THE UNIVERSITY OF NORTH CAROLINA
AT
CHAPEL HILL

Occupational Health Studies Program
Department of Epidemiology
School of Public Health
(919) 966-4181

The University of North Carolina at Chapel Hill
NCNB Plaza, Suite 32 322A
Chapel Hill, N.C. 27514

January 27, 1987

R. Paul Wilms, Director
Division of Environmental Management
Department of Natural Resources and
Community Development
State of North Carolina
512 North Salisbury Street
Raleigh, NC 27611

Dear Mr. Wilms,

In your letter of March 21, 1986, to Jonathan Howes, Chairman of the Affairs and Policy Committee, N. C. Academy of Sciences, you requested the Academy "to conduct an evaluation of toxic air pollutants and acceptable ambient levels slated for regulation by the state". As Chairman of the Academy's Air Toxic Panel, I am pleased to submit to you the Panel's Report and Recommendations and the recommended acceptable ambient levels for the chemicals submitted to the Academy for review.

The Panel has applied the guidelines contained in its Report and Recommendations to each of the chemicals on the list submitted for review. We have developed recommendations for each chemical, with the exception of nine non-carcinogenic compounds. Recommendations for these nine chemicals, identified on the list with an asterisk, are being deferred for further evaluation and review by an ad hoc or standing advisory committee to be subsequently appointed; the evidence for toxicity of these nine chemicals require more intensive evaluation than the Air Toxics Panel could provide within the limitations of our resources. In addition, for the 57 carcinogenic chemicals on the list, the Panel could only go so far as to identify whether the chemical fell into EPA's carcinogen classification scheme as a Group A carcinogen (human carcinogen) or a Group B carcinogen (probable human carcinogen). The Panel's recommended guidelines were then applied to these carcinogens to compute the air concentration at which an additional cancer risk of 1 in 1 million exposed persons would be incurred by ambient exposure to Group A carcinogens or a risk of 1 in 100,000 exposed persons for exposure to Group B Carcinogens. However the Air Toxic Panel did not have the time or resources to review the unit risk estimates upon which these guidelines are based. We therefore recommend that the ad hoc or standing advisory committee review these estimates prior to their use for regulatory purposes.

I would like to emphasize our Panel's recommendation on pages 26 and 27 of our report that a standing advisory committee on toxic air pollutants be appointed to deal with deferred, unresolved and recurrent issues related to the development or revision of AAL's for toxic air pollutants.

The Members of the Air Toxics Panel are pleased to have been of service to the State, and we trust that the product of our work will provide a sound scientific basis for your toxic air pollutant regulatory program.

Sincerely,

Carl M. Shy

Carl. M. Shy, M.D.
Chairman, Air Toxics Panel

CMS/vlm

Enclosures: Report and Recommended AAL's

cc: Jonathan Howes, N. C. Academy of Sciences
Dean, School of Public Health
Robert Harris, Chairman, Air Quality Committee
Environmental Management Commission

REPORT AND RECOMMENDATIONS
OF THE AIR TOXICS PANEL
OF THE NORTH CAROLINA ACADEMY OF SCIENCES

TO THE DIVISION OF ENVIRONMENTAL MANAGEMENT
NORTH CAROLINA DEPARTMENT OF NATURAL RESOURCES AND
COMMUNITY DEVELOPMENT

FINAL REPORT

SEPTEMBER, 1986

AIR TOXICS PANEL, N.C. ACADEMY OF SCIENCES

Carl M. Shy, M.D., Dr.P.H.
Panel Chairman
Professor of Epidemiology
School of Public Health, 201H
University of North Carolina
at Chapel Hill
Chapel Hill, N.C. 27514
966-4181

Richard N. Andrews, Ph.D.
Director
Institute for Environmental
Studies
311 Pittsboro Street, 256H
University of North Carolina
at Chapel Hill
Chapel Hill, N.C. 27514
966-2358

Philip A. Bromberg, M.D., Head
Division of Pulmonary Medicine
724 Clinical Sciences Bldg., 229H
University of North Carolina at
Chapel Hill
Chapel Hill, N.C. 27514
966-2531

Walter Dauterman, Ph.D.
Toxicology Program
North Carolina State University
P.O. Box 7333
Raleigh, N.C. 27695
737-2274

Harold Imbus, M.D.
Health & Hygiene, Inc.
4605 East Dundus Dr.
Greensboro, N.C. 27407
854-2303

John Mennear, Ph.D.
National Institute of
Environmental Health
Sciences
P.O. Box 12233
Research Triangle Park,
N.C. 27709
541-4178

James Popp, Ph.D., Head
Division of Experimental
Pathology & Toxicology
Chemical Industries
Institute of Toxicology
P.O. Box 12137
Research Triangle Park,
N.C. 27709
541-2070

Woodhall Stopford, M.D.,
M.S.P.H.
Occupational Medicine
Department of Community
and Family Medicine
P.O. Box 2914
Duke Medical Center
Durham, N.C. 27710
684-6677

Research Assistant to the Panel

Paige Tolbert, M.S.P.H
Doctoral Student
Department of Epidemiology
School of Public Health, 201H
University of North Carolina
at Chapel Hill
Chapel Hill, N.C. 27514

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While the members of the Air Toxics Panel of the North Carolina Academy of Sciences take full responsibility for the contents of this report, Panel members wish to acknowledge the excellent work of Paige Tolbert who functioned as the Panel's research assistant. As such, Ms. Tolbert researched and synthesized the literature referenced in the report, put into clear and precise English the deliberations and recommendations of the Panel, and throughout contributed substantially to the total effort. The Panel also wishes to cite the contribution of Mr. Joseph Padgett, officer of the U.S. Environmental Protection Agency, who served as an important source of information on EPA policy and on the procedures followed by other states in developing guidelines for toxic air pollutants. Reviewers of draft versions of this report were Drs. Michael Hogan and David Hoel of the National Institute of Environmental Health Sciences, Drs. Russell Christman and Alvis Turner of the Department of Environmental Sciences and Engineering, University of North Carolina, and Drs. Theodore Taylor and Charles G. Smith of the North Carolina Division of Health Services; their contributions are also gratefully acknowledged.

EXECUTIVE SUMMARY

At the request of the North Carolina Division of Environmental Management, an Air Toxics Panel was formed within the North Carolina Academy of Sciences to review the list of substances proposed for regulation as toxic air pollutants and to recommend a suitable approach for determining acceptable ambient levels for these pollutants. After reviewing the experience of nineteen states which had air toxics control programs in place, the Panel makes the following recommendations:

1. Develop air guidelines for those chemicals to which there is potential for exposures that may lead to adverse effects as a result of industrial emissions in North Carolina and which either (a) have been assigned a threshold limit value (TLV) by the American Conference of Governmental Industrial Hygienists or (b) are listed by the U.S. Environmental Protection Agency as carcinogens in the category of Group A (human carcinogens) or Group B (probable human carcinogens) or (c) are considered by the North Carolina Division of Health Services to be of public health concern. Criteria pollutants and biologically inert dusts are excluded from consideration; the latter can be considered as suspended particulate matter, already regulated as a criteria pollutant.
2. Potentially toxic chemicals chosen for the list of toxic air pollutants should be categorized by type of toxicity

based on adverse effects at near ambient levels. A category-specific approach is then proposed for deriving an acceptable ambient level. Four categories of toxicity are recommended: acute irritants, acute systemic toxicants, chronic toxicants, and carcinogens.

3. The Panel recommends a factored TLV approach to develop acceptable ambient levels for acute irritants, acute systemic toxicants and chronic toxicants. If no TLV exists for chemicals determined to pose a public health threat in North Carolina or if adverse health effects have not been accounted for in the derivation of the TLV, the Panel recommends using the no observed effect level (NOEL) reported in the toxicological literature. Under this system, the TLV or NOEL will be the starting point for applying a series of safety factors, depending on the category of toxicity into which the chemical falls. These adjustment and safety factors address the following concerns:

   (a) Adjustment for continuous exposure: use a 4-fold factor.

   (b) Variability in human susceptibility: use a 10-fold factor for all non-carcinogens.

   (c) Uncertainties inherent in studies of chronic effects: use a 2-fold factor for all chronic toxicants.

(d) Severity of effect: use a 2-fold factor for irreversible or life threatening effects.

For each chemical, the appropriate factors should be multiplied by each other to derive a composite factor. The composite factor should be applied to the TLV or NOEL to derive the acceptable ambient level for that chemical. Appendix E provides a decision tree to derive these acceptable ambient levels for any chemical classified as an acute irritant, acute systemic or chronic toxicant.

