDs so that it is available to emergency planners and responders and the public at large

PRACTICAL ISSUES FOR THE NAC/AEGL COMMITTEE ON CANCER RISK ASSESSMENTS

- Selecting the appropriate risk level
  - 1993 NAS guidance indicates a range of 10^{-4} to 10^{-6}
  - Acceptable cancer risk for lifetime exposures has ranged from 10^{-4} to 10^{-6} for US federal agencies
  - The risk level used by the NAS for the development of EEGLs and SPEGLs was 10^{-4}
  - The risk level used by the NAS for the development of SMACs is 10^{-4}

NAS AEGL SUBCOMMITTEE RESPONSE TO CHEMICALS WITH NO AEGL-1 VALUES

- **Believes the NAC/AEGL Committee should try to set AEGL-1 values for all chemicals**

  ---- use non-sensory, reversible toxicity data

  ---- develop a rationale and methodology for deriving AEGL-1 values in the absence of data

  ---- modify AEGL-1 definition to accommodate new endpoints

ARGUMENTS AGAINST DERIVING DIFFERENT AEGL-1 ENDPOINTS

- If the public has no sensory perception of the chemical, why set an AEGL-1 value?

- Setting an AEGL-1 value at a level that is below the odor threshold could be confusing and, hence, dangerous.

- The purpose of the AEGL-1 is sensory detection, so in the absence of sensory effects, an AEGL-1 value is not appropriate.

- It is not scientifically credible to set an AEGL-1 value that is not based on a known toxicological endpoint.

- What is the practical value of an AEGL-1 that is not based on some toxicological parameter?

ARGUMENTS FOR DERIVING DIFFERENT AEGL-1 ENDPOINTS

- For emergency responders, the AEGL-1 values serve as the threshold for notification, regardless of whether or not it can be detected by the public.

- In the absence of an AEGL-1 value, the notification threshold level becomes arbitrary and responders are left with no guidance.

- The AEGL-1 value provides a third data point for understanding the steepness of the dose/response curve and insight into the hazardous nature of the chemical. This may influence the emergency response actions taken.

- The AEGL values are used not only by emergency responders, but for emergency planning and emergency prevention.

- For purposes of emergency planning and prevention, it provides an important reference point for determining how far below the AEGL-2 is a level that could be considered reasonably protective.

- AEGL-1 values set by the NAC/AEGL Committee help to eliminate arbitrary decisions on reasonably safe levels.

Issues on Definitions

- Current exclusionary statement re. "Hypersusceptible" individuals

- Current clarification statement re. description on effects below the AEGL level being defined.

- Addition of language to cover non-sensory effects or other approaches to setting AEGL-1 values that are currently "N/A"

Suggested Options for AEGL-2 Definitions

1. NAS recommendation:

AEGL-2 is the airborne concentration (expressed as ppm or mg/m3) of a substance at or above which it is predicted that the general population, including "susceptible" individuals, could experience irreversible or other serious, long lasting effects or impaired ability to escape.

(No reference to hypersusceptibility or effects below AEGL-2)

2. Alternative A:

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

(No reference to hypersusceptibility, but reference to effects below AEGL-2)

3. Alternative B:

AEGL-2 is the airborne concentration (expressed as ppm or mg/m3) of a substance at or above which it is predicted that the general population, including "susceptible" individuals, could experience irreversible or other serious, long lasting effects or impaired ability to escape. Certain "hypersusceptible" individuals subject to unique or idiosyncratic responses may experience these adverse effects at concentrations below the AEGL-2 level.

(Additions of revised language on hypersusceptibility, but no reference to effects below AEGL-2)

Potential Elements in AEGL-1 Definitions

- Airborne concentrations at or above may cause:
  -notable discomfort (irritation)
  -objectionable odors (annoyance)*
  -subclinical, non-sensory toxic effects*

- However, the effects are:
  -not disabling*
  -transient*
  -reversible*

* represent proposed additions

SUGGESTED OPTIONS FOR AEGL-1 DEFINITION

- **NAS recommendation:**

AEGL 1 - is the airborne concentration (expressed as ppm or mg/m3) of a substance at or above which it is predicted the general population, including "susceptible" individuals, could experience notable discomfort or irritation. However, the effects are not disabling and these effects are transient and reversible upon cessation of exposure. Airborne concentrations below the AEGL-1 represent exposure levels that could produce mild odor, taste, or other sensory perceptions. (Some "hypersusceptible" individuals could experience notable discomfort or irritation below the AEGL-1.)

- **Option A:**

AEGL 1 - is the airborne conctration (expressed as ppm or mg/m3) of a substance at or above which it is predicted the general population, including "susceptible" individuals, could experience notable discomfort or irritation. However, the effects are not disabling and these effects are transient and reversible upon cessation of exposure. Airborne concentrations below the AEGL-1 represent exposure levels that could produce mild odor, taste, or other sensory perceptions.

(No reference to hypersusceptibility)

- Option B:

AEGL-1 - is the airborne concentration (expressed as ppm or mg/m3) of a substance at or above which it is predicted the general population, including "susceptible" individuals, could experience notable discomfort, or irritation. These effects are not disabling and are transient and reversible upon cessation of exposure. Airborne concentrations below the AEGL-1 represent exposure levels that could produce mild odor, taste, or other sensory perceptions. However, certain "hypersusceptible" individuals subject to unique or idiosyncratic responses may experience notable discomfort or irritation at concentrations below the AEGL-2 level.

(Revised language on hypersusceptibility)

- Option C:

AEGL-1 is the airborne concentration (expressed as ppm or mf/m3) of a substance at or above which it is predicted the general population, including "susceptible" individuals, could experience notable discomfort, irritation, or other reversible toxicity that may not be based on sensory effects. These effects are not disabling and are transient and reversible upon cessation of exposure. Airborne concentrations below the AEGL-1 represent exposure levels that could produce mild odor, taste, or other sensory perceptions. However, certain "hypersusceptible" individuals subject to unique or idiosyncratic responses may experience notable discomfort or irritation at concentrations below the AEGL-2 level.

(Revised language on hypersusceptibilty and language on reversible, non-sensory effects)

Proposed language that could be Footnoted to the NAS/AEGL Definitions to Provide Clarification.

Option A:

Airborne concentrations below AEGL-1 represent exposure levels that could produce mild odor, taste, or irritation. Airborne concentrations below AEGL-2, but at or above the AEGL-1, represent exposure levels that may cause notable discomfort and reversible toxicity. Airborne concentrations below AEGL-3, but at or above AEGL-2, represent exposure levels that may cause irreversible or other serious, effects or impaired ability to escape. While the AEGL values should protect susceptible members of the population, it is recognized that, due to their unique or idiosyncratic responses, some hypersusceptible individuals may not be protected. As the concentration increases above each AEGL level there is both an increasing probability of occurrence and severity of effects associated with that AEGl concentration level.

(Language developed by George Rush at NAS meeting)

Option B:

Airborne concentrations below AEGL-1 represent exposure levels that could produce mild odor, taste, or irritation. Airborne concentrations below AEGL-2, but at or above the AEGL-1, represent exposure levels that may cause notable discomfort and reversible toxicity, that may or may not be based on sensory

perception. Airborne concentrations below AEGL-3 but at or above AEGL-2, represent exposure levels that may cause irreversible or other serious, effects or impaired ability to escape. While the AEGL values should protect susceptible members of the population, it is recognized that, due to their unique or idiosyncratic responses, some hypersusceptible individuals may not be protected. As the concentration increases above each AEGL level there is both an increasing probability of occurrence and severity of effects associated with that AEGl concentration level.

(Includes language to address AEGL-1 values based on approaches other than sensory data)

Attachment 6

Chlorine - NAS Comments

Consider n value of 1

Based on best lethality studies

Pediatric asthmatics

Are they covered by protecting adult asthmatics?

Chlorine inhalation studies with normal subjects and subjects with airway hyperreactivity

1. Rotman et al. 1983
   - 0.5 ppm for 4 hours:
     - Healthy volunteers (8):
       - FEV_1 - no change (97% of control value)
       - Raw - no change (105% of control value)
     - Atopic individual:
       - FEV_1 - 81% of control value
       - Raw - ~double control value
   - 1.0 ppm for 4 hours
     - Healthy volunteers (8):
       - FEV_1 - 91% of control value
       - Raw - 144% of control value
     - Atopic individual:
       - FEV_1 - 45% of control value
       - Raw - ~3X control value... respiratory symptoms

D'Alessandro et al., 1996 (no controls, exposure through mask)
- 0.4 ppm for 1 hour
  - ~~Healthy volunteers (5)~~
    - ~~FEV_1 - no significant response~~
    - ~~Raw - no significant response~~
  - Subjects with airway hyperresponsiveness/asthma (5)
    - FEV_1 - no significant response
    - Raw - no significant response
- 1.0 ppm for 1 hour
  - Healthy volunteers (5)
    - FEV_1 - significant response (4% relative decrease)
    - Specific Raw - significant response (39% relative increase)
  - Subjects with airway hyperresponsiveness/asthma (5)
    - FEV_1 - 16% relative decrease
    - Specific Raw - 108% relative increase.... respiratory symptoms

Health Criteria Needs for Risk Assessment and Emergency Response Planning

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Attachment 7

Disclaimer

Direct policy-related questions to

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U. S. Department of Transportation
400 Seventh Street, S. W.
Washington, DC 20590

Overview of Presentation

- Background
- Evolution of the Emergency Response Guidebook
- Nature of accidental releases
- Issues related to health criteria

Background

- Work for the USDOT over past 10 years
  - Emergency Response Guidebook (1990, 1993, 1996, 2000)
  - Transportation Risk Assessment (1998-1999)
  - Performance Measures (1999)

Background
Transportation Risk Assessment

- In-depth risk profiles for six chemicals with over 95 % of TIH* commodity flow and over 90 % of total TIH* risk
- Gasoline, other flammables, and explosives
- Highway and rail only
- Excludes non-TIH* chemicals and radioactive and infectious substances

*Substances that pose a Toxic by Inhalation Hazard

Background
Transportation Risk Assessment

- Routes developed based on
  - Hazardous Materials Incident-reporting System (HMIS) database
  - Commodity flow data from US Census Bureau
  - Association of American Railroads 1 % Waybill Data
- 1 million 10-year periods simulated to develop statistical risk distributions
- Effect of sheltering included
- Intercomparison of risk

Background
Performance Measures

- Quantify relationship between regulations and lives saved
- Obtain insights on how regulations can be made more effective

Background
Emergency Response Guidebook

- Developed by the US DOT to assist fire-fighters, policemen and other emergency response personnel
- Focuses on the first 30 minutes following a transportation accident
- More than 1300 substances are cross-referenced by name and by identification number
- Each entry points to one of 62 hazard guides which gives information on
  - fire and explosion hazards
  - potential health hazards
  - fire-fighting techniques
  - mitigation strategies
  - first-aid procedures

Background
Emergency Response Guidebook

- Entries color coded to show a toxic-by-inhalation hazard (TIH)
- Initial Isolation and Protective Action Distances for 615 TIH substances (including generics, synonyms, mixtures, and water-reactive materials)

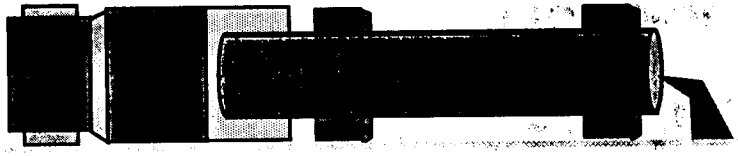
Background
Emergency Response Guidebook

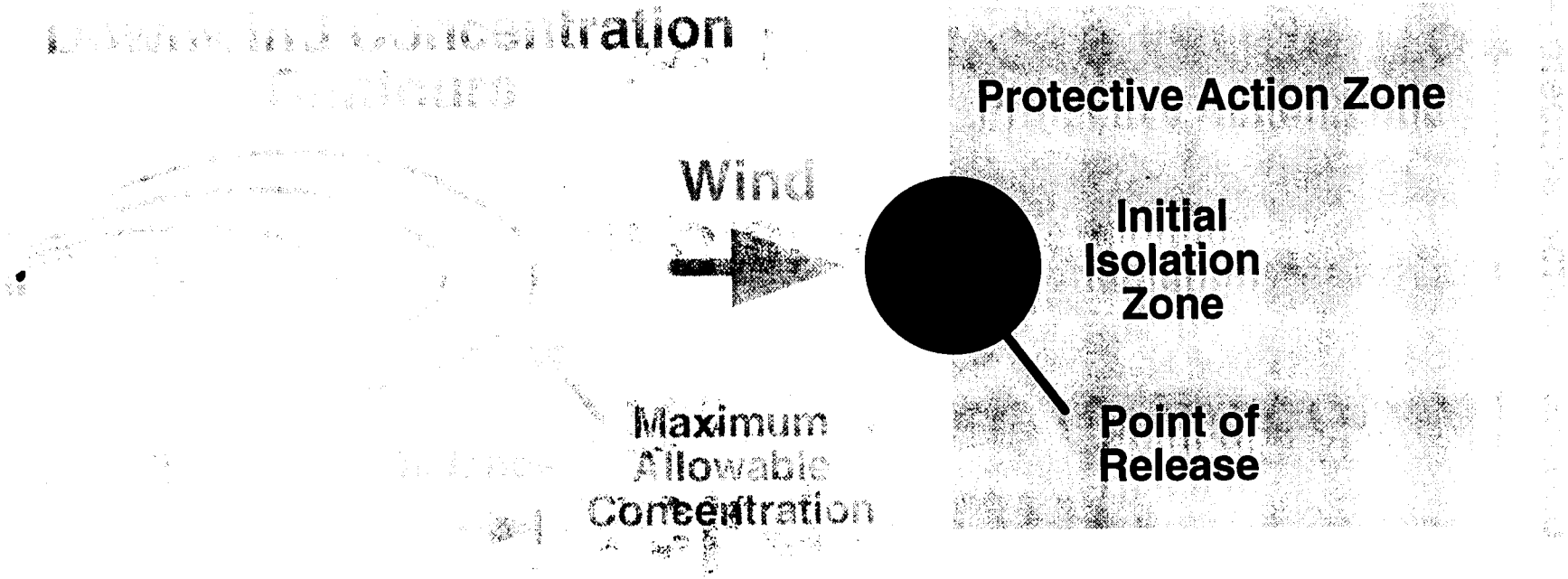
- List of TIH chemicals maintained by USDOT
- List developed from
  - UN criterion: volatility/toxicity (vapor pressure/LC_{50})
  - Other evidence that material poses a TIH risk
- List contains many poorly characterized chemicals as well as mixtures and generics

Background
Emergency Response Guidebook

- Initial Isolation Distances range from 100 to 3000 ft
- Protective Action Distances range from 0.1 to 7+ miles
- Two entries provided for each material:
  - Small spill: up to 55-gal drum, standard cylinder, or many small packages
  - Large spill: everything else

Initial Isolation and Protective Action Distances





Corresponding Table Entry

		Small Spill			Large Spill		
		First ISOLATE in all directions (feet)	Then, PROTECT persons downwind		First ISOLATE in all directions (feet)	Then, PROTECT persons downwind	
ID#	Material		DAY (miles)	NIGHT (miles)		DAY (miles)	NIGHT (miles)
1005	AMMONIA	500	0.1	[illegible]	500	0.3	[illegible]