4. For carcinogens, the Panel recommends a combined technology-based and risk assessment approach. Using the potency estimates developed by the Carcinogen Assessment Group of the Environmental Protection Agency, the State should calculate the incremental air concentration (i.e., the concentration attributable to an emission source, regardless of background levels) that would be associated with an additional cancer risk of 1 in 1,000,000 exposed persons for Group A carcinogens and a risk of 1 in 100,000 exposed persons for Group B carcinogens. These concentrations constitute an action level. Any emission source releasing a carcinogen resulting in incremental ambient air concentrations exceeding the action level should be required to apply added control technology, but cost and feasibility issues should be considered for existing emission sources. A proposed Standing Advisory Committee on Toxic Air Pollutants may consider modifying the action level in cases

in which well designed human studies or data regarding mechanisms of action, pharmacokinetics or species differences appear not to have been taken into account by the Carcinogen Assessment Group in the estimate of carcinogenic potency. If the impact on ambient air is estimated still to exceed the action level after application of added control technology, the emission source should be given the option of applying to the State for a variance.

5. The Panel proposes the establishment of a Standing Advisory Committee on Toxic Air Pollutants to deal with recurrent or unresolved issues, to review the application of these recommended criteria to any chemical selected for inclusion in the list of toxic air pollutants, to consider any modifications in recommended action levels for carcinogens, to consider whether air guidelines should be modified when there are multiple emission sources in the same localized area, and to assist the State in reviewing variance requests.

TABLE OF CONTENTS

ABBREVIATIONS

AAL	- Acceptable Ambient Level
ACGIH	- American Conference of Governmental Industrial Hygienists
CAG	- EPA's Carcinogen Assessment Group
DEM	- North Carolina Division of Environmental Management
DHS	- North Carolina Division of Health Services
EPA	- U.S. Environmental Protection Agency
IARC	- International Agency for Research on Cancer
LOEL	- Lowest Observed Effect Level
NAS	- National Academy of Sciences
NATICH	- National Air Toxics Information Clearinghouse
NCAS	- North Carolina Academy of Sciences
NESHAP	- National Emission Standard for Hazardous Air Pollutants
NIOSH	- National Institute for Occupational Safety and Health
NIEHS	- National Institute of Environmental Health Sciences
NOEL	- No Observed Effect Level
NTP	- National Toxicology Program (NIEHS)
OSHA	- Occupational Safety and Health Administration
STAPPA/-ALAPCO	State and Territorial Air Pollution Program Administrators/Association of Local Air Pollution Control Officials
STEL	- Short-Term Exposure Limit
TLV	- Threshold Limit Value
TWA	- Time-Weighted Average

I. HISTORY AND CHARGE OF THE PANEL

As part of a three-phase study for the North Carolina Division of Environmental Management (DEM), Radian Corporation conducted a survey to define the nature and extent of toxic air pollution in North Carolina. The report, North Carolina Air Toxics Survey: Identification of Pollutant Emission Sources, published in April 1985, concluded that "the toxic air pollution problem in North Carolina is significant" [Radian, 1985]. The authors estimated that there are several thousand point sources which may be emitting pollutants at levels toxic to nearby residents. The report included a list of 67 toxic air pollutants of concern in North Carolina based upon probable emissions from industries identified within the state and the findings of other states developing air toxics programs.

The list of pollutants in the Radian report was subsequently reviewed by staff of the North Carolina Division of Health Services (DHS) and DEM to determine which chemicals should be targeted for regulatory action. Following additions and deletions, the final list was composed of 80 chemicals.

To develop acceptable ambient levels (AALs) for these chemicals, DHS and DEM proposed a factored Threshold Limit Value (TLV) approach. The following types of occupational guidelines established by the American Conference of Governmental Industrial Hygienists (ACGIH) were proposed as starting points in the derivation of AALs:

1) Threshold Limit Value - Time-Weighted Average (TLV-TWA) - the time-weighted average concentration for a normal 8-hour workday and a 40-hour workweek, to which the ACGIH has determined that nearly all workers may be repeatedly exposed, day after day, without adverse effect.

2) Threshold Limit Value - Short-Term Exposure Limit (TLV-STEL) - a 15-minute time-weighted average exposure which the ACGIH has determined should not be exceeded at any time during a work day. [ACGIH, 1985].

To account for differences between occupational exposure as addressed by the ACGIH and community exposure as addressed by the state's air toxics program, a factor of 1/200 was applied to TLV-TWAs (averaging time, 24 hours) and 1/10 to TLV-STELs (averaging time, 15 minutes) to derive the AALs for community exposure. In the case of chemicals for which the ACGIH had not developed a TLV, the state proposed to use as a starting point: 1) guidelines established by the National Institute of Occupational Safety and Health (NIOSH); 2) guidelines established by the Occupational Safety and Health Administration (OSHA); or finally, in the absence of federal guidelines, 3) the recommendation of DHS.

Industry representatives responded to the proposed program with several major objections:

1. The TLVs are being used out of context and are not applicable to the intended purpose.

2. The safety factor is, for the most part, judgmental and does not have a rigorous basis.
3. Research to establish existing background concentrations of the pollutants is necessary.
4. Extensive studies need to be conducted prior to setting any AALs.

In the wake of these objections, DEM decided to seek a peer group review of the state's air toxics proposal. DEM requested a review by an expert panel from the North Carolina Academy of Sciences, an independent, non-profit corporation established in 1902 to foster understanding of science in North Carolina and to promote scientific research and education in the state's academic institutions. (Letter requesting NCAS assistance attached, Appendix A).

The Air Toxics Panel of the N.C. Academy of Sciences was convened in April 1986. Its membership includes experts in pulmonary and occupational medicine, epidemiology, toxicology, and policy analysis. Specifically, the panel's charge was:

1) to review the list of air pollutants proposed for regulation and recommend additions or deletions,

and

2) to recommend a suitable approach for determining AALs.

The panel met bi-weekly from April through July, and the recommendations flowing from the panel's deliberations are presented in this report.

II. OTHER STATE PROGRAMS

A search of the database of the National Air Toxics Information Clearinghouse (NATICH) indicates that as of June 1986, nineteen states had air toxics control programs in place and 22 had programs under development [NATICH, 1986]. A summary of structural and policy aspects of the state programs is presented in Appendix B. The structural basis of these programs ranges from informal guidelines to formally promulgated regulations. Some programs address a specified list of pollutants while others address all chemicals meeting the state's definition of toxic air contaminants. Some apply only to new sources whereas others apply to both new and existing sources.

Regarding methodology for deriving AALs, 31 states rely wholly or in part upon a factored TLV approach, as DEM originally proposed for North Carolina. The factor applied to the TLV varies considerably from state to state, as does the averaging time. For the purpose of comparing safety factors used in conjunction with different averaging times, an "equivalent safety factor" can be derived using a system developed by the Commonwealth of Virginia. For instance, a factor used with a 1-hour averaging time is multiplied by 1/5 to derive the "equivalent safety factor" based on a 24-hour averaging time, while a factor used with an annual averaging time is multiplied by 5 to obtain the 24-hour equivalent. The 24-hour equivalent safety factor ranges from 1/10 (e.g., New York - low toxicity

chemicals) to 1/73,000 (e.g., Massachusetts - certain high toxicity chemicals). Appendix C presents the equivalent safety factors being used in a sample of states. Twenty-four states use risk assessment for carcinogens to derive AALs associated with a specified "acceptable level of risk" [NATICH, 1986]. Typically, the "acceptable level of risk" is defined as a risk of one additional cancer in 100,000 or one in 1,000,000 exposed persons [STAPPA/ALAPCO, 1984].

III. PANEL RECOMMENDATIONS

In making its recommendations, the panel has striven to devise an approach which is rational yet simple. Given the scientific uncertainties inherent in the assessment of health risks from ambient air pollution, the approach outlined here should not be considered a precise method distinguishing safe from unsafe levels of contaminants, but rather a means to establish flexible guidelines which can be used to raise flags of concern and set priorities for action. The panel has exercised its best judgment in addressing the issues involved in air guideline development, many of which are questions more of policy than of science; final policy decisions must, of course, be made by the State. Furthermore, it should be pointed out that the guidelines discussed herein are directed toward prevention of human health effects; ecotoxic effects are not addressed.

The decision tree for the overall approach proposed by the panel is presented in Appendix D and, for purposes of illustration, sample air guidelines derived using the proposed approach are presented in Appendix G.

A. Criteria for Selecting Chemicals for Air Guideline Development

Recommendation: Develop air guidelines for those chemicals which meet any of the following criteria and to which there is potential for exposures that may lead to adverse effects as a result of industrial emissions in North Carolina:

1) those chemicals for which the ACGIH has developed a TLV,

2) those chemicals listed by EPA as carcinogens in the category of Group A ("Human Carcinogens") or Group B ("Probable Human Carcinogens"),

or 3) any other chemicals considered by DHS to be of public health concern.

Criteria pollutants should be excluded. Biologically inert dusts should be considered as suspended particulate matter and therefore already regulated as criteria pollutants. Pollutants listed under Section 112 of the Clean Air Act (NESHAP) should not be excluded, although in the case of those source categories that have a NESHAP emissions regulation, the federal regulations should take precedence. It may be most expedient to consider DEMs current list of 80 chemicals first because preliminary groundwork regarding toxicity and occurrence in North Carolina

has been accomplished. Specific compounds which are members of classes of chemicals on the list and which are determined to be biologically inert should be deleted.

If a new chemical meeting any of the above criteria will be introduced into North Carolina as a result of the location of new industry or process changes in existing industry, air guidelines for that chemical should be developed. Sources intending to emit such chemicals can use the ACGIH and EPA lists as checklists to anticipate guideline development. (New sources will not be able to predict whether a chemical to be emitted will meet Criterion 3 above but this classification is expected to be unusual).

B. Categorization of Chemicals

Recommendation: Categorize chemicals by type of toxicity (based on adverse effects at near ambient levels) and use a category-specific approach. If a chemical falls into more than one category, develop an air guideline for each category and select the guideline which affords the greatest degree of protection.

The following categories of toxicity are suggested:

I. Acute Irritants - those chemicals associated with irritation at the site of contact immediately or shortly after a single exposure of eight hours or less. (Excludes agents such as asthma-inducing agents whose action involves an immune response; these are included in Category II, below).

II. Acute Systemic Toxicants - those chemicals associated with adverse effects at sites distant from the site of contact, immediately or shortly after a single exposure of eight hours or less.

III. Chronic Toxicants - those chemicals associated with adverse effects only after multiple (>1) or prolonged (>8 hrs) exposures.

IV. Carcinogens - those chemicals classified by EPA as Group A or Group B carcinogens.

Group A ("Human Carcinogens") - those chemicals for which there is sufficient evidence from epidemiologic studies to support a causal association between exposure to the agent and cancer.

Group B ("Probable Human Carcinogens") - those chemicals for which there is sufficient evidence of carcinogenicity from animal studies and limited or inadequate evidence from epidemiologic studies. In some cases, known physical or chemical properties of an agent and results from short-term tests provide additional substantiation.

EPA's definitions of "sufficient evidence", "limited evidence", and "inadequate evidence" are presented in Appendix F.

C. Factored TLV Approach for Non-Carcinogens (Categories I, II, and III)

Recommendation: Use a factored TLV approach to develop AALs for acute irritants, acute systemic toxicants, and chronic toxicants. Appendix E presents a table of adjustment and safety factors addressing the following concerns: 1) adjustment for continuous exposure, 2) variability in human susceptibility, 3) uncertainties inherent in studies of chronic effects, and, 4) severity of effect. For each chemical, the appropriate factors from Appendix E should be multiplied by each other to determine a composite factor. The composite factor should be applied to the TLV (or NOEL) to derive the AAL for that chemical.

In the case of chemicals which fall into either of the following categories, use the no observed effect level (NOEL) for the effect of concern as the starting point and apply appropriate factors:

1) Any chemical which the State determines poses a public health threat in North Carolina but for which there is no TLV.

or

2) Any chemical which the State determines has health effects not accounted for by ACGIH in the derivation of the TLV, at concentrations below the TLV.

For such chemicals, if only the lowest observed effect level (LOEL) for the effect of concern has been reported, the NOEL should be estimated by LOEL/5.

Rationale: Acute and chronic toxicants generally exhibit threshold concentrations below which no adverse effects are observed. A prudent approach to the control of these chemicals, therefore, would be to maintain ambient levels below the concentration that would produce adverse health effects in sensitive subgroups of the general population. Unfortunately, there is little information on the effects of community exposure to most chemicals. A substantial effort, however, has been devoted to the assessment of threshold levels in occupational settings. Although unmodified application of these occupational guidelines to community exposures would be inappropriate, the panel believes that adjustments can be made in the TLVs to reflect differences between community and occupational exposures and differences in susceptibilities to toxic exposures of persons in the community vs. the work environment.

The panel proposes to use the ACGIH TLVs as the starting point for developing air guidelines for non-carcinogens. For over 40 years, the ACGIH TLV Committee has been assessing threshold levels of industrial chemicals in the workplace. The Committee is composed of experts who bring to bear their scientific and practical experience with the chemicals and their knowledge of the published literature. The TLV determinations represent their best judgment of safe occupational levels given the present state of knowledge. TLVs are reviewed annually and revised to reflect new information as appropriate [Stokinger, 1964; ACGIH, 1986]. Over 650 chemicals have been assigned TLVs.

Although the ACGIH handbook explicitly cautions against the use of TLVs in the evaluation or control of community air pollution nuisances or in estimating the toxic potential of continuous uninterrupted exposures [ACGIH, 1985], the panel feels that adjustments to the TLV specifically addressing differences between occupational and community settings obviates this objection. Most states with air toxics programs have elected to use a factored TLV approach. By employing multiple safety factors on a case by case basis, as outlined below, the panel's approach is less arbitrary than that used in states applying a single safety factor to TLVs.

As indicated above in the recommendation, the NOEL is recommended as the starting point in certain situations. When the NOEL must be used and only the LOEL for the effect of concern has been reported, the NOEL should be estimated using a factor of 1/10. Weil and McCollister [1963] found that in a comparison of NOELs and LOELs for a sample of toxicants, the ratio of LOEL to NOEL was less than 5 in 96% of the comparisons. Thus, in the absence of direct evidence for the NOEL itself, we suggest using a factor of 1/5 to derive an estimate of the NOEL from the reported LOEL if this appears to be appropriate.

The following are the bases for the factors the panel proposes be applied to the TLV (or, in certain cases, the NOEL):

1) Variation in population susceptibility -- A factor should be applied to all TLVs to account for variation in population susceptibility. The TLV does not always

accomodate variation in susceptibility within the occupational setting [Steinberg, 1982]. The TLV handbook [ACGIH, 1985] states:

> Because of wide variation in individual susceptibility, however, a small percentage of workers may experience discomfort from some substances at concentrations at or below the threshold limit; a smaller percentage may be affected more seriously by aggravation of a pre-existing condition or by development of an occupational illness.

Furthermore, whereas industrial workers are generally healthy adults, the general population includes children, the elderly, the chronically ill and other sensitive subgroups. Vessel [1984] reported that variability in individual response to therapeutic drugs varied from 3 to 40 fold. Other research supports intra-species variability factors of 18 or more [Mantel & Bryan, 1961; Oser, 1969; Krasovskii, 1976; Munro & Krewski, 1981]. A factor of 10 has traditionally been used by EPA, and is generally being proposed by other states for use in their air toxics programs [Dourson & Stara, 1983]. We propose a factor of 10 to account for variation in susceptibility across the general population.

2) Continuous exposure -- In the case of chronic toxicants, adjustment for continuous exposure must be made. Because TLV-TWAs are set for 8-hour exposure periods, 5 days a week, a factor of 168 hours per week divided

by 40 hours per week, or roughly 4, should be applied to the TLV-TWA for chronic toxicants. Because the effects of acute toxicants are short-term and not generally cumulative, and because an averaging time of 15 minutes for agents with STELs and 1 hour for agents with only TWAs is proposed, no such adjustment is necessary for acute toxicants [Strauss, Hattis, & Ashford, 1986]. Therefore, we propose a factor of 4 to adjust for continuous exposures only for Category III chemicals (chronic toxicants).

3) Uncertainty inherent in studies of chronic effects -- In the case of chronic toxicants, an additional safety factor of 2 is proposed in order to reflect the greater degree of uncertainty that accompanies studies of chronic effects relative to studies of acute effects. Because chronic studies require information over a relatively long period, experimental and observational data, particularly in studies involving humans, are prone to gaps. Exposure information is typically deficient since environmental monitoring is generally not performed continuously over the relevant time period. Even if a complete profile of exposure over time is available, it is not generally clear how exposure should be integrated to determine cumulative dose and whether peak exposure values, mean concentration, or rapid fluctuation in ambient levels

are most relevant to the induction of effect. Furthermore, with respect to assessing response, effects of chronic exposure are often subtle and detection of a gradual change in a health parameter may be difficult. In establishing TLVs for chronic toxicants, the ACGIH TLV Committee occasionally applies a safety factor to reflect the uncertainties involved in chronic studies but this is not done in a consistent fashion. We therefore suggest that a factor of 2 be applied in the case of chronic toxicants because the difficulties inherent in relating dose and effect in such studies are not generally reflected in the TLV.

4) Severity of effect -- In light of the uncertainty inherent in setting AALs, it is prudent to exercise greater caution in regulating those pollutants whose health effects are more serious and for which the consequences of setting an AAL that is too high are grave. Two categories of severity are suggested, with a safety factor of 2 being applied to the latter:

   a) Agents eliciting reversible and non-life threatening effects at concentrations that might reasonably be expected to occur in the ambient air. Examples of such effects include mucous membrane irritation, dermatitis, narcosis, weight change, nausea, asthma attacks, reversible change in pulmonary function,

reversible change in serum enzyme levels, temporary liver enlargement, peptic ulcers, acute bronchitis. No additional safety factor is proposed for these agents.

b) Agents eliciting irreversible or life-threatening effects at concentrations that might reasonably be expected to occur in the ambient air. Examples of such effects include: pneumoconiosis, emphysema, cirrhosis, irreversible kidney damage, immune suppression, demyelination, coronary heart disease, seizures, coma, fetotoxicity. A safety factor of 2 is proposed for these agents. In situations in which acute exposures to a chemical may lead to a life-threatening condition, a severity factor of as much as 5 may be warranted. We propose that this judgment be reviewed by the standing advisory committee.