Emergency Response Guidebook

- Our involvement began with the 1990 ERG
- 1990 methodology
  - Source based on Wu-Schroy Model (46 chemicals) and ARCHIE algorithm
  - Dispersion based on Pasquill-Gifford stability class D and 10 mph wind speed
  - Time-dependent Gaussian puff model

use of hydrazine

Emergency Response Guidebook

- 1990 methodology

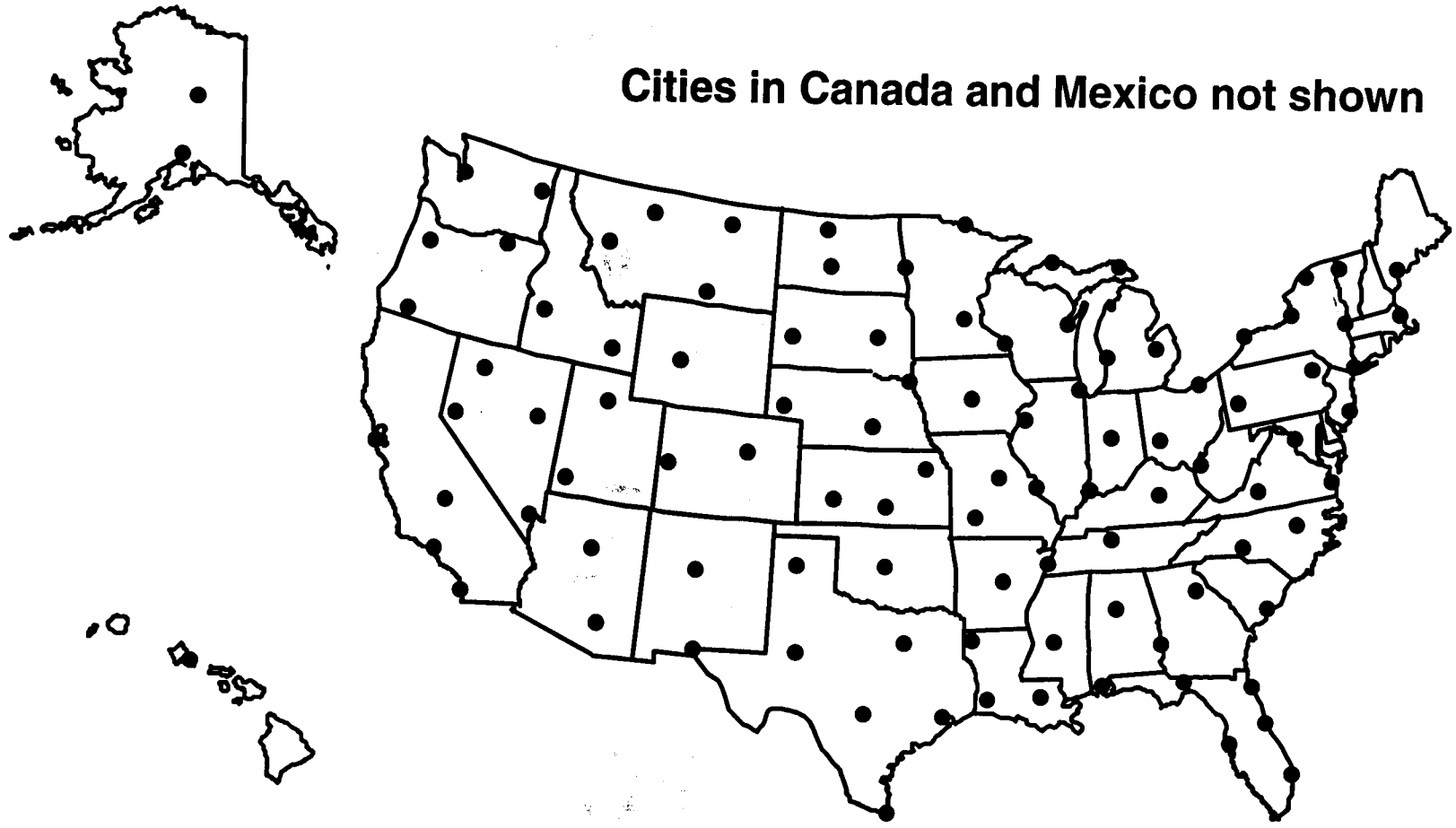
Limit	Characteristics	Organization	%
ERPG-2	1 hr, emergency	AIHA	9
SPEGL	1 hr, emergency	NRC/NAS	1
TLV-STEL	15-min, occupational	ACGIH	13
TLV-C	instant, occupational	ACGIH	2
EEGL	1 hr, occupational	NRC/NAS	3
3 × TLV-TWA	15-min, occupational	ACGIH	35
$0.1 \times LC_{50}$	varies	varies	20
LC_{LO}	varies	varies	7
Other	—	—	10

Guidelines: Percent used in emergency response

Emergency Response Guidebook

- **Improvements**
  - Day/night separation
  - Expanded to cover Canada and Mexico
  - Dispersion based on climatology of 110 cities in North America
  - Fully statistical analysis
    - » Develop statistical distributions
    - » Model large number of events
    - » Level of Protection = probability that individual will not experience specified adverse health effect

Dispersion Distributions based on 110 Cities



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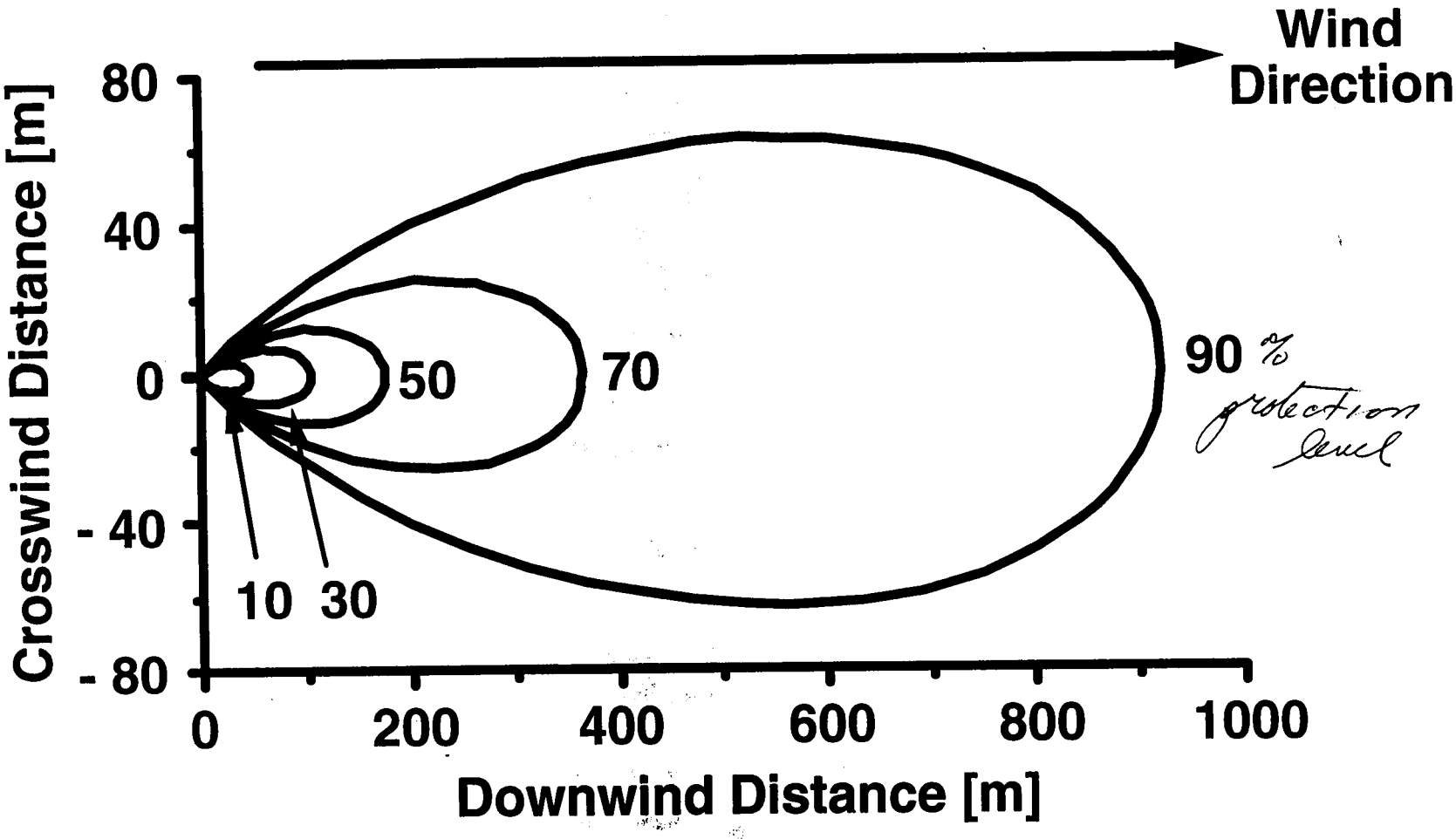
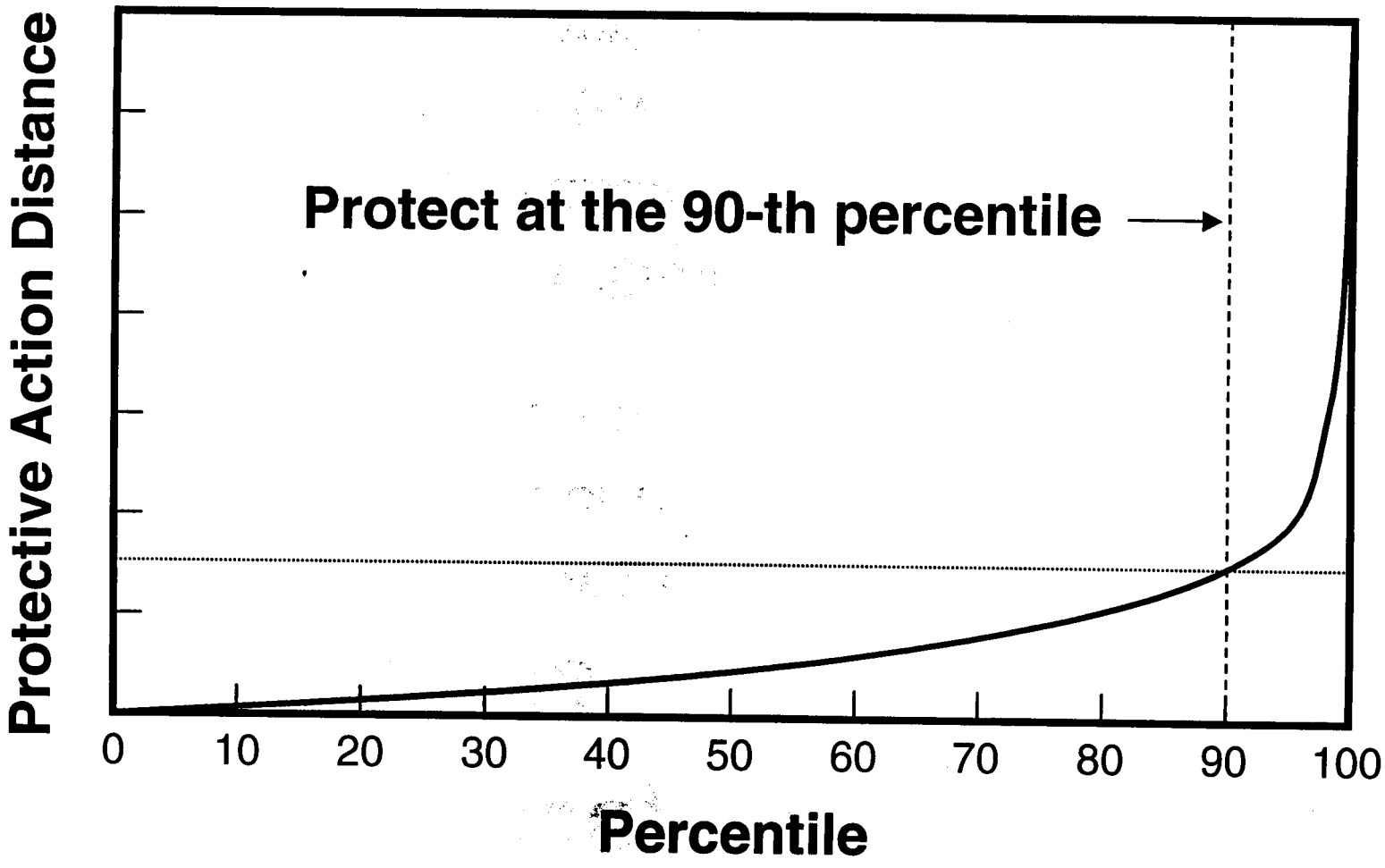
Footprints for Different Percentiles



Emergency Response Guidebook



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Emergency Response Guidebook

- **Improvements**
  - Source models for gases, liquids, liquefied gases
  - Enforced container authorizations
  - Release fraction from historical data on container performance
  - Geographical distribution reflects commodity flow
  - Water-reactive substances
  - Chemical agents (transportation, criminal)
  - Mixtures and generics
  - Chemical properties
  - Heavy-gas effects

Emergency Response Guidebook

- **Improvements**
  - Revised set of surrogate health criteria
  - Panel of toxicologists with extensive experience with health criteria for acute exposures
  - ERPG-2 criterion of choice
  - $0.01 \times LC_{50}$ where good LC_{50} data exist
  - Miscellaneous criteria used otherwise

Current Health Criteria

Basis of Health Criteria	%	%
ERPG for chemical of concern	23	
ERPG for structurally similar chemical	11	
Subtotal for ERPGs		34
LC_{50} for chemical of concern	51	
LC_{50} for structurally similar chemical	5	
Subtotal for LC_{50}		56
LC_{LO} for chemical of concern	6	
LC_{LO} for structurally similar chemical	< 1	
Subtotal for LC_{LO}		6
AIHA Emergency Exposure Level	2	
NRC Emergency Exposure Guidance Level	< 1	
ACGIH TLV for structurally similar chemical	< 1	
Subtotal for alternate health-based values		3
Oral toxicity data		< 1
Total		100

Nature of Accidental Releases

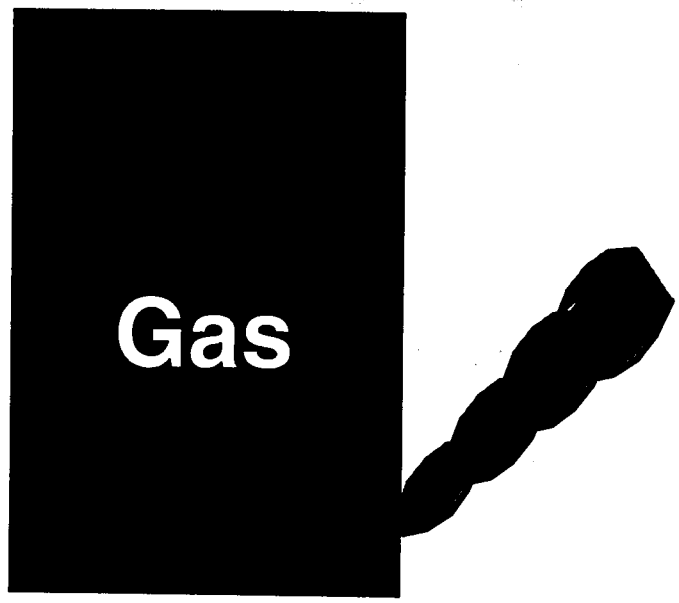
- Problem has three parts
  - Determining the source emission rate
  - Estimating downwind dispersion
  - Combining health criteria with downwind concentration predictions to obtain hazard distances
- Each part poses unique problems that must be addressed using the best-available information