The effect most likely to occur at low doses is the effect that should be considered here. Thus, this excludes effects that would not be expected to occur at ambient or near ambient levels (including normal variation). In cases where there is uncertainty regarding whether to assign a severity factor of 1 or 2, a factor of 1 should be used because safety factors have been incorporated elsewhere in the derivation of AALs.

The panel suggests treating reproductive and developmental toxicants as Category II (Acute Systemic Toxicants) or Category III (Chronic Toxicants), as appropriate. Although little is known about the dose-response relationships of these agents, the panel felt present evidence did not exclude threshold effects and therefore a factored TLV approach appears appropriate at present. The Standing Advisory Committee may wish to revise the approach for reproductive and developmental toxicants as knowledge regarding their dose-response relationships improves.

D. Risk Assessment/Technology Approach for Carcinogens (Category IV)

Recommendation: In the case of carcinogens, the Panel proposes a combined technology-based and risk assessment approach subject tomodification by the Standing Committee on a case-by-case basis. Using the potency estimates developed by the Carcinogen Assessment Group (CAG) of EPA, the State should calculate the incremental air concentration (i.e. concentration attributable to emission source, regardless of background level) that would be associated with an additional cancer risk of 10^{-6} for Group A carcinogens and a risk of 10^{-5} for Group B carcinogens; these concentrations constitute the action levels. In cases in which well designed human studies or data regarding mechanism (epigenetic vs. genetic), pharmacokinetics, or species differences appear not to have been taken into account by CAG in the estimate of potency, the Standing Advisory Committee may modify the action level as appropriate. Any source releasing a

carcinogen at an emission rate which modelling indicates would cause the action level to be exceeded should be required to apply control technology. Control technologies required for existing sources should take into account cost and feasibility issues, while new sources should be required to apply state-of-art technology if the action level is exceeded. If the post-control impact on ambient air is estimated still to exceed the action level, the source should be given the option of applying to DEM for a variance. In the variance procedure DEM should consider such relevant factors as:

- the quality of animal and human data on which the risk assessment is based
- new information not yet reflected in the CAG potency estimate
- the potential for population exposure to the polluting source, e.g., the proximity of residences to the fence-line of the polluting source
- the potential for achieving the action level by alternative control strategies, e.g., alternate siting, lower emissions, modifications of process, etc.

DEM may seek the input of the proposed standing air toxics advisory panel on these issues, particularly in the area of the quantitative risk assessment.

Rationale: The panel recommends controlling EPA's Group A and Group B carcinogens. Although the EPA carcinogen classification system has not yet been approved by OMB and is therefore

technically "interim", it is presently being used internally at EPA and is not likely to be substantially altered [McGaughy, 1986]. The criteria used by EPA are very similar to those of the International Agency for Research on Cancer. Chemicals are classified qualitatively by weight of scientific evidence without consideration of potency (criteria are listed in Appendix F). This qualitative classification system allows separate treatment of chemicals with different levels of evidence for human carcinogenicity; i.e., known human carcinogens can be regulated with greater stringency than chemicals not definitively associated with human cancer. The panel does not recommend regulating "possible" carcinogens (EPA's Group C carcinogens) unless they are associated with other types of toxicity, although DEM, DHS, or the proposed Standing Advisory Committee (see below) may choose to reconsider this exclusion. The panel felt that the EPA classification system was preferable to IARC's because of the following considerations:

1) the chemicals that have been classified include those considered by IARC as well as the National Toxicology Program (NTP),
2) EPA has performed potency calculations for each of the carcinogens on its list, and
3) EPA updates its classifications as new evidence becomes available, whereas IARC addresses chemicals in batches and does not have a systematic approach for updating classifications of individual chemicals [McGaughy, 1986].

In November, EPA intends to publish in its Superfund Reportable Quantities Rule a table of the 187 chemicals classified by the Agency as Group A, B or C [Cogliano, 1986].

Carcinogenesis is qualitatively different from the processes leading to other toxic effects because events in a single cell can lead to the development of disease [Fialkow, 1974]. It has been argued that thresholds for activity of direct-acting carcinogens could result from saturation of deactivating enzymes or overwhelming DNA repair processes [Cornfield, 1977]. These phenomena would cause non-linearity in the dose-response curve, but because neither deactivation nor repair are instantaneous or complete [Office of Technology Assessment, 1981; California DHS, 1986], an absolute threshold is not implied. In theory, then, thresholds for direct-acting carcinogens are unlikely, although non-linearities in the dose-response curve may occur (low-dose extrapolation models will be discussed later). For indirect, or epigenetic, carcinogens (e.g., chemicals which stimulate activating enzymes or cause cellular proliferation) a threshold level of effect is plausible as the mechanisms postulated resemble those of classical toxicants [Weisburger & Williams, 1983]. Most carcinogens cannot presently be classified as having a genetic or epigenetic mechanism, however [IARC, 1983; California DHS, 1985]. The panel agrees with the reasoning taken by federal agencies [U.S. Interagency Regulatory Liaison Group, 1979; Food Safety Council, 1980; Office of Technology Assessment, 1981; Samuels & Adamson, 1985] that a no-threshold assumption is generally appropriate for carcinogens.

The panel considers the use of TLVs developed for carcinogens to be an inappropriate approach to managing carcinogens. In setting TLVs for carcinogens, the ACGIH frequently uses the level at which no carcinogenic effect is observed to derive "an approximate threshold of neoplastic response" [ACGIH, 1985; Stokinger, 1977]. Even in the absence of a threshold, however, a no effect level will occur in every epidemiological or toxicological study investigating sufficiently low doses and the apparent threshold of response will simply reflect limitations of sample size and study power, not an absolute biological phenomenon. Because TLVs are based on the premise of a threshold, the panel recommends an alternative approach for carcinogens.

Two alternative approaches to managing carcinogens are commonly considered: 1) a technology-based approach, and 2) risk assessment and management. Technology-based approaches are straight-forward and simple. Specified control technology is required of sources emitting carcinogens. Drawbacks of a pure technology approach stem from the lack of consideration of health risk or of the potency of different carcinogens. For instance, if there is no potential for population exposure near the source, the cost of control technology may not be warranted. On the other hand, situations may arise in which unreasonable health risks are posed by operation of a facility even after state-of-the-art control technology has been installed.

The panel considers the final policy alternative, risk assessment, to be the only currently viable way to incorporate health risk considerations into the management of carcinogens. Risk assessment, as practiced by EPA's Carcinogen Assessment Group makes maximal use of all of the relevant information known about an agent to derive the best estimate of risk associated with that agent. Problems with risk assessment arise not from the process itself but rather from gaps in the information base. Where gaps exist, CAG has had to make assumptions. A discussion of some of these assumptions follows:

1) Low Dose Extrapolation - One of the greatest sources of uncertainty in risk estimates arises from extrapolation of the dose-response curve to low doses. Animal and sometimes occupational data involve exposures orders of magnitude higher than those which might be encountered by the general population in ambient air. To extrapolate downward, a model must be formulated. Postulated extrapolation models fall into two categories: 1) tolerance distribution (e.g., probit function), and 2) mechanistic. Tolerance distribution models posit a level above which the dose will produce a singular response, e.g., cancer, with certainty. Due to inter-individual variation in tolerance levels, a smooth dose-response curve for the aggregate population results. Because these models do not take into account the stochastic nature of carcinogenesis, the panel

considers them to be less biologically plausible than mechanistic models. Mechanistic models, in contrast, strive to incorporate current understanding of the mechanisms of carcinogenesis. Examples of mechanistic models include the one-hit, multi-hit, linearized multi-stage, unconstrained multi-stage and Weibull [Armitage & Doll, 1961; Pike, 1966; Crump, 1976; Rai & Van Ryzin, 1981; Crump, 1981]. The relative merits of the various mechanistic models have been extensively debated [Crump, 1977; Guess & Hoel, 1977; Hartley & Sielken, 1977; Carlborg, 1981; Haseman, et al, 1981]. These models all tend to provide a good fit to experimental data in the observed dose range but diverge increasingly in their risk predictions at progressively lower doses. When extrapolations must be performed over a dose range of more than several orders of magnitude, estimates of risk tend to vary over a similar range [OSHA, 1980; Office of Technology Assessment, 1981]. Unfortunately, while the extrapolation model has a profound effect on risk estimates at very low doses, it is generally agreed that the models are untestable and unprovable in that a prohibitively large quantity of data would be necessary to determine which model provides the best fit at low doses [Office of Technology Assessment, 1981; Brown, 1984]. Although the question of which model is appropriate will not likely be resolved by goodness-of-

fit arguments, theoretical considerations and elucidation of biological mechanisms hold some promise. Hoel [1980] and Crump, et al, [1976] have proposed that regardless of the shape of the dose-response curve for an agent acting in isolation, the risk associated with low doses of an agent acting in concert with other influences will typically be additive over background risk. Hoel [1980] has done calculations which indicate that this will be the case whenever the agent is added to an environment in which other agents acting by a similar mechanism are responsible for even as little as one percent of the background level of the cancer in question. Such situations are expected to be the norm. In these situations, Hoel [1980] and Crump, et al, [1976] have shown that the most appropriate low dose extrapolation model would be approximately linear in the low dose region. CAG is presently deliberating whether to use the 95% upper confidence bound of the linearized multi-stage model or a linear extrapolation of ED (the dose associated with a 10% increase in cancer) in its future potency calculations. A comparison of potency calculations by these two methods for about 180 chemicals indicates a close correlation [Cogliano, 1986].

2) Inter-Species Extrapolation - A second source of uncertainty stems from the use of animal data to predict

human response. It is necessary to consider not only differences in scale, but also inherent differences in the handling of agents. There are a number of units that might be used to perform the scale adjustment: weight, body surface area, lung surface area (inhalation studies), metabolic rate, total food intake (ingestion studies), lifespan. CAG has tentatively concluded that the most appropriate scaling unit for carcinogens is body surface area (or, equivalently, the 2/3 power of weight), based on limited data from chemotherapeutic agents [Anderson, 1984]. Regarding pharmacokinetics, any known inter-species differences in absorption, distribution, metabolism, and elimination that are relevant to a particular agent are taken into account by CAG in calculating potency in humans [USEPA, 1984]. A final factor that is not explicitly taken into consideration by CAG is the greater diversity in humans compared to laboratory animals with respect to genetic constitution, nutritional status, disease states, and exposure (historic and concurrent) to a variety of environmental agents including initiators and promoters. Crouch and Wilson [1979] have compared potencies (in $[\text{mg/kg body weight/day}]^{-1}$) of nine chemical carcinogens for which there are dose-response data in humans, rats and mice, and found that humans tended to be as sensitive as the more sensitive laboratory animal. CAG

thus has an empirical basis for its decision to use data from the most sensitive animal species in its calculations of human potency [USEPA, 1984].

3) Generalizability of Studies in Humans - Even if human dose-response data are available, confidence in risk assessments must be tempered by consideration of the generally poor quality of data and possible confounding and bias. In addition, there is the issue of generalizability from the study group to the population as a whole. In general, however, fewer assumptions are required when using human rather than animal data [Day, 1985], and CAG relies on human data as much as possible. Even negative human data are used: well-conducted epidemiological studies finding no excess risk of cancer are used to reduce the upper bound of the risk estimate [USEPA, 1984].

The panel feels that the assumptions used by CAG are conservative but not unrealistic. Given the unavoidable fact that full information is not available on every carcinogen, the process used by CAG provides a reasonable upper bound risk estimate, i.e., the true risk is not likely to be greater than the risk estimate. Because risk estimates entail a high degree of uncertainty, they cannot be relied on as precise measures of absolute risk. The fact that risk assessments are performed in a consistent manner, however, implies that they can be used to compare risks from different sources, and to suggest priorities for action.

The panel proposes that CAGs potency estimates be used to develop for each carcinogen an action level, defined as the increment in ambient concentration associated with a risk of 10^{-6} for Group A carcinogens and 10^{-5} for Group B carcinogens. The definition of "acceptable risk" is necessarily a policy judgment, not a scientific determination. It is therefore outside the purview of this advisory panel. Risk levels in the range of 10^{-5} to 10^{-6} have been widely used by other regulatory agencies [Flamm, 1986], and the panel therefore suggests this range on the basis of precedent. The panel recommends more stringent action levels for Group A carcinogens -- concentrations associated with a 10^{-6} risk, as opposed to a 10^{-5} risk for Group B carcinogens -- because Group A chemicals have greater weight of evidence for their human carcinogenicity.

Our proposed approach does not rely on these action levels as precise barometers of risk, but rather as guideposts. Through installation of the recommended control technology, it is expected that most post-control emissions will cause increments in ambient levels much lower than the action level. On the other hand, the proposed variance procedure would allow the action level to be exceeded under certain circumstances.

E. Standing Advisory Committee

Recommendation: Establish a standing advisory committee on toxic air pollutants to deal with recurrent or unresolved issues such as:

1) Whether the factored TLV approach has been appropriately applied to each chemical selected for inclusion in the list of toxic air pollutants. (This provides a peer-review of the State's application of these proposed guidelines).
2) Whether agents having adverse reproductive or developmental effects should be treated as Category II or III toxicants or evaluated by means of risk assessment.
3) Whether health risks from exposure to complex mixtures of chemicals should receive special consideration, requiring some modification in air guidelines for individual chemicals within the mixture.
4) Whether air guidelines should be modified when there are multiple sources of the same toxic air pollutant in a localized area.
5) Whether uncertainties in each step of the carcinogenic risk assessment process can be incorporated into the development or revision of air guidelines for carcinogenic air pollutants, particularly in the case of epigenetic carcinogens.

The Panel would also be available for consultation by DEM and DHS regarding guidelines for individual chemicals (e.g., choice of severity factor) and variance requests (e.g., consideration of new data not incorporated into risk estimate).

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APPENDIX A

Letter from Paul Wilms, Director, DEM, Requesting NCAS Assistance, March 21, 1986

State of North Carolina
Department of Natural Resources and Community Development
Division of Environmental Management
512 North Salisbury Street • Raleigh, North Carolina 27611
Air Quality Section

James G. Martin, Governor
S. Thomas Rhodes, Secretary

R. Paul Wilms
Director

March 21, 1986

Mr. Jonathan B. Howes, Chairman
Affairs and Policy Committee
N. C. Academy of Science, Inc.
Center For Urban and Regional Studies
University of North Carolina
Hickerson House 067A
Chapel Hill, NC 27514

Dear Mr. Howes:

The Division of Environmental Management requests the North Carolina Academy of Sciences to conduct an evaluation of toxic air pollutants and acceptable ambient levels slated for regulation in the state. It is proposed that the Academy select a qualified panel to examine the list of air toxics, recommend additions or deletions to the list, determine a suitable approach for establishing acceptable ambient levels and document quantitative acceptable ambient levels to control air toxics. Attached for your consideration is a description of the project.

Funding for the Academy has been allocated in the amount of $10,000 through an agreement with the Environmental Protection Agency. For funding purposes EPA would contract with the Radian Corporation located in the Research Triangle Park, and Radian would establish a subcontract with the Academy to conduct the project. It is anticipated that the contract between EPA and Radian will be effective toward the end of this month at which time the subcontractual arrangements with the Academy could proceed. Project costs incurred by the Academy would be billed to the Radian Corporation in accordance with the subcontract. The date targeted for project completion is July 1, 1986.

After careful consideration, the Division of Environmental Management has concluded that the N.C. Academy of Sciences is the most appropriate scientific body to conduct the evaluation. The peer group evaluation which the Academy can provide is an essential step toward the successful implementation of an air toxics program in North Carolina.

Additional materials to further describe the proposed air toxics program will be forthcoming.

(2)

Please do not hesitate to contact me or my staff if you have questions. I look forward to hearing from you at your earliest convenience.

Sincerely,

R. Paul Wilms

/mdgK3

Attachment

APPENDIX B

Survey of State Air Toxics Programs

SURVEY OF STATE AIR TOXICS PROGRAMS

State	Status of Air Toxics Control Program	Basis for Air Toxics Control Program	Scope of Air Toxics Control Program	Basis for Some or All Acceptable Ambient Concentrations or Standards	Comments
Alabama	In place	Promulgated general regulation prohibiting air pollution; informal guidelines	Not limited to specific list of pollutants, sources, or source categories	Acceptable ambient concentrations (2.5% TLV/hr)	Program applies to all pollutants emitted by new sources.
Alaska					Control technology requirements for sources of specified pollutants. Risk assessment used on case-by-case basis. Toxic emissions inventory.
Arkansas	In place	Informal guidelines	Not limited to specific list of pollutants, sources, or source categories	Acceptable ambient concentration (1% TLV)	All sources controlled through permit program. Control technology requirements used for sources of specified pollutants.
Arizona	In place	Informal guidelines	Specified list of pollutants	Acceptable ambient concentrations, some original health effects research	Risk assessment used on a case-by-case basis
California	In place (implemented 1/1/84)		Specific list of pollutants -- 47 candidates for regulation	Compound-specific	Control technology requirements used for sources of specified pollutants. Risk assessment used on case-specific basis. Extensive research efforts: source tests, ambient monitoring, dispersion modeling, ambient exposure, pollutant research on benzene, ethylene dibromide, and ethylene dichloride

State	Status of Air Toxics Control Program	Basis for Air Toxics Control Program	Scope of Air Toxics Control Program	Basis for Some or All Acceptable Ambient Concentrations or Standards	Comments
Colorado	In preparation	Promulgated regulations (tentative)	Specific list of pollutants (tentative)		Toxics inventory in progress.
Connecticut	In preparation	Promulgated regulations	Specific list of pollutants	Acceptable ambient concentrations based on TLV	Control technology requirements for sources of specified pollutants. Risk assessment used on a case-by-case basis.
Delaware	In preparation		Not limited to specific list of pollutants, sources, or source categories	Acceptable ambient concentrations based on TLV	Control technology requirements for sources of specified pollutants. Risk assessment used on a case-by-case basis.
Florida	In preparation	Promulgated regulations	Specific list of pollutants	Acceptable ambient concentrations based on TLV	Control technology requirements for sources of specified pollutants. Risk assessment used on a case-by-case basis.
Georgia	In place	Informal guidelines	Specific list of pollutants	Acceptable ambient concentrations: 1% TLV/ 24 hr if not known human carcinogen; 0.33% TLV/ 24 hr if known human carcinogen	
Hawaii	No program				
Idaho	In preparation		Not limited to specific list of pollutants, sources, or source categories	Acceptable ambient concentrations	Control technology requirements used for sources of specified pollutants. Risk assessment used on case-by-case basis.