Source Types

- Compressed gases
- Ordinary liquids
- Liquefied gases

- Exposure depends heavily on source type

Compressed Gases



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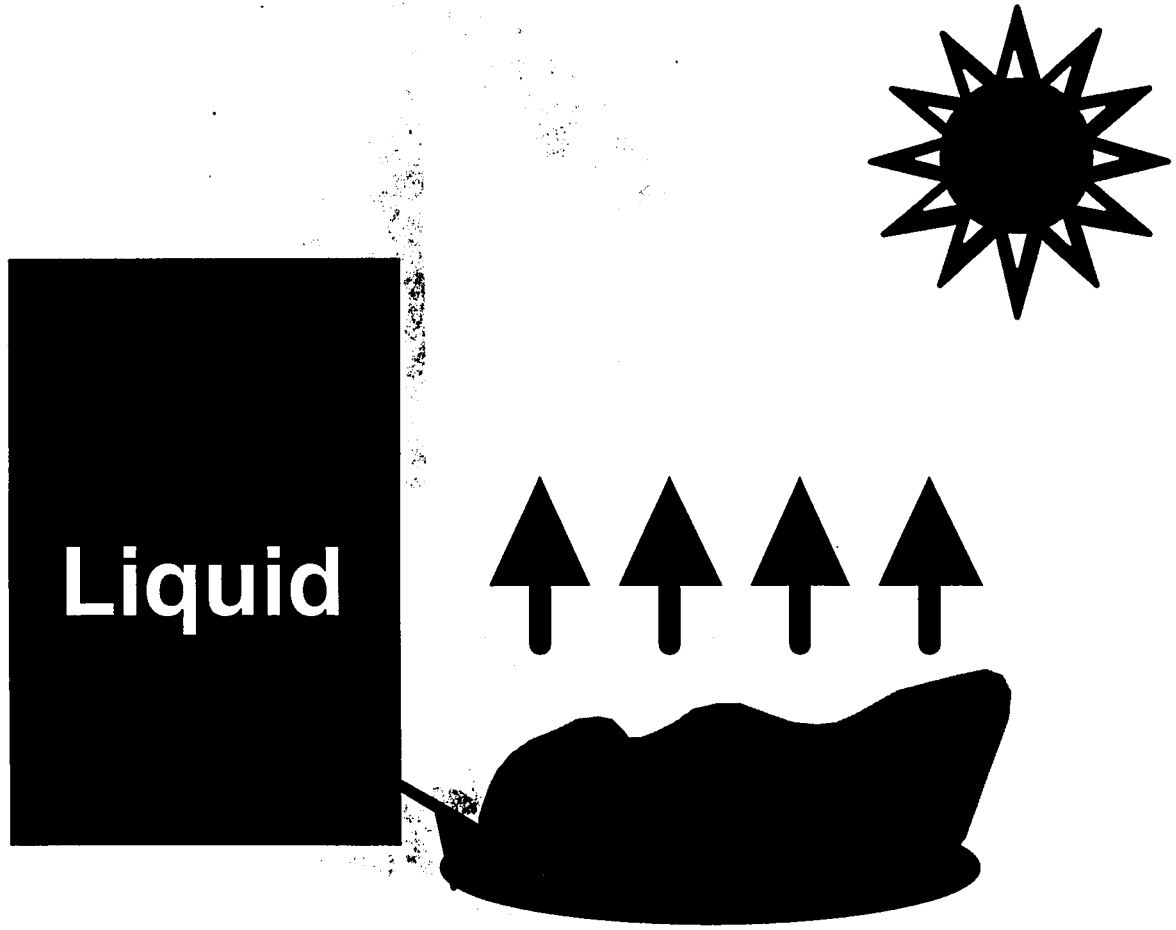
Ordinary Liquids



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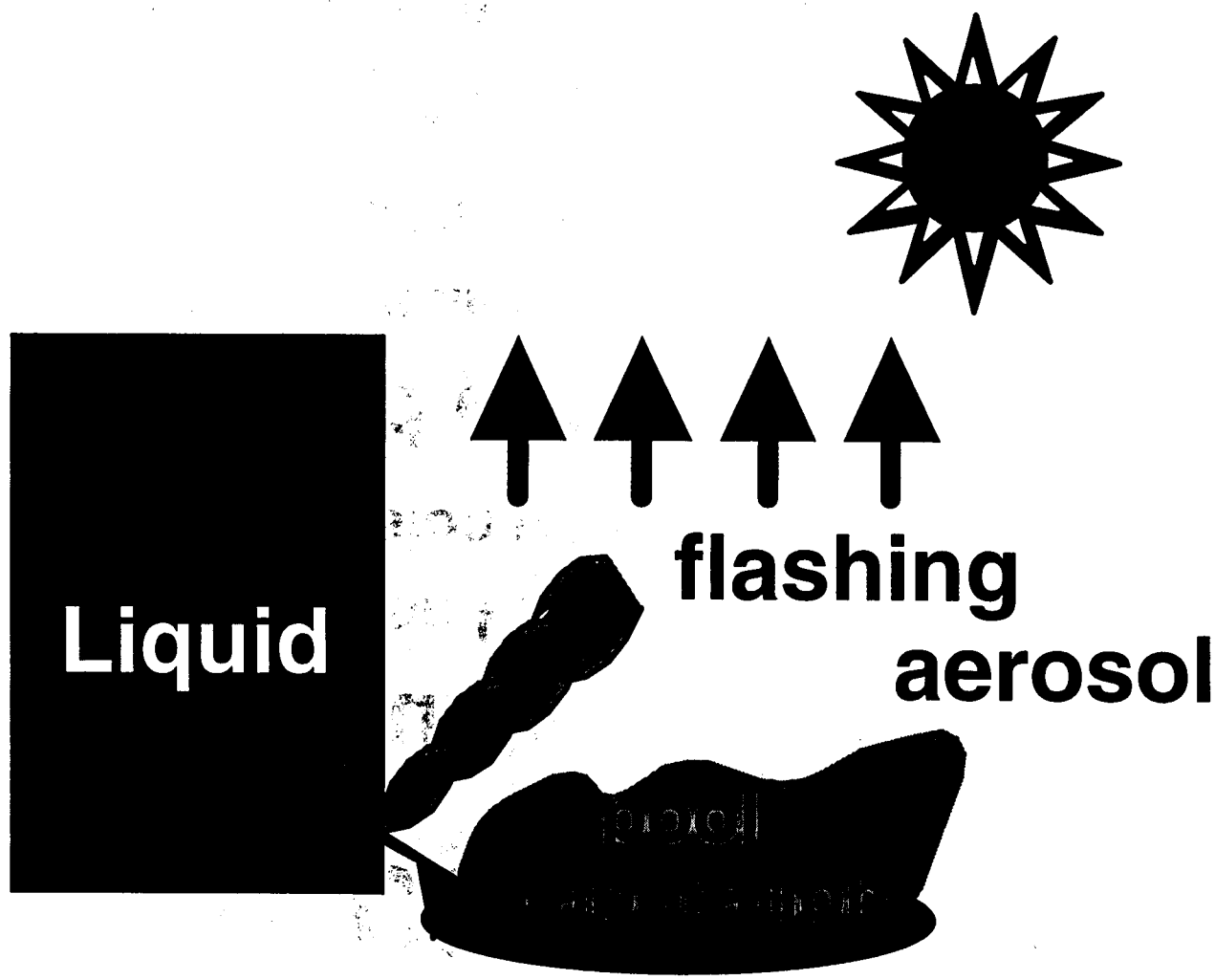
Liquefied Gases



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Source Characteristics

- **Ordinary liquids**
  - Pool evaporation key mechanism
  - Smallest emission rate all else being equal
- **Compressed gases**
  - Blowdown typically under 15 min.
  - Intermediate emission rate all else being equal
- **Liquefied gases**
  - Flashing (aerosol) + pool evaporation
  - Largest emission rate all else being equal

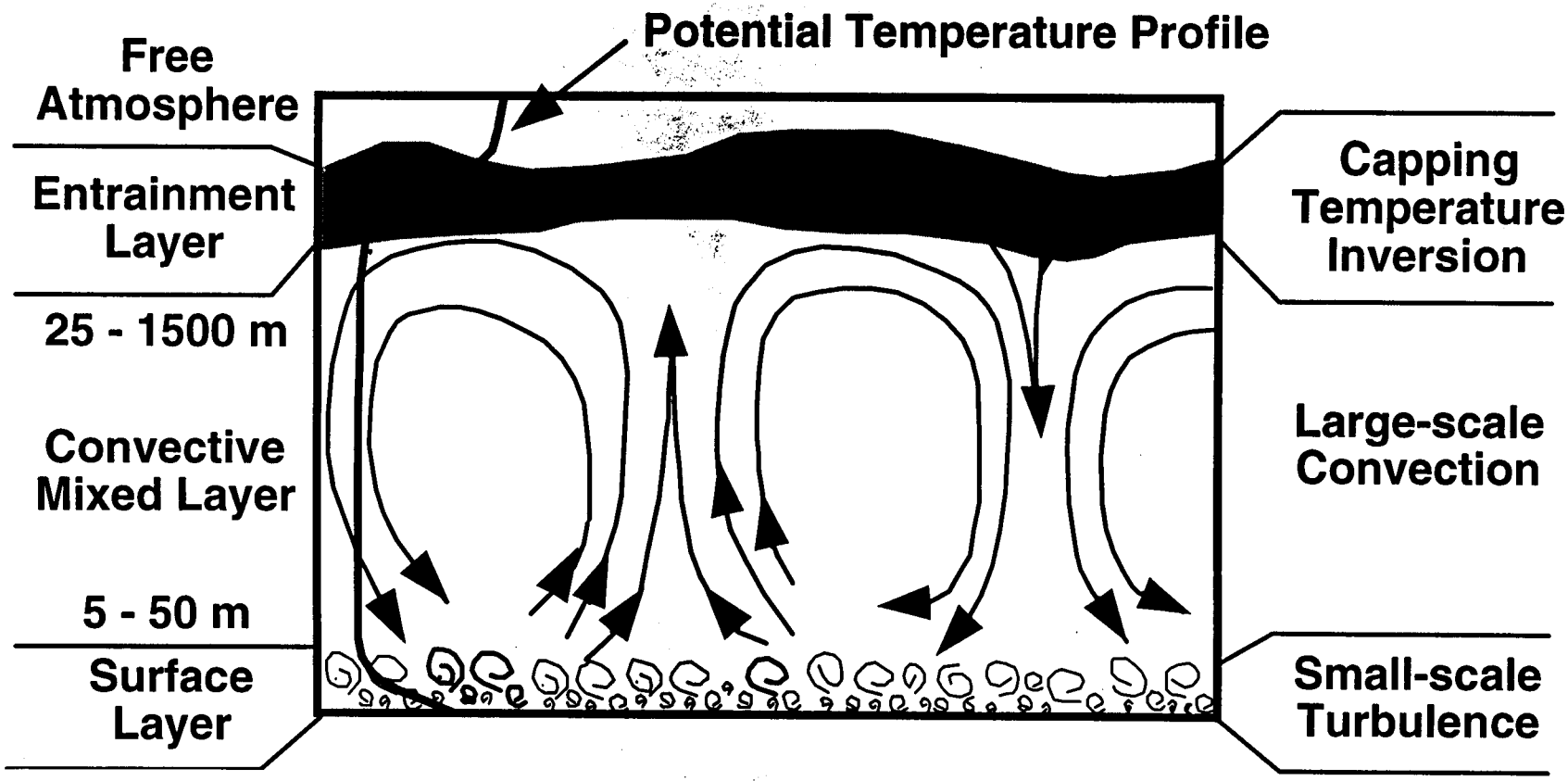
Source Characteristics

- Event often short lived with large release over short period of time (5 – 15 min.)
- Problem further complicated by fire, reaction with standing water, and heavy-gas effects

Atmospheric Dispersion

- Governs downwind concentration
- Depends heavily on time of day and prevailing meteorology
  - bright sunny day => best dispersion
  - overcast day or night => intermediate dispersion
  - clear night => worst dispersion
- Plume inhomogeneous in both space and time

Daytime Atmosphere



Daytime Plume

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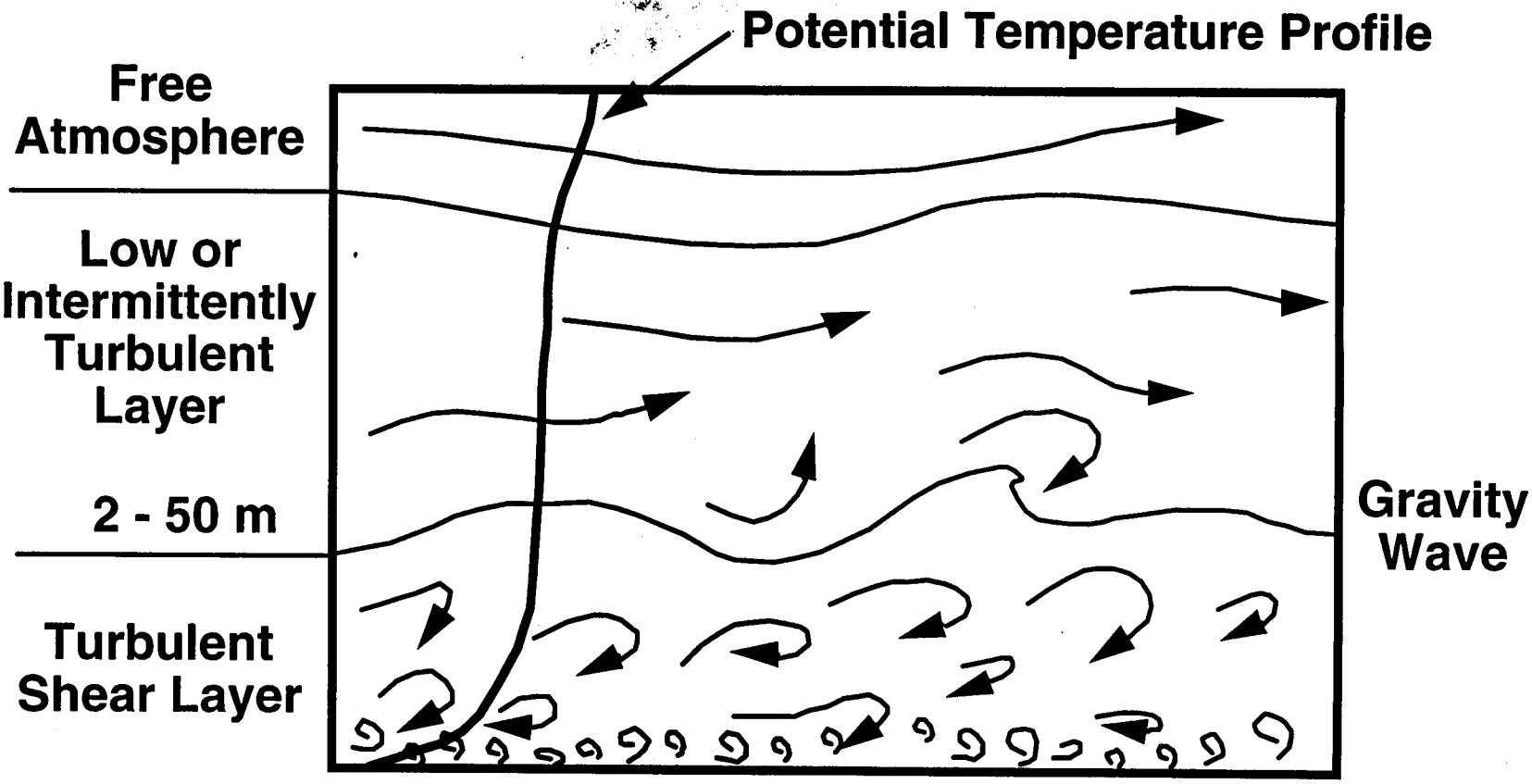
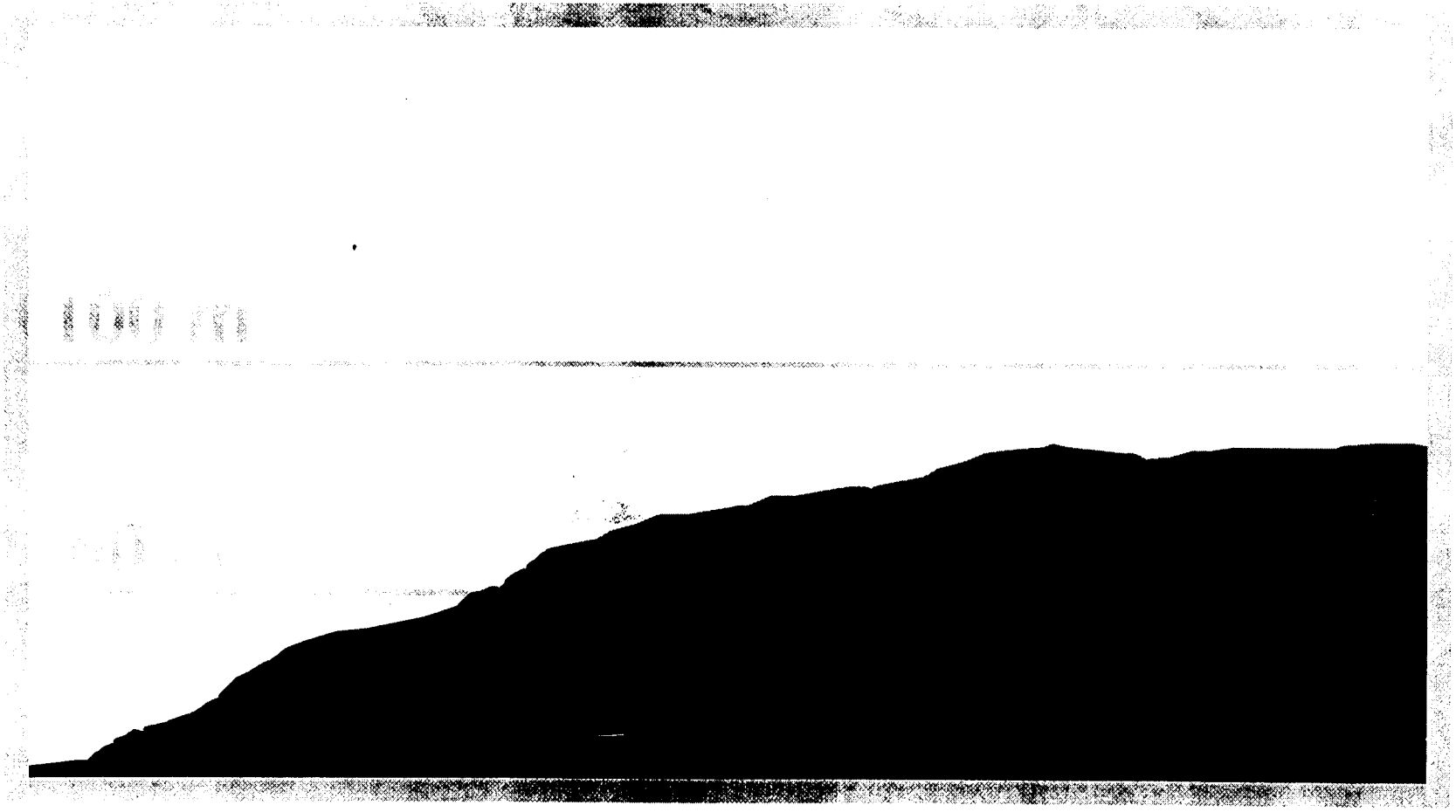
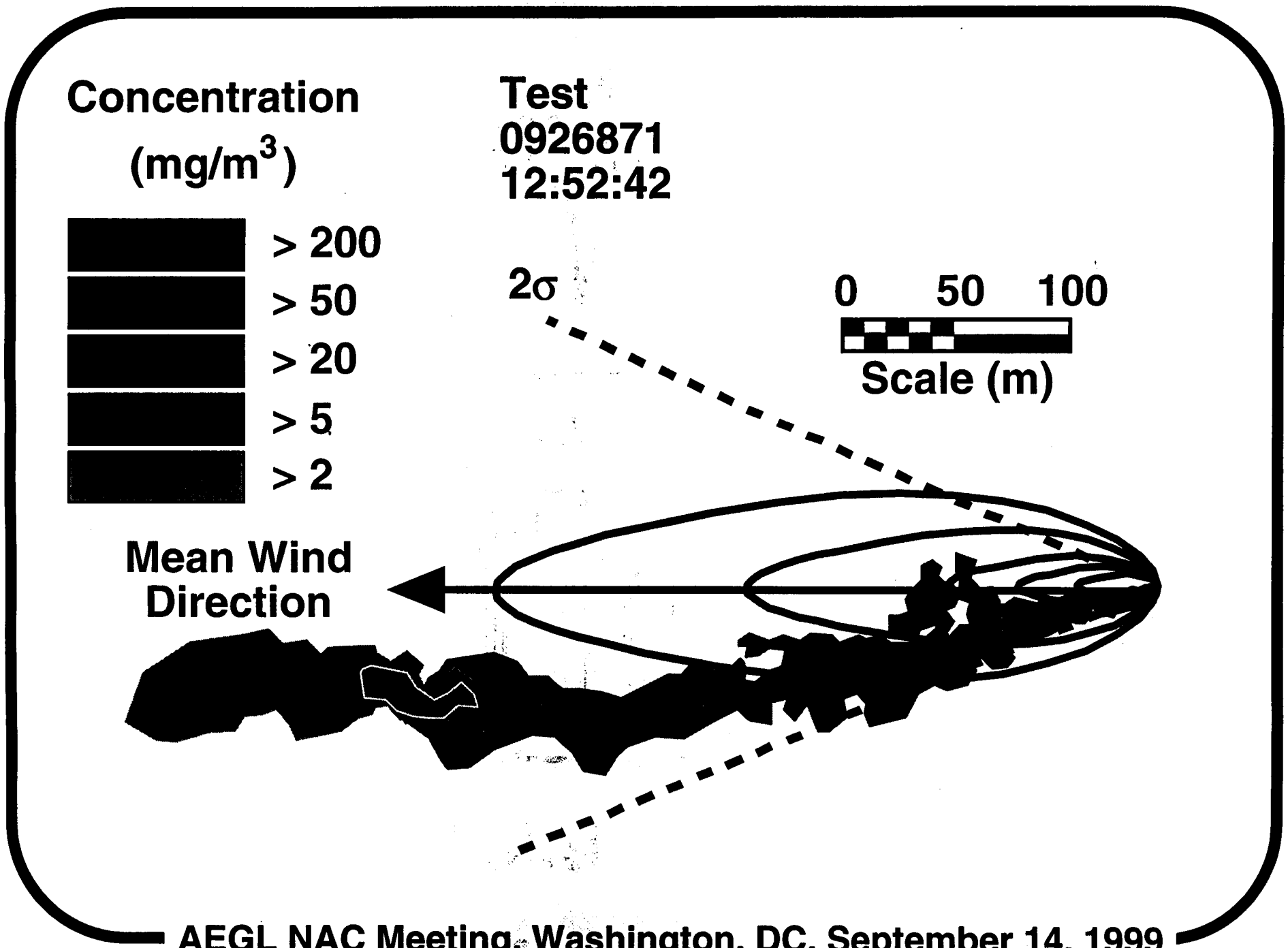
Nighttime Atmosphere