State	Status of Air Toxics Control Program	Basis for Air Toxics Control Program	Scope of Air Toxics Control Program	Basis for Some or All Acceptable Ambient Concentrations or Standards	Comments
Illinois	In place	Informal guidelines	Not limited to specific list of pollutants, sources, or source categories	Acceptable ambient concentration: 0.33% TLV if non-carcinogen; some standards based on original health effects research	Control technology requirements used for sources of specified pollutants. Risk assessment used on case-by-case basis; currently reviewing risk assessment procedures of other agencies. Methods development: ambient monitoring, dispersion modeling, emergency response, indoor/outdoor lead levels, emissions modeling for lead from slag pile.
Indiana	In preparation	Informal guidelines (tentative)	Specified list of pollutants (tentative)		
Iowa	In preparation	Informal guidelines	Not limited to specific list of pollutants, sources or source categories	Acceptable ambient concentrations	
Kansas	No program				
Kentucky	In place	Promulgated regulations (tentative)	Specified list of pollutants (tentative)	Acceptable ambient concentrations, except for H_2S, gaseous fluoride, and total fluoride, pollutant level must be non-harmful	Control technology requirements will be used for sources of specified pollutants. Risk assessment will be used on a case-by-case basis (tentative).
Louisiana	No program				

State	Status of Air Toxics Control Program	Basis for Air Toxics Control Program	Scope of Air Toxics Control Program	Basis for Some or All Acceptable Ambient Concentrations or Standards	Comments
Maine	In preparation: air toxics emissions inventory will determine regulatory approach		Not limited to specific list of pollutants, sources, or source categories	Safety factor on TLV (tentative); original health effects research will be used	Control technology requirements will be used for sources of specified pollutants. Risk assessment will be used on a case-by-case basis (tentative).
Maryland	In preparation	Promulgated regulations	Not limited to specified list of pollutants, sources, or source categories	Acceptable ambient air concentrations based on TLV	Control technology requirements used for sources of specified pollutants. Risk assessment used on case-by-case basis.
Massachusetts	In preparation	Promulgated regulations; informal guidelines	Not limited to specific list of pollutants, sources or source categories	Acceptable ambient concentrations based on occupational limits	Control technology requirements for sources of specified pollutants.
Michigan	In place	Promulgated regulations	Not limited to specified list of pollutants, sources, or source category	Acceptable ambient air concentrations based on TLV, original health effects research (toxics model)	Control technology requirements used for sources of specified pollutants. Risk assessment used on case-by-case basis. Have developed models and applications for emissions from landfills and landfill excavation, time scaling factors for different averaging times, dilution factor matrix.
Minnesota	In place (new sources); in preparation for existing sources (1-87)	Informal guidelines	Not limited to specified list of pollutants, sources, or source categories	Acceptable ambient air concentrations (1% TLV), original health effects research	State of Michigan framework used as policy for new sources. Risk assessment used on case-by-case basis. Conducting ambient monitoring.

State	Status of Air Toxics Control Program	Basis for Air Toxics Control Program	Scope of Air Toxics Control Program	Basis for Some or All Acceptable Ambient Concentrations or Standards	Comments
Missouri	In preparation	Promulgated regulations; informal guidelines	Not limited to specific list of pollutants, sources or source categories		
Montana	In preparation	Informal guidelines	Not limited to specified list of pollutants, sources, or source categories	Formally adopted ambient standards for F- and H_2S; acceptable ambient air concentrations for others TLV/42	BACT required for all permitted sources with uncontrolled emissions >25 tons/year.
Nevada	In place	Promulgated regulations	Not limited to specific list of pollutants, sources or source categories	Acceptable ambient concentrations based on TLV	Control technology requirements for sources of specified pollutants. Risk assessment used on case-by-case basis.
New Hampshire	In preparation	Promulgated regulations	Not limited to specific list of pollutants, sources, or source categories	Acceptable ambient concentrations (1% TLV)	Regulation Amendment is expected to be required for enforcement of the guidelines. Developing methods for solid absorbent collection of various VOCs and monitoring of ambient TRS.
New Jersey	In place		Specific list of pollutants. Not limited to specific sources and source categories	Formally adopted standards	Control technology requirements used for sources of specified pollutants. Risk assessment used on a case-by-case basis. Ambient monitoring of non-traditional sources such as landfills.
New Mexico	In preparation				

State	Status of Air Toxics Control Program	Basis for Air Toxics Control Program	Scope of Air Toxics Control Program	Basis for Some or All Acceptable Ambient Concentrations or Standards	Comments
New York	In place	Informal guidelines	Not limited to specific list of pollutants, sources or source categories	Acceptable ambient concentrations based on TLV; some original health effects research	Regulate all sources of air toxics. Have pollutant research program and results of toxicity tests.
North Carolina	In preparation				
Oklahoma	In preparation	Promulgated regulations	Not limited to specific list of pollutants, sources or source categories	Acceptable ambient concentrations based on TLV, some original health effects research	Control technology requirements for sources of specified pollutants. Risk assessment used on case-by-case basis.
Oregon	In place		Not limited to specific list of pollutants, sources or source categories	Acceptable ambient concentrations based on TLV	Program in place for control of fluorides from aluminum plants and H_2S and mercaptans from kraft mills. Some other plants controlled by permit on case-by-case basis.
Pennsylvania	In place and evolving		Not limited to specific list of pollutants, sources or source categories	Acceptable ambient concentrations based on TLV, some original health effects research	Emissions inventory for air toxics.
Rhode Island	In preparation	Promulgated regulations	Specific list of pollutants	Acceptable ambient concentrations	Control technology requirements for sources of specified pollutants. Risk assessment on case-by-case basis.
South Carolina	In place	Informal guidelines	Limited to specific list of pollutants. Not limited to specific sources, or source categories	Acceptable ambient air concentrations (1/420 TLV)	Air toxics program being developed may lead to specific regulations.

State	Status of Air Toxics Control Program	Basis for Air Toxics Control Program	Scope of Air Toxics Control Program	Basis for Some or All Acceptable Ambient Concentrations or Standards	Comments
South Dakota	No program				
Texas	In place	Informal guidelines	Not limited to specific list of pollutants, sources, or source categories	Formally adopted ambient standards (Guidelines are 1% occupational standard for 30-min. max and 0.1% occupational standard for annual max.); original health effects research	Control technology requirements used for sources of specified pollutants. Developing data base for 800 substances. Conducting R&D in source testing, ambient monitoring, emergency response procedures, ambient exposure assessment, assessment of human exposure to complex mixtures of contaminants.
Utah	No program				
Vermont	In place for new sources; new program for existing and new sources in preparation	Not yet decided; probably will be formal guidelines	Specific list of pollutants	Acceptable ambient concentrations (1/420 TLV)	Control technology requirements used for sources of specified pollutants. Risk assessment used on a case-by-case basis.
Virginia	In place	Promulgated regulations	Specific list of pollutants	Acceptable ambient concentrations based on TLV	
Washington	In place	Promulgated regulations; informal guidelines	Specific list of pollutants	Acceptable ambient concentrations based on TLV	Control technology requirements for sources of specified pollutants. Risk assessment used on case-by-case basis. Toxic emissions inventory.
West Virginia	No program				

State	Status of Air Toxics Control Program	Basis for Air Toxics Control Program	Scope of Air Toxics Control Program	Basis for Some or All Acceptable Ambient Concentrations or Standards	Comments
Wisconsin	In preparation	Informal guidelines (tentative)	Not limited to specific list of pollutants, sources, or source categories (tentative)	Formally adopted ambient standards (2.4% TLV) (tentative)	Control technology requirements will be used for sources of specified pollutants. Risk assessment will be used on a case-by-case basis (tentative).
Wyoming	No program				

Sources: NATICH, 1986 and Radian, 1985

APPENDIX C

Equivalent Safety Factors Applied to TLVs in Various States

EQUIVALENT SAFETY FACTORS APPLIED TO TLVs IN VARIOUS STATES*

State or Agency	Averaging Time	Safety Factor Applied to TLV	Equivalent Safety Factor[a]
Alabama	1 hour	1/40	1/200
Arkansas	24 hour	1/100	1/100
Connecticut	8 hour	1/200 (known carcinogens)	1/400
	8 hour	1/100 (suspect carcinogens)	1/200
	8 hour	1/50 (others)	1/100
Georgia	24 hour	1/300 (known human carcinogens)	1/300
	24 hour	1/100 (not known human carcinogens)	1/100
Illinois	24 hour	1/300 (non-carcinogens)	1/300
Indiana	24 hour	1/100	1/100
Michigan	8 hour	1/100	1/200
Minnesota	8 hour	1/100	1/200
Mississippi	24 hour	1/30	1/30
Montana	Annual	1/42	1/10
Nevada	8 hour	1/10	1/20
New Hampshire[b]	NA	1/100	NA
New York	Annual	1/300 (high-moderate toxicity)	1/60
	Annual	1/50 (low toxicity)	1/10

EQUIVALENT SAFETY FACTORS APPLIED TO TLVs IN VARIOUS STATES*

State or Agency	Averaging Time	Safety Factor Applied to TLV	Equivalent Safety Factor[a]
Rhode Island	24 hour	1/100	1/100
South Carolina	NA	1/420	NA
Texas	30 minute	1/100	1/1000
	Annual	1/1000	1/200
Vermont	Annual	1/420	1/84
	24 hour	1/420	1/420
Virginia	24 hour	1/100 (carcinogens)	1/100
	24 hour	1/60 (non-carcinogens)	1/60
Wisconsin	NA	1/42	NA
Wyoming	Annual	1/42	1/10
	24 hour	1/50	1/50
	1 hour	1/300	1/1500

[a]Based on calculations by the Commonwealth of Virginia, under typical conditions and non-varying emission rates, the highest 1 hour concentration of a pollutant will be 25 times as high as the annual mean, 5 times the 24 hour mean, and 2.5 times the 8 hour mean. Thus an 8 hour concentration x 1/2 = the 24 hour and the annual x 5 = 24 hour concentration.

[b] Program is not finalized; the safety factor is tentative.