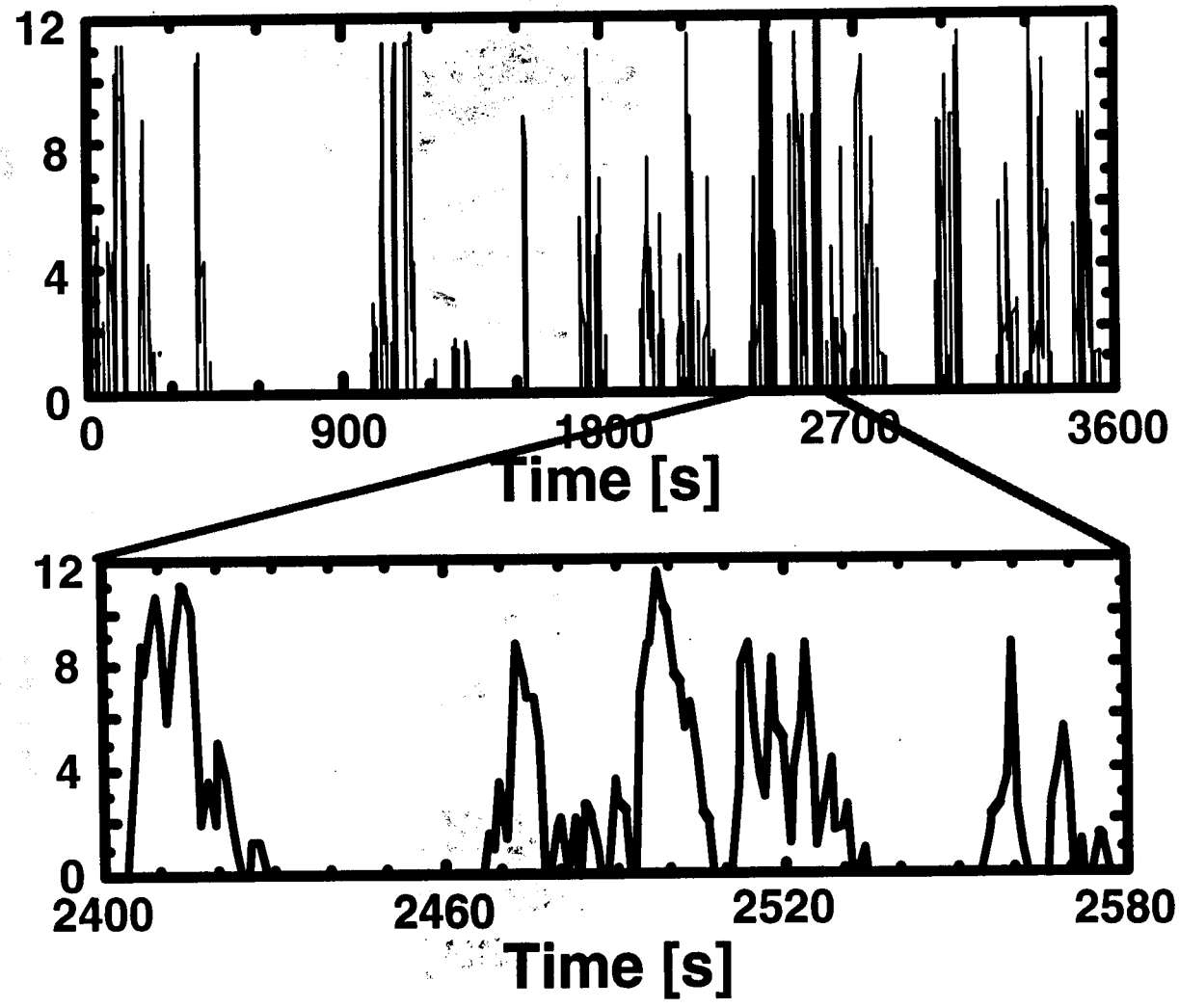


Nighttime Plume



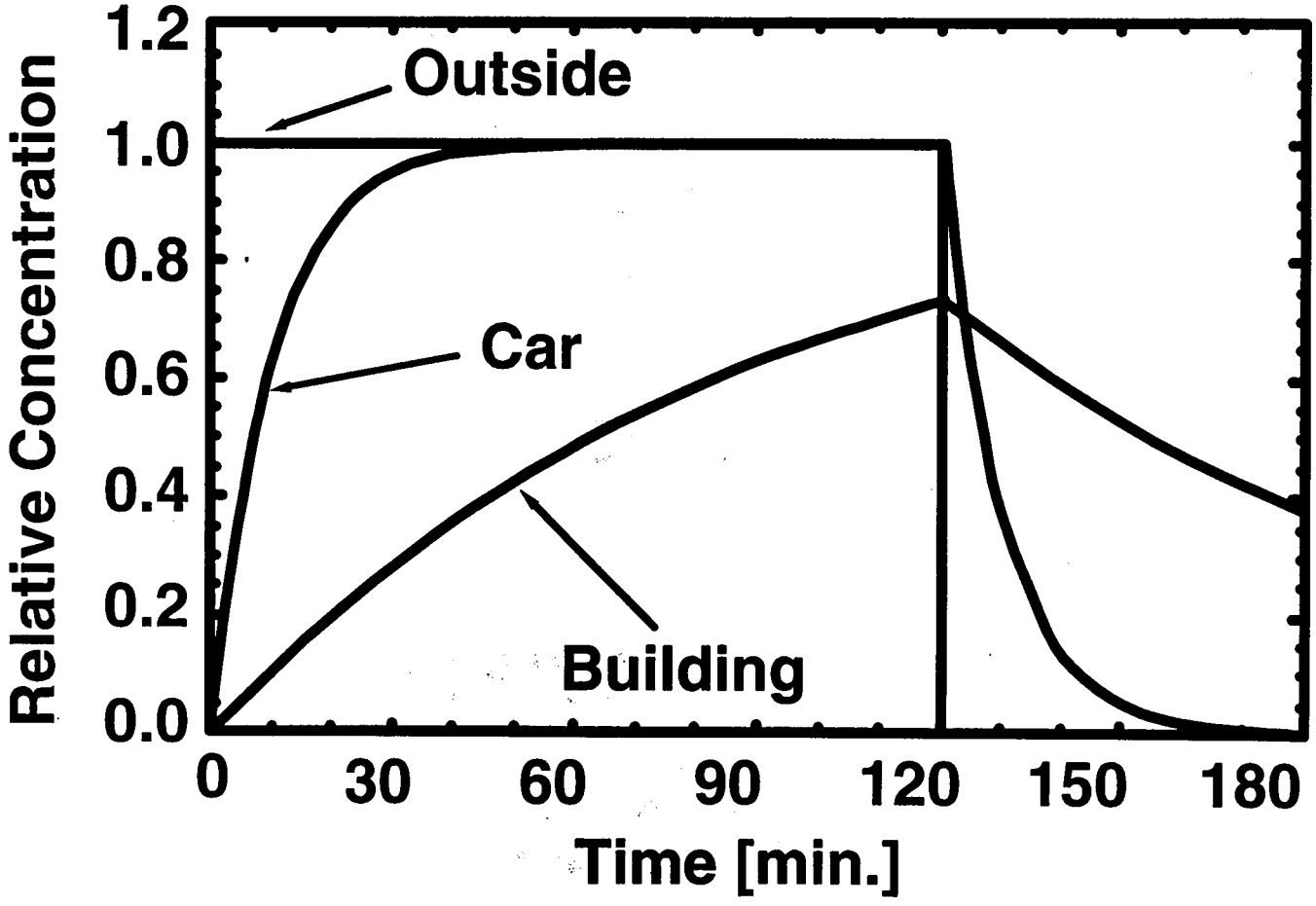

Concentration
(mg/m3)
> 200
> 50
> 20
> 5
> 2
Test
0926871
12:52:42
2σ
0 50 100
Scale (m)
Mean Wind
Direction

Temporal Variation



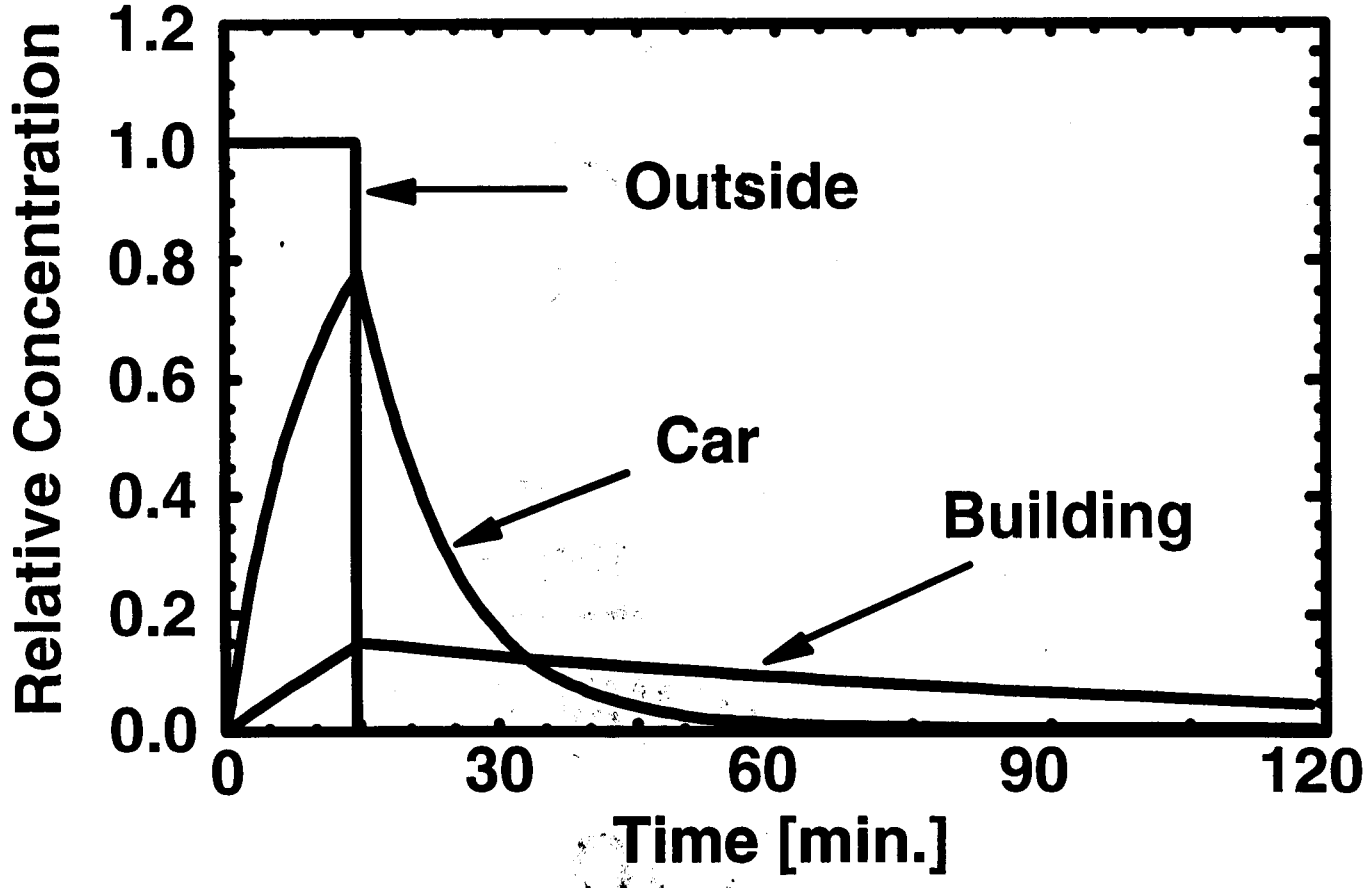
Effect of Sheltering

120 Minute Release



Effect of Sheltering

15 Minute Release



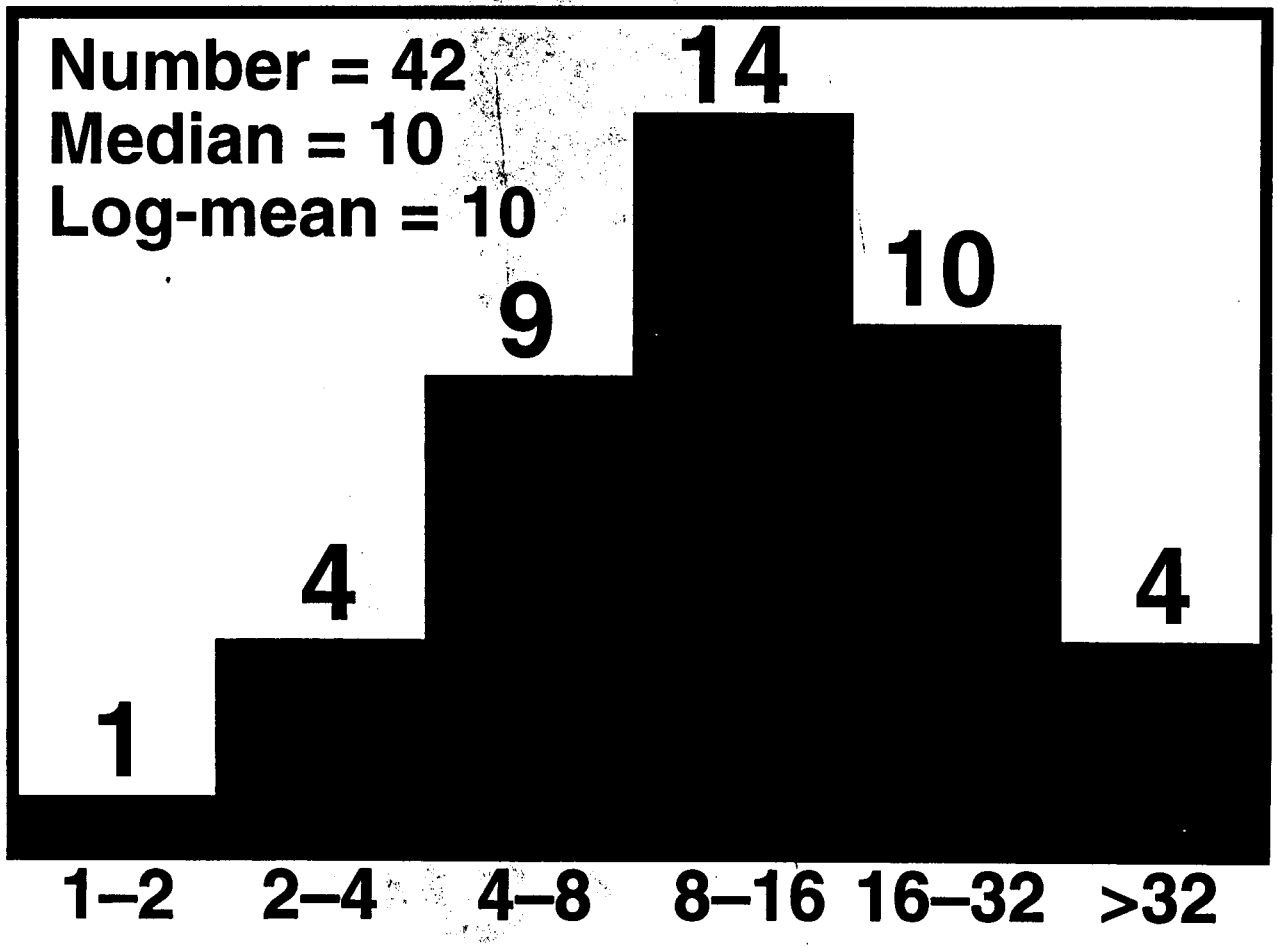
Health Criteria Issues

- Surrogate criteria
- Exposure time adjustment(s)
- Quantitative and scalable criterion definition
- Nonlinear exposure/dose/response relationships and real-world concentration variability

Surrogate Data

- Need for surrogate data will always exist
- Overly conservative health criteria are of little practical value
- Surrogate data must be consistent with established criteria
- Peer-reviewed procedure for assigning surrogate values should receive high priority

ERPG-2 / TLV-TWA



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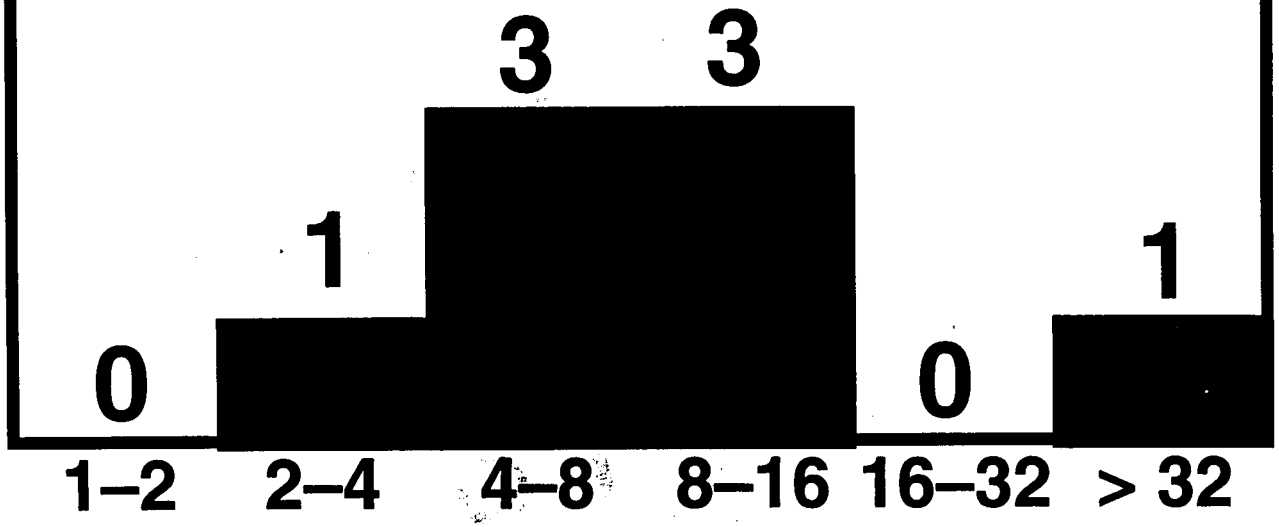
ERPG / TLV-C

With Carcinogen
Number = 8
Median = 7
Log-mean = 8

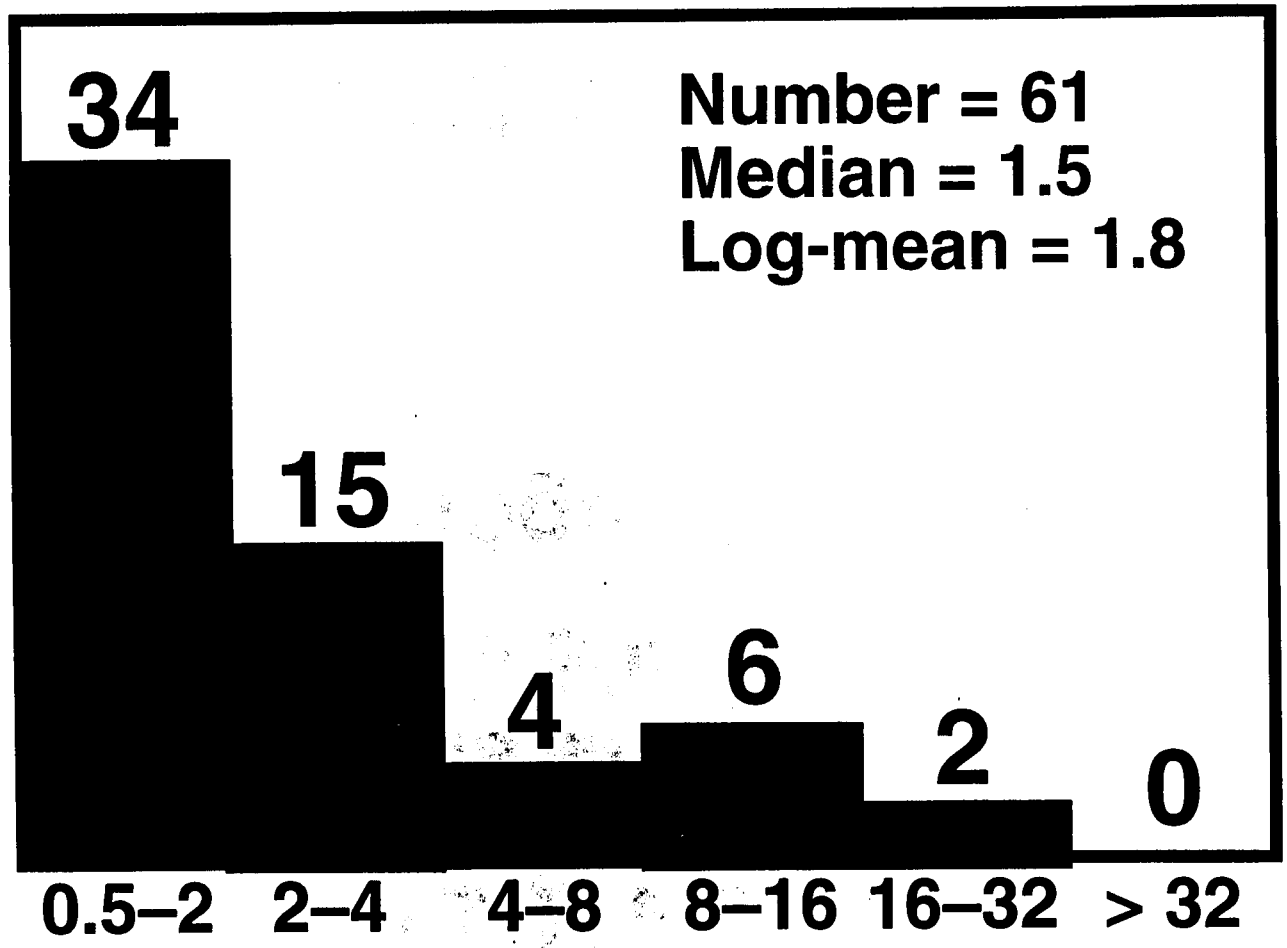
No Carcinogens
Number = 7
Median = 6
Log-mean = 6



Observations

- Carcinogens are outliers with ratios of 25 - 500
- With carcinogens removed
  - Number = 33
  - Median = 8
  - Log Mean = 8.3
- 3 × TLV-TWA is conservative
- Poor correlation with emergency response criteria

$100 \times ERPG\text{-}2 / LC_{50}$ (norm)



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LC_{50} Surrogate Criteria

- Both ERPG and LC_{50} based on acute inhalation toxicity
- Well defined effect
- Carcinogenic effects absent
- $0.01 \times LC_{50}$ gives value usually within factor of 2 of ERPG

LC_{50} Surrogate Criteria

- Potential Problems
  - Different end point
  - Questionable origin of some data
  - Conflicting values
  - Species/population correction often required
  - Exposure time correction typically needed

Exposure Time Adjustment

- Many emergency exposures are 15 min. or less
- Emergency response data are normalized to 1 hr
- Many other health criteria are for longer exposure times
- Exposure-time adjustment chemical specific

Exposure Time Adjustment

- **Exposure time 15 min. to 1 hr**

$$C_{corrected} = ERPG \times (t_{ref} / t_{actual})^{1/2}$$

- **Exposure time less than 15 min.**

$$C_{corrected} = 2 \times ERPG$$

Quantitative and Scalable Criterion Definition

- LC_{50} based on well-defined end-point
  - Fatalities are easy to measure
  - Most studies use rats and follow standard test protocol
- Emergency response criteria need to be similarly well defined

Quantitative and Scalable Criterion Definition

- **Risk assessment requires that effect be quantified and scalable**
  - How can effects be related to concept of temporary and permanent injury?
  - What happens for exposures at levels above criteria (but below the next highest criteria)?
  - What fraction of the population will experience each consequence level?

Quantitative and Scalable Criterion Definition

- **Ideal: multiple discrete effect levels with percentiles affected**

Population Affected [%]	Medical Attention	Hospitalization Required	Severe Injury	Death
1	0.1	1	3	5
10	0.2	2	15	25
30	0.5	5	25	50
50	1	10	50	100
70	2	20	100	200
90	5	50	250	400
99	10	100	500	800

Nonlinear Response Relationships

- Animal studies are based on constant concentration
- Real-world concentrations are highly transient
- Very little is known about averaging and recovery characteristics of humans

Summary and Conclusions

- Analysis of accidental releases involves three components
  - Source characterization
  - Dispersion analysis
  - Impact of chemical concentrations on the general population

Summary and Conclusions

- **Most chemical accidents produce brief, time-varying exposures**
  - Outdoor exposures combine brief episodes of high concentration interspersed with periods of clean air
  - Indoor exposures are usually lower, lagged, and more uniform
  - Non-linear response to exposure may greatly impact the real-world effects

Summary and Conclusions

- Practical use of health criteria often require
  - Adjustment of exposure time
  - Use of surrogate data
- Risk assessments require more quantitative and scalable effects

Benchmark Dose Procedures: Application to Ethylene Oxide

Judy A. Strickland and Jeffrey S. Gift
National Center for Environmental Assessment
U.S. Environmental Protection Agency

Benchmark Dose Software
Purpose

Facilitate the fitting of a mathematical function to dose-response data and the determination of a benchmark dose (BMD) that is associated with a pre-selected benchmark response (BMR).

Benchmark Dose Software Version 1.1b

- http://www.epa.gov/ncea/bmds.htm
- **BMDS Help Manual**
- **Jeff Gift, Project Manager**
  - **gift.jeff@epa.gov**
  - **919-541-4828**

Benchmark Dose Publications

- The Use of the Benchmark Dose Approach in Health Risk Assessment, EPA/630/R-94/007
- Benchmark Dose Technical Guidance Document, EPA/600/P-96/002A, Draft

Dichotomous Model

- **Pr (response) = γ + (1- γ)F(dose; α, β. .)**
  - **F(dose; α, β. .) = cumulative distribution function. When it approaches 0 as dose approaches 0, γ is background incidence**
  - **γ, α, β. . = parameters estimated by maximum likelihood methods**

Models

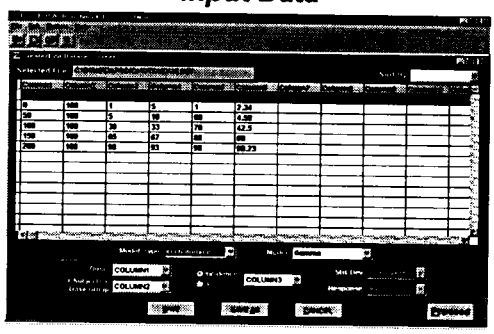
- **Three Types**
  - **Dichotomous (9)**
  - **Continuous (4)**
  - **Nested (3)**

Benchmark Dose Software
Calculating a BMD

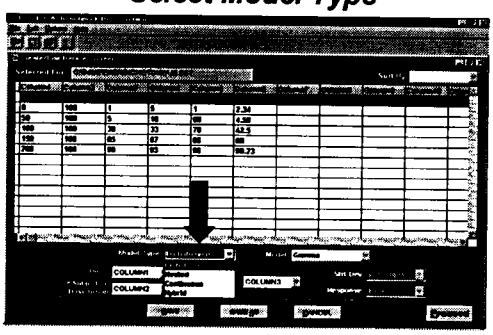
- Create or Import the data
- Select model type
- Select model
- Specify model parameters
- Run model
- Review textual & graphic results

National Center for Environmental Assessment

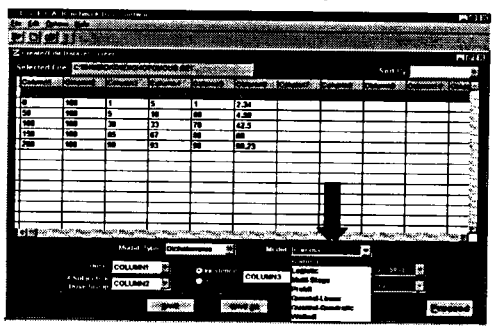
Benchmark Dose Software
Input Data



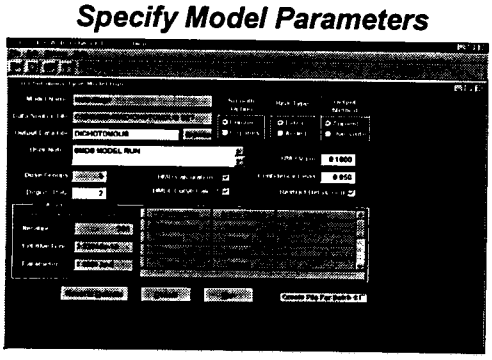
Benchmark Dose Software
Select Model Type



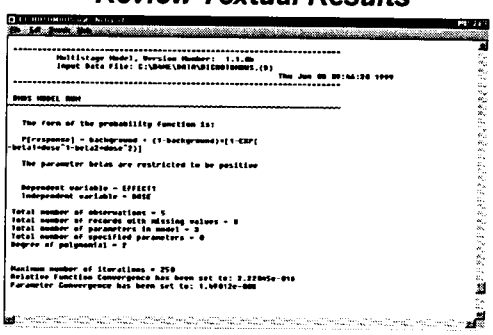
Benchmark Dose Software
Select Model



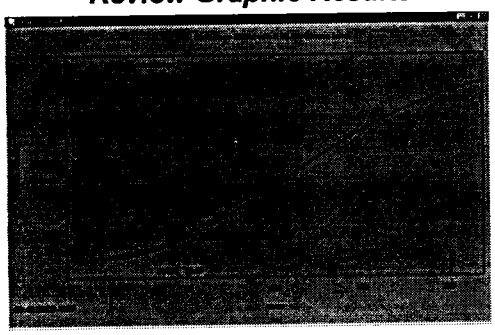
Benchmark Dose Software
Specify Model Parameters



Benchmark Dose Software
Review Textual Results



Benchmark Dose Software
Review Graphic Results

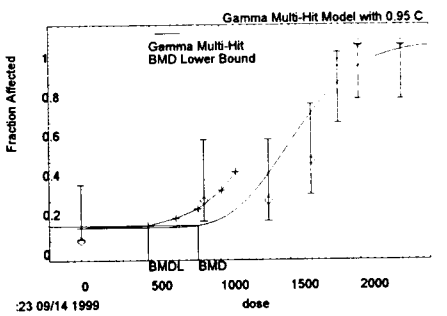


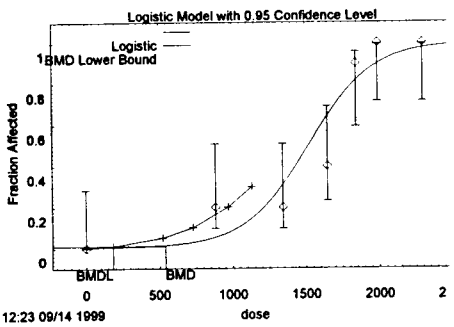
Jacobson et al., 1956

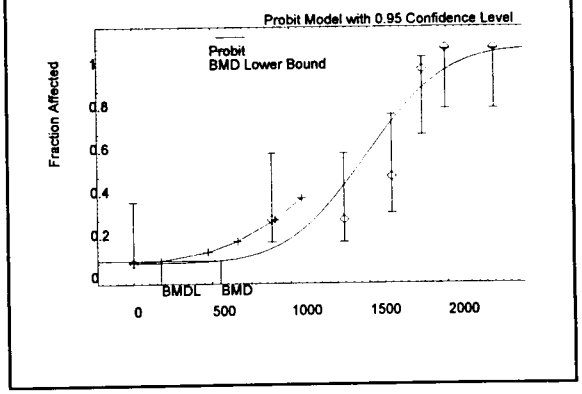
Concentration (ppm)	# Subjects	% Lethality
882	10	20
1343	10	20
1648	10	40
1843	10	90
1992	10	100
2298	10	100

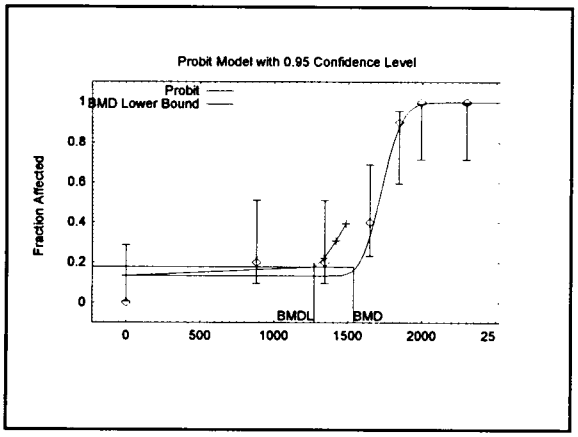
Benchmark Risk = 10%

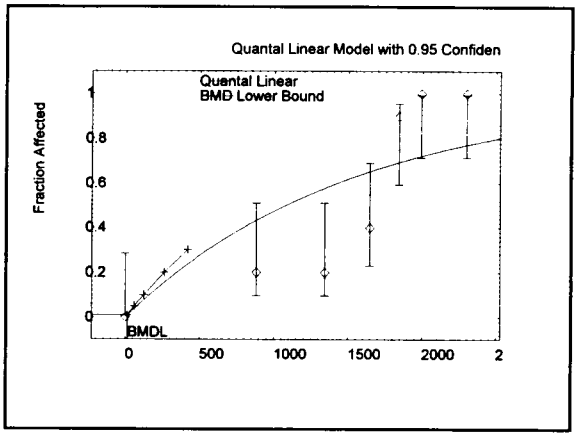
Model	p-value	MLE (ppm)	95% LCL (ppm)
Gamma	0.0816	1117	838
Logistic	0.0998	1045	728
Probit	0.1162	972	665
Log probit	0.667	1573	1337
Quantal linear	0.0031	164	124
Quantal quadratic	0.0499	510	441
Weibull	0.1443	1054	785

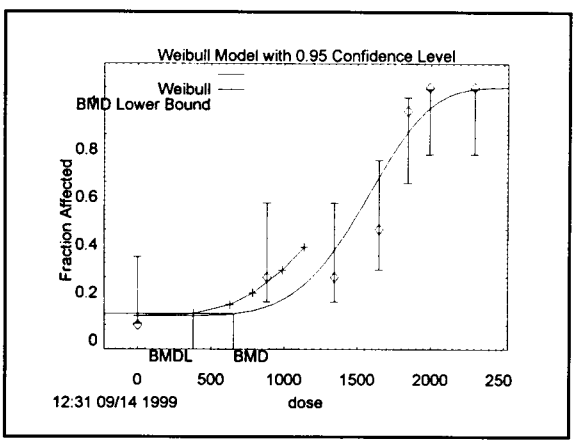












Benchmark Risk = 5%

Model	p-value	MLE (ppm)	95% LCL (ppm)
Gamma	0.0816	1013	680
Logistic	0.0998	884	521
Probit	0.1162	826	475
Log probit	0.667	1538	1271
Quantal linear	0.0031	80	60
Quantal quadratic	0.0499	356	308
Weibull	0.1443	911	629

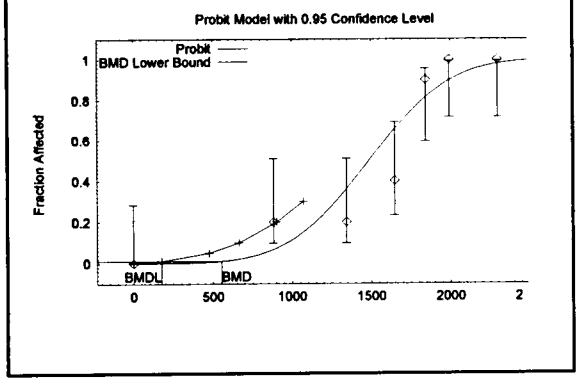
Benchmark Risk = 1%

Model	p-value	MLE (ppm)	95% LCL (ppm)
Gamma	0.0816	838	481
Logistic	0.0998	541	182
Probit	0.1162	554	175
Log probit	0.667	1474	1155
Quantal linear	0.0031	16	12
Quantal quadratic	0.0499	158	136
Weibull	0.1443	656	379

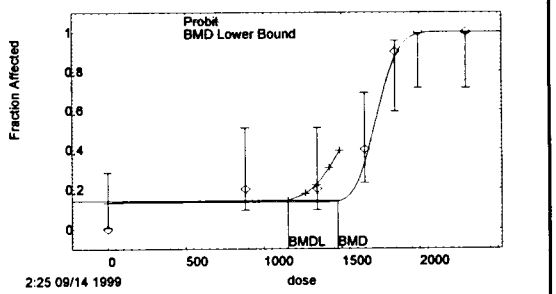
Benchmark Responses & Doses

	Log Probit		Probit	
Benchmark Response	MLE (ppm)	95% LCL (ppm)	MLE (ppm)	95% LCL (ppm)
1%	1474	1155	554	175
5%	1538	1271	826	475
10%	1573	1337	972	665

Probit, Benchmark Response = 1%



Log probit, Benchmark Response = 1%



Benchmark Results for Snellings et al., 1982a

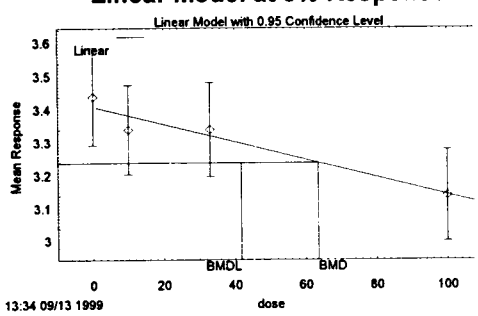
Model	Response	p-value	MLE (ppm)	95% LCL (ppm)
Linear	10%	0.6946	127	83
	5%		64	42
	1%		13	8
Polynomial	10%	0.3932	127	56
	5%		64	21
	1%		13	4

Snellings et al., 1982a

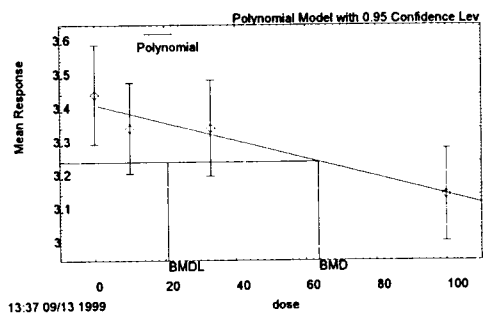
Concentration (ppm)	# Dams	Mean Wt Males (g)	Std. Dev.
0	19	3.4	0.4
10	22	3.3	.03
33	20	3.3	0.3
100	21	3.1	0.2

She did not separate developmental data by litter. All pups were averaged

Snellings et al, 1982a Linear Model at 5% Response



Snellings et al, 1982a Polynomial Model at 5% Response



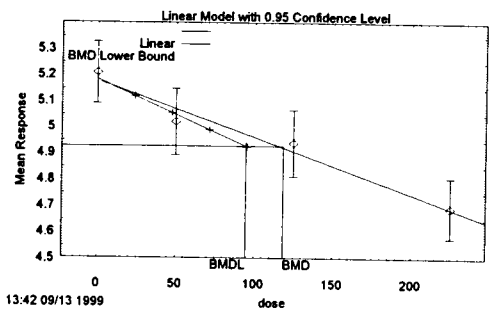
BRCC, 1993

Concentration (ppm)	# Dams	Mean Wt (g)	Std. Dev.
0	23	5.161	0.248
50	20	4.972	0.2766
125	20	4.891	0.2745
225	24	4.644	0.2899

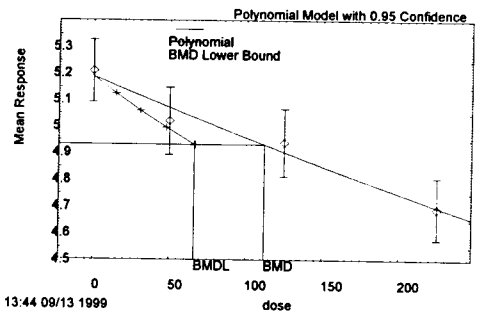
Benchmark Results for BRCC, 1993

Model	Response	p-value	MLE (ppm)	95% LCL (ppm)
Linear	10%	0.3231	237	189
	5%		118	95
	1%		24	19
Polynomial	10%	0.1361	238	173
	5%		112	66
	1%		22	12
Power	10%	0.1572	236	174
	5%		101	40
	1%		14	0.6

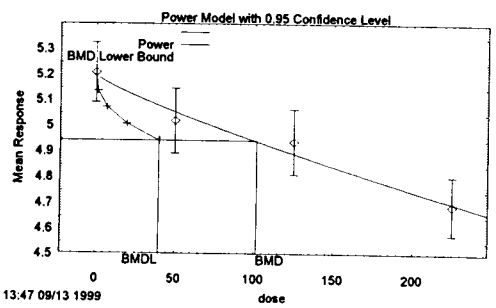
BRRC, 1993
Linear Model at 5%Response



BRRC, 1993
Polynomial Model at 5%Response



BRRC, 1993
Power Model at 5%Response



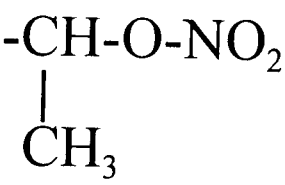
ACUTE EXPOSURE GUIDELINE LEVELS (AEGLs)

FOR

OTTO FUEL II

(Cas No. 106602-80-6)

(Propylene Glycol Dinitrate; CAS No. 6423-43-4)



ORNL Staff Scientist: Sylvia Talmage
Chemical Manager: William Bress
Chemical Reviewers: Robert Snyder, William Pepelko, Kenneth Still
NAC 15 Meeting, September 14, 1999

Attachment 9

Otto Fuel II

Introduction:

Three components:

1,2-propylene glycol dinitrate (PGDN, 75%) - explosive
dibutyl sebacate (23%) - desensitizer
2-nitrodiphenylamine (2%) - stabilizer

Only PGDN volatilizes at temperatures up to 45 °C
Dibutyl sebacate and 2-nitrodiphenylamine are of low acute oral toxicity
Therefore, the derived values pertain to both Otto Fuel II and PGDN

Human Studies

Occupational Exposures of U.S. Navy personnel

Complaints of headaches, nasal congestion, eye irritation, dizziness, etc.

No ataxia, headaches, nasal congestion during 29 torpedo maintenance procedures
Subclinical change (decrease) in eye movement velocity (516.6 vs 479.3 msec)
~400 grab samples: concentrations of 0.00-0.22 ppm
Exposure duration: 30-60 minutes
(Horvath et al., 1981)

No deaths or cardiac arrhythmias, but increased incidences of myocardial infarction and angina pectoris over 10-year period
(Forman et al., 1987)

No spontaneous abortions (limited number of personnel)
(NHRC, 1986)

Human Experimental Study (Stewart et al., 1974)

Total of 20 participants
Exposures 0.0-1.5 ppm for 1 to 8 hours

HUMAN RESPONSE TO PROPYLENE GLYCOL DINITRATE[a]							
	0.0 ppm 1-8 hr	0.03 ppm 1 hr 4 hr 8 hr	0.1 ppm 1 hr 4 hr 6 hr	0.21-0.26 ppm 1 hr 2 hr 8 hr	0.33-0.37 ppm 1 hr 2 hr 8 hr	0.5 ppm 1 hr 2 hr 7.3 hr	1.5 ppm 1 hr 3.2 hr
Number of subjects	17	2 3 3	2 3 3	3 3 12	3 3 3	3 3 3	2 6
Number detecting odor	0	0 0 0	0 0 0	2 3 2	1 2 2	1 1 2	2 6
Number developing mild headache	1	0 1[b] 0	0 1[b] 1*	0 2 5	0 3 1	1* 2 0	0 0
Number developing severe headache	0	0 0 0	0 0 0	0 0 6	0 0 2	0 1 ** 3	2 6
Number developing eye irritation	0	0 0 0	0 0 0	0 0 1	0 1 0	0 0 0	2 6
Number with changed VER	0	0 0 0	0 0 0	0 0 0	0 ? 3	3 3 3	2 6
Number with abnormal Romberg	0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 ** 3	- -

[a]Modified from Stewart et al. (1974).
[b]This individual developed a mild headache during each of the control exposures.
* Basis for AEGL-1.
** Basis for AEGL-2 (exposure duration of 6 hours).

Effects in humans (Stewart et al., 1974)

Headache

- Nitrate and nitrite esters are vasodilators
- Vasodilatation of dural arteries ➜ headache
- Action due to nitric oxide (NO)
- Same action as nitroglycerin used to treat angina

Central nervous system effects

- Disruption of the VER (subclinical)
- Disequilibrium
- No changes in cognitive functions

Effects: Concentrations and Exposure Durations

No headache	Mild headaches	Severe headaches
0.03 ppm for 8 hours	0.1 ppm after 6 hours	0.2 ppm for 8 hours
0.1 ppm for 3-4 hours	0.2 ppm (0.21-0.26) for 2 hours	0.3 ppm for 8 hours
0.2 ppm for 1 hour	0.35 ppm for ≥2 hours	0.5 ppm for 2 hours
0.35 ppm for 1 hour	0.5 ppm for 1.25 hours	1.5 ppm for 1 hour

Time Scaling

Based on k values of ~0.5 for mild headaches and ~1.6 for severe headaches, the value of n in the concentration-exposure duration relationship ($c^n \times t = k$) is 1.

Derivation of AEGL-1 and AEGL-2

The AEGL-1 values are based on the threshold for mild headaches: 0.1 ppm for 6 hours and 0.5 ppm for 1 hour.

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

Uncertainty factors:

Susceptible subpopulations: none identified

The elderly or those with cardiac problems (e.g., angina) are not necessarily more susceptible to vasodilators as vasodilators are used to treat the symptoms of coronary insufficiency. However, those individuals on vasodilators could receive an extra dose if exposed during an accidental release.

Nitric oxide, responsible for the vasodilatation effect, is administered to premature infants to treat hypertension during the first days of life.

Blood nitrates were not increased during the exposures.

Therefore, an intraspecies uncertainty factor of 3 was chosen to cover the normal range of sensitivity (to induction of headaches) in the human population.

PROPOSED AEGL VALUES

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

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

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

Animal Studies

No deaths following single exposures of ≤8 hours

Monkeys:

- 70-100 ppm for 6 hours (Jones et al., 1972)
  - Convulsions, vomiting, pallor, cold extremities, semiconsciousness
- 10, 15, or 33 ppm for 90 days (Jones et al., 1972)
  - No toxic signs, normal weight gain
  - Some histological changes
- 2 ppm for 4 hours (Mattsson et al., 1981)
  - Some changes in VER
  - No change in cognitive behavior

Dogs, rats, guinea pigs:

- 10, 15, or 33 ppm for 90 days (Jones et al., 1972)
  - Methemoglobinemia (up to 23%); decreases in hemoglobin and hematocrit (dog)
  - Some histological changes

Rats:

- 199 ppm for 4 hours (Jones et al., 1972)
  - No toxic signs (methemoglobin level of 23.5%)

Derivation of AEGL-3

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

Interspecies uncertainty factor: 3

The monkey is an appropriate species for extrapolation to humans.

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

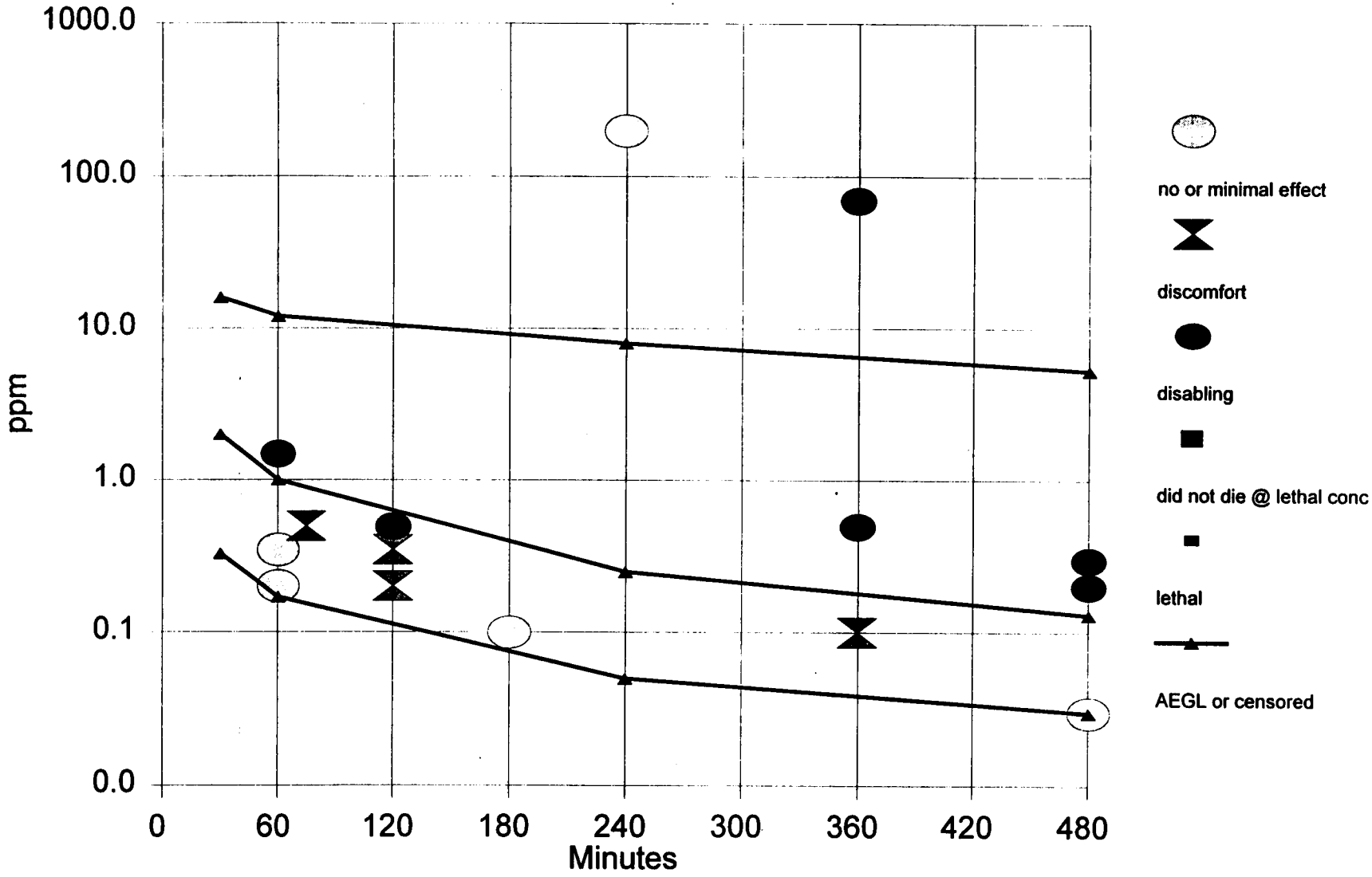
PGDN has some CNS depression properties; the threshold for CNS depression (for anesthetics) does not differ widely among species or individuals.

Intraspecies uncertainty factor: 3

The 6-hour 70 ppm concentration was divided by a total uncertainty factor of 10 and scaled across time using n = 1 for the 8-hour value and n = 3 for the 30 minute and 1- and 4-hour values.

Chemical Toxicity - TSD All Data

OTTO FUELS II



Definitions

Saccades: synchronized eye tracking movements.

Visual evoked response (VER): complex waveform representing the summed electrical activity of many neurons in response to a flash of light; measured over the visual cortex of the brain.

Romberg test: a 1-minute test of postural stability; feet together and parallel and eyes closed.

Modified Romberg tests may include a wider stance, crossing of arms, and/or feet placed heel to toe.

Failure to maintain an upright posture with eyes closed indicates a dorsal column lesion whereby proprioception is lost. The positive Romberg test does not indicate vestibular or cerebellar disease.

Heel to toe test: a test of postural stability with one foot placed in front of the other.

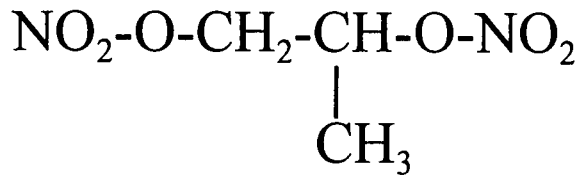
ACUTE EXPOSURE GUIDELINE LEVELS (AEGLs)

FOR

OTTO FUEL II

(Cas No. 106602-80-6)

(Propylene Glycol Dinitrate; CAS No. 6423-43-4)



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Therefore, the derived values pertain to both Otto Fuel II and PGDN

Appendix A

National Advisory Committee (NAC)
for Acute Exposure Guideline Levels (AEGLs) for Hazardous Substances
Final Meeting 14 Highlights
The Old Post Office, Rm. M-09
1100 Pennsylvania Avenue
Washington, D.C.
June 14-16, 1999

INTRODUCTION

George Rusch (NAC Chairman) opened the meeting and welcomed all participants. The meeting agenda (Attachment 1) and participants (Attachment 2) are attached. The NAC/AEGL Meeting 13 highlights (Appendix A) were reviewed and approved unanimously as is (Appendix B) based on the motion made by Bob Benson, seconded by Dave Belluck.

STATUS REPORTS AND GENERAL INTEREST ITEMS

29th OECD Meeting Overview

Roger Garrett provided an overview of the OECD meeting held June 7-11, 1999, in Paris, France. Ten OECD countries (technical representatives), four international organizations, and one OECD secretariat were represented at the meeting. Roger Garrett explained that the meeting provided a good platform for a collective effort (both national and international) to improve the scope of support for the AEGL program. The Standing Operating Procedures (SOPs) and five interim status chemicals (aniline, arsine, chlorine, fluorine, and hydrazine) from the National Advisory Committee on Acute Exposure Guidelines Levels (NAC/AEGL) were presented at the OECD meeting. The two primary issues were: (1) to evaluate and reach a consensus on the scientific approach for developing AEGLs, and (2) to seek participation and resource support for the AEGL program. The AEGL program and its methodologies were favorably received and appreciated, and the participants were impressed with the "transparency" (openness) of the methodologies and rationales presented in the SOP, Technical Support Documents (TSDs), and Summary Tables. Questions arose regarding some aspects of the SOP although no consensus was achieved on these issues. These focused primarily on uncertainty factors (magnitude and justification), carcinogenicity, dosimetry, time scaling, and resource support for the AEGL program. George Rusch stated that there was a difference of opinion in the overall philosophy in application of uncertainty factors. For example, the National Academy of Sciences Committee on Toxicology (NAS/COT) has expressed some concern that the uncertainty factors may be to small while some OECD members said they are inappropriate and should not be used at all.

The need and usefulness of an international effort to develop AEGLs was recognized. The fact that chemical spills and emergencies do not recognize political borders necessitates the need for an international, universal approach to responding to such emergencies. Fritz Kalberlah said industry representatives at the OECD meeting were also supportive of the AEGL process and the need for international involvement. Roger Garrett stated that in such an environment, the AEGLs may be utilized in different ways by different countries and their application adjusted under different umbrellas of risk management.

National Academy of Sciences/Committee on Toxicology (NAS/COT)
The status of deliberations by the NAS/COT Subcommittee on AEGLs were discussed by Roger Garrett. The NAS/COT has been reviewing the SOPs and 10 interim-status AEGLs. Additionally, they have also been presented with 10 additional AEGL TSDs to provide a broader perspective of the NAC/AEGL work. An Interim Letter Report (Attachment 3) from the NAS/COT was distributed that provided information regarding their review of the SOP and the AEGL Interim values/TSDs (Attachment 4). Roger Garrett focused on the major issues of incomplete sections in the SOPs, uncertainty factor application/justification, time scaling, use of a NOEL, AEGL-1 issues (specifically, where AEGL-1 values were not developed) and cancer risk. A written response to NAS/COT concerns is planned.

Incomplete sections of the SOPs
Incomplete sections of the SOPs (carcinogenicity, hypersusceptible populations, clarification of precision of values, dosimetry adjustments, and alternate methodologies) will be expanded/revised as required and resubmitted to the NAS/COT in a timely fashion to the next NAS/COT meeting.

Time scaling
The NAS/COT suggested that when empirically derived values of n for the equation, $C^n \times t = k$, are unavailable, the AEGL values should be derived using an $n = 3$ when scaling from longer time periods to shorter periods and an $n = 1$ when scaling from shorter time periods to longer periods. This practice would encompass a greater range of possible concentration-time relationships and provide somewhat lower AEGL values than would be attained using a default of $n = 2$. It was the general consensus of the NAC/AEGL that this approach be adopted (Appendix C).

Dosimetry issues
Although the NAS/COT originally indicated some concern regarding the lack of dosimetric adjustment in the development of AEGLs, it was the consensus of the NAC/AEGL that dosimetry adjustments will not be routinely performed because the existing EPA dosimetry models for gases and vapors have not been validated. Consistent with NAS/COT recommendations, an attempt at dosimetry adjustment will be considered for particulate matter. The SOP will be amended to include brief discussion of methodologies such as particulate matter dosimetry and minute-volume scaling factors.

AEGL-1 issues
The NAS/COT expressed concern regarding the absence of AEGL-1 values for some chemicals. The NAC/AEGL will attempt to set AEGL-1 values where possible. However, for some chemicals the AEGL-l level simply may not be feasible or appropriate and would be of limited use and validity for the emergency planner.

Carcinogenicity
There was extensive discussion regarding the issue of how carcinogenic potential will factor into the development of AEGLs. This topic was discussed in-depth following Dr. Edward Calabrese's presentation/discussion of his single-exposure carcinogen database and is presented under the General Interest Items.

Uncertainty factors
For some uncertainty factors, more definitive justification is required. For example, an uncertainty factor of 3 for intraspecific variability for chemical irritants should not be routinely used with a justification of "mechanism of action is similar and unlikely to vary among individuals." Attention must also be given to

consistency of uncertainty factor application and justification. In many cases, the uncertainty factor issues are chemical-specific. A suggestion was made by George Alexeeff that the NAC/AEGL may, depending on availability of resources, want to investigate variability in responses to chemical irritants.

Alternate methodologies

A discussion of alternate methodologies (e.g., benchmark dose, categorical regression) will be added to the SOP as suggested by the NAS/COT. Collaborative efforts are currently underway with EPA/RTP regarding categorical regression. Where appropriate, these methodologies may be applied to the development of AEGLs.

Interim Chemical Status Reports

Chemical-specific comments from the NAS/COT were briefly discussed by Robert Young and Cheryl Bast. For most of the chemicals, aniline (Attachment 5), arsine (Attachment 6), chlorine (Attachment 7), hydrazine (Attachment 8), dimethylhydrazine (Attachment 9), and methyl hydrazine (Attachment 10), the discussions focused on the effect of calculating AEGL values using a time-scaling factor (n) of 1 or 3 rather than a default of 2 (see above discussion) or the fact that more extensive justification of uncertainty factors was required. Where applicable, tables were presented showing the effect of this adjustment. For 1,2-dichloroethene (Attachment 11), additional data (from a GLP industry study report) has become available necessitating revisit of the current AEGLs. James Barter (PPG) expressed concerns regarding the differential toxicity of the 1,2-dichloroethene isomers and that this may be a moot issue because little or none (<0.5%) of the *cis* isomer is used. Additional deliberations on this chemical was tabled until the new data become available. For phosphine (Attachment 12), NAS/COT concerns will be addressed (i.e., absence of AEGL-1, justification of rationale for previously approved AEGLs) and considered at the next NAC/AEGL meeting. The TSDs and summary tables for these chemicals will be revised accordingly.

General Interest Items

- Hypersusceptible/Hypersensitive Individuals

George Rodgers provided information in response to the NAS/COT request for a more definitive and thorough delineation of a hypersusceptible subpopulation as it pertains to the AEGL process. He noted that the hypersusceptible subpopulation may be defined as that which exhibits an idiosyncratic response or a response that lies outside of or is discontinuous with the range of normal responders. He provided information from the field of anesthesiology to demonstrate the effects of age on anesthetic gas effects. It is likely that the issue hypersusceptiblity may most often be a chemical-specific issue. The hypersusceptible individual may be impossible to identify and, therefore, difficult to protect. It has been estimated that in a chemical accident scenario involving perhaps 1,000-2,500 individuals, the hypersusceptible subpopulation may only encompass one or two individuals.

- Single-exposure carcinogen database

Edward Calabrese presented an overview of his Single Exposure Carcinogen Database (Attachment 13). Following an explanation of the need for such a database, the terms used in the database were defined and the procedure for identifying and extracting data elements for inclusion in the database were explained. The database contains approximately 5500 studies involving 800 chemicals. Positive responses were reported predominately via the oral, injection, and dermal routes by genotoxic carcinogens. Positive reports were reported following single exposures for a wide variety of chemicals on a broad range of species and strains. He will provide some search results to George Rusch on irritant chemicals requested by the NAC/AEGL.

• Acute exposure carcinogenicity issue

There was extensive discussion in response to the NAS/COT concerns regarding the use of cancer risk in the development of AEGLs. The NAS/COT indicated that a consensus on this issue by the NAC/AEGL was needed and that also should be incorporated into the SOP document. Additionally, chemical-specific cancer issues would need to be incorporated into the TSDs. Roger Garrett presented a synopsis of the scientific status of acute exposure cancer response issues. Following extensive discussion it was the consensus of the NAC/AEGL that a cancer notation be included in the Executive Summary AEGL table. The notation would include carcinogenic potential regardless of route and whether or not the risk is quantifiable. This notation would be especially relevant for those chemicals for which a cancer risk (determined by the method described by the NAS) comes within range of the AEGL values determined using noncancer endpoints. The Appendix currently included in TSDs on chemicals with quantifiable carcinogenicity data will be retained and will include 10^{-4}, 10^{-5}, and 10^{-6} risk levels. A discussion regarding the cancer risk and its relevance will be included in this Appendix, the Executive Summary, and text body of the TSD where appropriate. A motion to accept this position was made by Ernest Falke and seconded by Richard Niemeier (Appendix D). The motion passed unanimously. These issues will be included in the SOP.

AEGL PRIORITY CHEMICALS

Hydrogen sulfide, CAS No. 7783-06-4

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

Cheryl Bast reviewed the previous NAC/AEGL deliberations on hydrogen sulfide (Attachment 14) explaining that the AEGL-1 was currently based on threshold for annoyance. Cheryl Bast presented exposure values provided by Zarena Post (unable to attend) that were obtained near an oil refinery. The described exposure was of approximately 0.5-8 hours duration and involved low levels of additional chemicals (sulfur dioxide, toluene, benzene, methyl-tert-butyl ether). The issue of discussion focused on whether or not to set AEGL-1 levels 5 times greater than the odor threshold or to set levels that are below ambient air levels (i.e., odor threshold). The issue will be revisited at the next meeting.

Perchloromethyl mercaptan, CAS No. 594-42-3

Chemical Manager: Zarena Post, Texas NRCC
Author: Claudia Troxel, ORNL

Claudia Troxel presented a summary of the limited available data on perchloromethyl mercaptan and also described the basis and rationale for the draft AEGL values (Attachment 15) (Loren Koller substituted for Zarena Post). AEGL values were presented using the traditionally applied default *n* of 2 for time scaling as well as the NAS/COT-suggested *n* values of 1 and 3. Comments to the chemical manager from those NAC members who responded to the previously circulated TSD suggested reduction of the total uncertainty factor from 100 to 30. Initially, concern was expressed regarding the validity of an AEGL-1 and several options were considered: (1) no value, (2) use odor threshold as presented in draft TSD, and (3) use subacute study and uncertainty factors. AEGL-1 values were based on the threshold for irritation of 0.079 ppm from a 13-week exposure. The resulting 30-min., 1-hr, 4-hr, and 8-hr AEGL-1 values were 0.018, 0.014, 0.009, and 0.006 ppm, respectively, and incorporated a total uncertainty factor of 10 (a long-term study was utilized to derive values for a short-term effect). The motion for these AEGL-1 values was provided by Bob Snyder

and seconded by John Hinz. The motion passed [YES: 18; NO: 7; ABSTAIN: 0] (Appendix E). Following extensive discussion, it was the consensus of the NAC/AEGL to base the AEGL-2 on minimal reversible effects in rats following repeated exposures to 0.58 ppm. The resulting 30-min., 1-hr, 4-hr, and 8-hr AEGL-2 values were 0.044, 0.035, 0.022, 0.014 ppm and incorporated a total uncertainty factor of 30 (10 for interspecies variability due to data limitations and a steep dose-response curve and 3 for intraspecies variability in response to an irritant). A motion by Bob Benson (seconded by Ernest Falke) to accept these values passed [YES: 20; NO: 6; ABSTAIN: 0] (Appendix E). AEGL-3 also involved extensive deliberations regarding the exposure-response determinant for the value and uncertainty factor application. A motion (made by Ernie Falke and seconded by Bob Benson) to accept the values of 0.38, 0.30, 0.075, and 0.038 ppm for the 30-min, 1 hr, 4 hr, and 8 hr AEGL-3, respectively, passed [YES: 21; NO: 4; ABSTAIN: 0] (Appendix E). These values were based on a nonlethal response of rats to 9 ppm and reflect a total uncertainty factor application of 30 (10 for interspecies and 3 for intraspecies).

SUMMARY OF REVISED AEGL VALUES (ppm) FOR PERCHLOROMETHYL MERCAPTAN					
Classification	**30-min**	**1-hr**	**4-hr**	**8-hr**	**Endpoint**
AEGL-1	0.018	0.014	0.009	0.006	threshold for irritation in rats from a 13-week study
AEGL-2	0.044	0.035	0.022	0.014	minimal reversible effects in rats following subchronic exposure to 0.58 ppm
AEGL-3	0.38	0.30	0.075	0.038	no effect level (9 ppm)for mortality in rats

Toluene, CAS No. 108-88-3

Chemical Manager: Larry Gephart, Exxon Biomedical Sciences, Inc.
Author: Tessa Long, ORNL

Larry Gephart provided an introduction (Attachment 16) and Tessa Long presented an overview of the extensive toluene database (Attachment 17). After discussion, the committee decided to base AEGL-1 values on eye and nose irritation and headache in humans exposed to 100 ppm for 6 hours. The resulting 30-min, 1-hr, 4-hr, and 8-hr AEGL-1 values were 120, 82, 41, and 29 ppm and incorporated a total uncertainty factor of 3 for intraspecies extrapolation. A motion by Loren Koller (seconded by David Belluck) to accept these values passed [YES: 20; NO: 1; ABSTAIN: 1] (Appendix F). The committee decided to base AEGL-2 values on confusion, uncoordination, nausea, and muscular weakness in humans exposed to 200 ppm for 8 hours. The resulting 30-min, 1-hr, 4-hr, and 8-hr AEGL-2 values were 270, 190, 94, and 67 ppm and incorporated a total uncertainty factor of 3 for intraspecies extrapolation. A motion was made by Loren Koller (seconded by David Belluck) to accept these values passed [YES: 21; NO: 1; ABSTAIN: 0] (Appendix F). The committee then decided to base AEGL-3 values on a 1-hour NOEL for death in mice of 6339 ppm. The resulting 30-min, 1-hr, 4-hr, and 8-hr AEGL-3 values were 900, 630, 320, and 220 ppm and incorporated a total uncertainty factor of 10 (3 for intraspecies and 3 for interspecies extrapolation). A motion by Loren Koller (seconded by Kyle Blackman) to unanimously accept these values (Appendix F).

SUMMARY OF PROPOSED AEGL VALUES (ppm) FOR TOLUENE					
Classification	**30-min**	**1-hr**	**4-hr**	**8-hr**	**Endpoint**

AEGL-1	120	82	41	29	eye and nose irritation and headache in humans
AEGL-2	270	190	94	67	confusion, nausea, muscular weakness, uncoordination in humans
AEGL-3	900	630	320	220	NOEL for death in mice

Tetrachloroethylene, CAS No. 127-18-4

Chemical Manager: William Bress, Vermont Dept. Health
Author: Claudia Troxel, ORNL

Claudia Troxel presented a review of the data available for tetrachloroethylene (Attachment 18). The committee discussed the validity of the value of the exponent n=2 obtained from the ten Berge reference, and decided to assume the value was correct. Ernie Falke will attempt to verify this value; if the value cannot be verified, the chemical will be brought back to the committee. After deliberation, the committee (remaining cognizant of CNS effects observed in humans exposed to 50 ppm for 4 hr) decided to base AEGL-1 values on irritation in humans exposed to 106 ppm for 1 hr. The resulting 30-min, 1-hr, 4-hr, and 8-hr AEGL-1 values were 50, 35, 18, and 12 ppm and incorporated a total uncertainty factor of 3 for intraspecies extrapolation. A motion by Steve Barbee (seconded by Richard Niemeier) to accept these values passed [YES: 21; NO: 2; ABSTAIN: 0] (Appendix G). The committee decided to base AEGL-2 values on a NOEL for ataxia in rats exposed to 1150 ppm for 4 hr. The resulting 30-min, 1-hr, 4-hr, and 8-hr AEGL-2 values were 330, 230, 120, and 81 ppm and incorporated a total uncertainty factor of 10 (3 for intraspecies and 3 for interspecies extrapolation). A motion by Bob Benson (seconded by Richard Niemeier) to accept these values passed [YES: 21; NO: 1; ABSTAIN: 0] (Appendix G). The committee decided to base AEGL-3 values on an estimated NOEL for death in mice and rats (highest concentration with no lethality). The resulting 30-min, 1-hr, 4-hr, and 8-hr AEGL-3 values were 690, 490, 240, and 170 ppm and incorporated a total uncertainty factor of 10 (3 for intraspecies and 3 for interspecies extrapolation). A motion was made by Tom Hornshaw (seconded by Steve Barbee). The committee unanimously accepted these values (Appendix G).

SUMMARY OF PROPOSED AEGL VALUES (ppm) FOR TETRACHLOROETHYLENE					
Classification	**30-min**	**1-hr**	**4-hr**	**8-hr**	**Endpoint**
AEGL-1	50	35	18	12	Irritation in humans
AEGL-2	330	230	120	81	NOEL for ataxia in rats
AEGL-3	690	490	240	170	Estimated NOEL for death (highest concentration with no lethality)

ADMINISTRATIVE ISSUES

Future meetings

The following meeting dates and locations have been proposed:

September 14-16, 1999 (Washington, D.C.)
December 6-8, 1999 (Washington, D.C.)
March 16-17, 2000 (Philadelphia or Rutgers University) (prior to SOT)

These highlights are submitted by Robert Young and Po-Yung Lu, ORNL.

LIST OF ATTACHMENTS

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

1. NAC/AEGL Meeting No. 14 Agenda
2. NAC/AEGL Meeting No. 14 Attendee List
3. Interim Letter Report of NAS/COT/AEGL
4. Summary of Chemical Specific Comments by NAS/COT/AEGL
5. Chemical Specific Comment Responses to NAS/COT/AEGL - Aniline
6. Chemical Specific Comment Responses to NAS/COT/AEGL - Arsine
7. Chemical Specific Comment Responses to NAS/COT/AEGL - Chlorine
8. Chemical Specific Comment Responses to NAS/COT/AEGL - Hydrazine
9. Chemical Specific Comment Responses to NAS/COT/AEGL - Dimethylhydrazine
10. Chemical Specific Comment Responses to NAS/COT/AEGL - Methylhydrzine
11. Chemical Specific Comment Responses to NAS/COT/AEGL - 1,2-Dichloroethene
12. Chemical Specific Comment Responses to NAS/COT/AEGL - Phosphine
13. The Single Exposure Carcinogen Database: Assessing the Circumstances During Which a Single Exposure to a Carcinogen Can Cancer - Edward Calabrese
14. Data Analysis of Hydrogen Sulfide - Cheryl Bast
15. Data Analysis of Perchloromethyl mercaptan - Claudia Troxel
16. Overview of Toluene - Larry Gephart
17. Data Analysis of Toluene - Tessa Long
18. Data Analysis of Tetrachloroethylene - Claudia Troxel

LIST OF APPENDICES

A. Approved NAC-AEGL-13 Meeting Highlights
B. Ballot for Minutes approval
C Ballot for approval on time scaling extrapolation
D. Ballot for approval on how to handle “carcinogenicity” issues in TSD
E. Ballot for Perchloromethyl mercaptan
F. Ballot for Toluene
G. Ballot for Tetrachloroethylene

NAC/AEGL Meeting: 9/14-16/99 Chemical: MINUTES FOR 6/14-16/99 MTG.

NAC Member	AEGL 1	AEGL 2	AEGL 3	NAC Member	AEGL 1	AEGL 2	AEGL3
George Alexeeff				Loren Koller			
Steven Barbee				Glenn Leach			
Lynn Beasley				Mark A. McClanahan			
David Belluck				John S. Morawetz			
Robert Benson				Deirdre L. Murphy (absent)			
Kyle Blackman				Richard W. Niemeier			
Jonathan Borak				William Pepelko			
William Bress				Zarena Post			
				George Rodgers			
George Cushmac				George Rusch, Chair			
Ernest Falke				Michelle Schaper			
Larry Gephart				Bob Snyder			
John Hinz				Thomas Sobotka			
Jim Holler				Kenneth Still			
Thomas C. Hornshaw				Patricia Ann Talcott			
Nancy Kim				Richard Thomas			
				Thomas Tuccinardi/ Doan Hansen			
				TALLY			

Appendix B

Accepted unanimous

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

~~AEGL 1~~ Motion: Mark McClanahan Second: John Hinz

AEGL 2 Motion: _____ Second: _____

AEGL 3 Motion: _____ Second: _____

Approved by Chair: _____ DFO: Paul S. Tobin Date: 9/14/99

Appendix C

NAC/AEGL Meeting: 9/14-16/99 **Chemical:** HYDROGEN SULFIDE

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

NAC Member	AEGL 1	AEGL 2	AEGL3
Loren Koller	Y		
Glenn Leach	Y		
Mark A. McClanahan	N		
John S. Morawetz	Y		
Deirdre L. Murphy (absent)	~~A~~		
Richard W. Niemeier	Y		
William Pepelko	Y		
Zarena Post	Y		
George Rodgers	Y		
George Rusch, Chair	Y		
Michelle Schaper	A		
Bob Snyder	Y		
Thomas Sobotka	A		
Kenneth Still	Y		
Patricia Ann Talcott	~~A~~		
Richard Thomas	A		
Thomas Tuccinardi/ Doan Hansen	A N		
TALLY	20/22		

PPM, (mg/m³)	10min 30 Min	60 Min	4 Hr	8Hr
AEGL 1	0.03 0.03 ( )	0.03 , ( )	0.03 , ( )	0.03 , ( )
AEGL 2	, ( )	, ( )	, ( )	, ( )
AEGL 3	, ( )	, ( )	, ( )	, ( )

AEGL 1 Motion: Falke **Second:** Niemeier

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

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

Approved by Chair: [signature] **DFO:** Paul S. Tobin **Date:** 9/15/99

106602-80-6 **Appendix D**

NAC/AEGL Meeting: 9/14-16/99 **Chemical:** OTTO FUEL (PROPYLENE GLYCOL DINITRATE; 6423-43-4

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

NAC Member	AEGL 1	AEGL 2	AEGL3
Loren Koller	A	A	A
Glenn Leach	A	A	A
Mark A. McClanahan	A	A	A
John S. Morawetz	Y	Y	
~~Deirdre L. Murphy~~ (absent)	A	A	A
Richard W. Niemeier	Y	Y	
William Pepelko	A	A	A
Zarena Post	Y	Y	
George Rodgers	Y	Y	
George Rusch, Chair	Y	Y	
Michelle Schaper	A	A	A
Bob Snyder	A	A	A
Thomas Sobotka	A	A	A
Kenneth Still	Y	Y	
~~Patricia Ann Talcott~~			
Richard Thomas	A	A	A
~~Thomas Tuccinardi~~/ Doan Hansen	A / Y	A / Y	A
TALLY	16/16	16/16	

PPM, (mg/m^3)	30 Min	60 Min	4 Hr	8Hr
AEGL 1	0.33 ,( )	0.17 ,( )	0.05 ,( )	0.03 ,( )
AEGL 2	2.0 ,( )	1.0 ,( )	0.25 ,( )	0.13 ,( )
AEGL 3	,( )	,( )	,( )	,( )

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

AEGL 2 Motion: Rodgers **Second:** Hinz

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

Approved by Chair: _____ **DFO:** Paul S. Tobin **Date:** 9/15/99