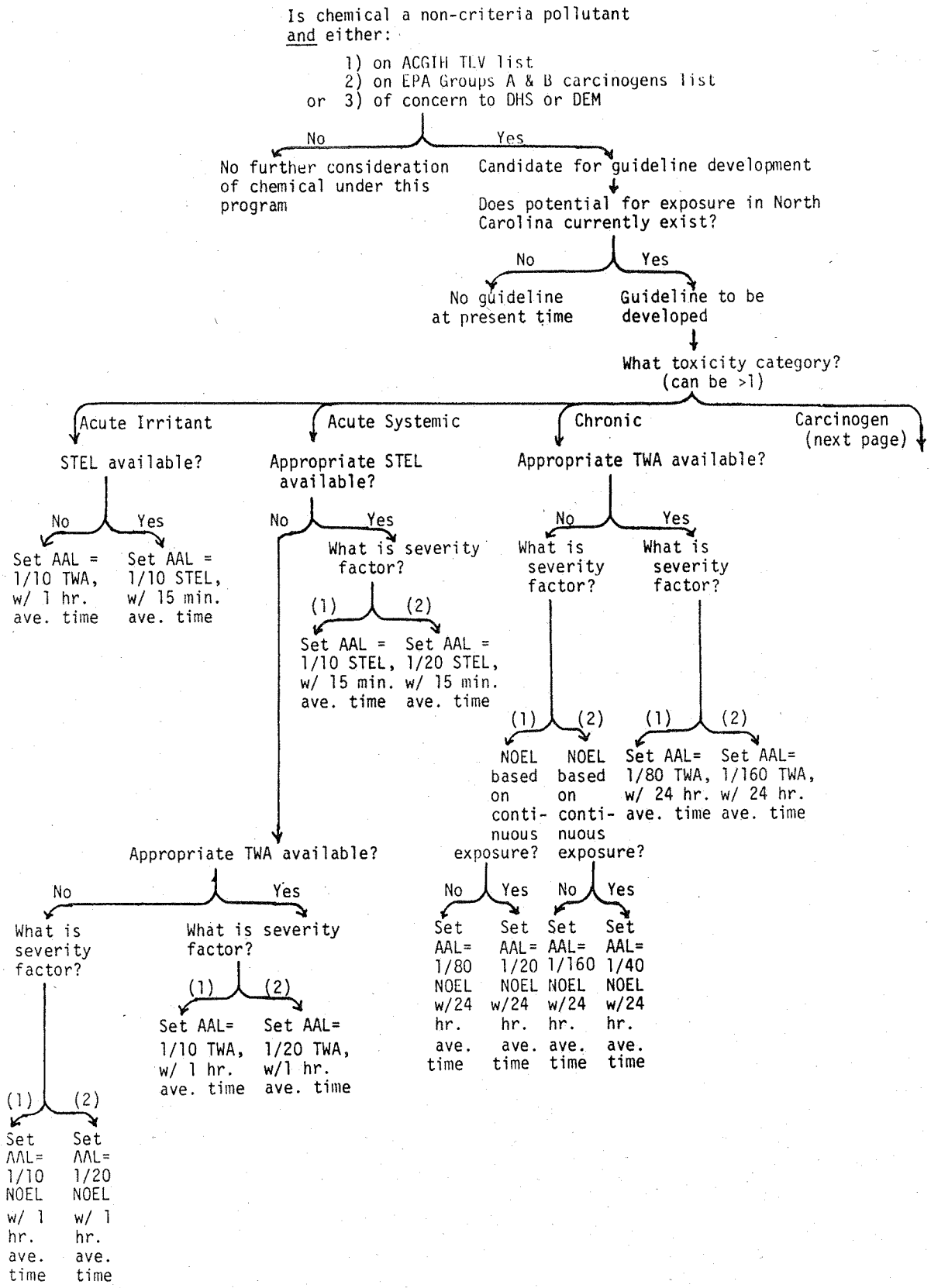
NA = Not available

*Compiled by Radian Corporation for DEM, April, 1985

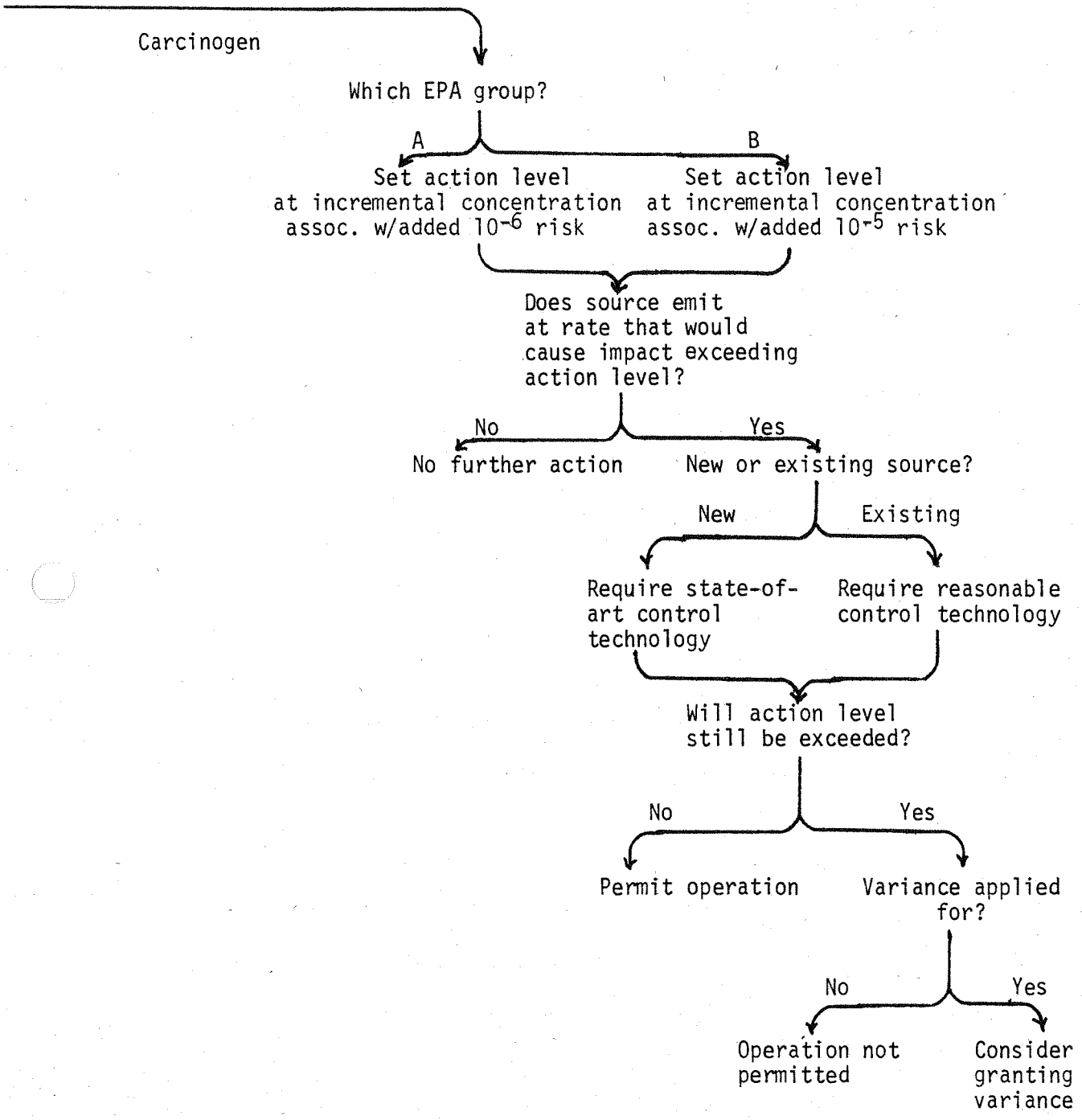
APPENDIX D

Decision Tree - Panel Proposal

DECISION TREE- PANEL PROPOSAL*



DECISION TREE (Cont'd)



*The approach recommended by the panel is simplified here for clarity of presentation. See text for a more complete description.

APPENDIX E

Suggested Safety and Adjustment Factors

SUGGESTED SAFETY AND ADJUSTMENT FACTORS FOR NONCARCINOGENS

	Starting point	Adjustment for continuous exposure	Factor to account for greater variation in susceptibility	Factor reflecting uncertainty inherent in studies of chronic effects	Factor for added conservatism due to severity of effect	Range of composite factor
Acute Irritants	TLV-STEL if avail.	--	10	--	--	10
	Otherwise, TLV-TWA					
Acute Systemic Toxicants	TLV-STEL if avail.	--	10	--	1 or 2	10 to 20
	Otherwise, TLV-TWA					
Chronic Toxicants	TLV-TWA	4	10	2	1 or 2	80 to 160

APPENDIX F

Excerpt, Proposed Guidelines for Carcinogen Risk Assessment,
EPA, 49 FR 46294, November 23, 1984

IV. Appendix—EPA Classification System for Evidence of Carcinogenicity From Human Studies and From Animal Studies (Adapted From IARC)

A. Assessment of Evidence for Carcinogenicity From Studies in Humans

Evidence of carcinogenicity from human studies comes from three main sources:

1. Case reports of individual cancer patients who were exposed to the agent(s).
2. Descriptive epidemiologic studies in which the incidence of cancer in human populations was found to vary in space or time with exposure to the agent(s).
3. Analytical epidemiologic (case-control and cohort) studies in which individual exposure to the agent(s) was found to be associated with an increased risk of cancer.

Three criteria must be met before a causal association can be inferred between exposure and cancer in humans:

1. There is no identified bias which could explain the association.
2. The possibility of confounding has been considered and ruled out as explaining the association.
3. The association is unlikely to be due to chance.

In general, although a single study may be indicative of a cause-effect relationship, confidence in inferring a causal association is increased when several independent studies are concordant in showing the association, when the association is strong, when there is a dose-response relationship, or when a reduction in exposure is followed by a reduction in the incidence of cancer.

The degrees of evidence for carcinogenicity* from studies in humans are categorized as:

1. Sufficient evidence of

*For purpose of public health protection, agents associated with life-threatening benign tumors in humans are included in the evaluation.

carcinogenicity, which indicates that there is a causal relationship between the agent and human cancer.

2. Limited evidence of carcinogenicity, which indicates that a causal interpretation is credible, but that alternative explanations, such as chance, bias, or confounding, could not adequately be excluded.

3. Inadequate evidence, which indicates that one of two conditions prevailed: (a) There were few pertinent data, or (b) the available studies, while showing evidence of association, did not exclude chance, bias, or confounding.

4. No evidence, which indicates that no association was found between exposure and an increased risk of cancer in well-designed and well-conducted independent analytical epidemiologic studies.

5. No data, which indicates that data are not available.

B. Assessment of Evidence for Carcinogenicity From Studies in Experimental Animals

These assessments are classified into five groups:

1. Sufficient evidence+ of carcinogenicity, which indicates that there is an increased incidence of malignant tumors or combined malignant and benign tumors§: (a) In multiple species or strains; or (b) in multiple experiments (preferably with different routes of administration or using different dose levels); or (c) to an unusual degree with regard to incidence, site or type of tumor, or age at onset. Additional evidence may be provided by data on dose-response effects, as well as information from short-term tests or on chemical structure.

2. Limited evidence of carcinogenicity, which means that the data suggest a carcinogenic effect but are limited because: (a) The studies involve a single species, strain, or experiment; or (b) the experiments are restricted by inadequate dosage levels, inadequate duration of exposure to the agent, inadequate period of follow-up, poor survival, too few animals, or inadequate reporting; or (c) an increase in the incidence of benign turmors only.

3. Inadequate evidence, which indicates that because of major qualitative or quantitative limitations, the studies cannot be interpreted as showing either the presence or absence of a carcinogenic effect.

4. No evidence, which indicates that there is no increased incidence of neoplasms in at least two well-designed and well-conducted animal studies in different species.

5. No data, which indicates that data are not available.

The categories "sufficient evidence" and "limited evidence" refer only to the strength of the experimental evidence that these agents(s) are carcinogenic and not to the power of their carcinogenic action.

C. Categorization of Overall Evidence

Group A—Human Carcinogen

This category is used only when there is sufficient evidence from epidemiologic studies to support a causal association between exposure to the agent(s) and cancer.

Group B—Probable Human Carcinogen

This category includes agents for which the evidence of human carcinogenicity from epidemiologic studies ranges from almost "sufficient" to "inadequate." To reflect this range, the category is divided into higher (Group B1) and lower (Group B2) degrees of evidence. Usually, category B1 is reserved for agents for which there is at least limited evidence of carcinogenicity to humans from epidemiologic studies. In the absence of adequate data in humans, it is reasonable, for practical purposes, to regard agents for which there is sufficient evidence of carcinogenicity in animals as if they presented a carcinogenic risk to humans. Therefore, agents for which there is inadequate evidence from human studies and sufficient evidence form animal studies would usually result in a classification of B2.

In some cases, the known chemical or physical properties of an agent and the results from short-term tests allow its transfer from Group B2 to B1.

Group C—Possible Human Carcinogen

This category is used for agents with limited evidence of carcinogenicity in animals in the absence of human data. It includes a wide variety of evidence: (a) Definitive malignant tumor response in a single well-conducted experiment, (b) marginal tumor response in studies having inadequate design or reporting, (c) benign but not malignant tumors with an agent showing no response in a variety of short-term tests for mutagenicity, and (d) marginal responses in a tissue known to have a high and variable background rate.

In some cases, the known physical or cehmical properties of an agent and results from short-term tests allow a transfer from Group C to B2 or from Group D to C.

Group D—Not Classified

This category is used for agent(s) with inadequate animal evidence of carcinogenicity.

Group E—No Evidence of Carcinogenicity for Humans

This category is used for agent(s) that show no evidence for carcinogenicity in at least two adequate animal tests in different species or in both epidemiologic and animal studies.

+ Under specific circumstances, such as the production of neoplasms that occur with high spontaneous background incidence, the evidence may be decreased to "limited" if warranted (e.g., there are widely diverging scientific views regarding the validity of the mouse liver tumor as an indicator of potential human carcinogenicity when this is the only response observed, even in replicated experiments in the absence of short-term or other evidence).

§ Benign and malignant tumors will be combined unless the benign tumors are not considered to have the potential to progress to the associated malignancies of the same morphologic type.

APPENDIX G

Sample Air Guidelines Using Proposed Approach

SAMPLE GUIDELINES USING PROPOSED APPROACH

Chemical	Health effects or symptoms at low levels	TLV-TWA	TLV-STEL	Adjustment for continuous exposure	Variation in susceptibility	Chronicity	Severity of effect	Composite factor	Suggested guideline	Averaging time
Acute Irritants										
Acetaldehyde	eye and respiratory tract irritation	100 ppm	150 ppm	-	10	-	-	10	15 ppm	15 min
Ammonia	eye and respiratory tract irritation	25	35	-	10	-	-	10	3.5	15 min
Acute Systemic Toxicants										
Hydrogen sulfide	respiratory tract irritation, conjunctivitis, keratosis, nervousness, nausea, headache, insomnia	10 ppm	15 ppm	-	10	-	1	10	1.5 ppm	15 min
Methyl isobutyl ketone	reversible renal damage	50	75	-	10	-	1	10	7.5	15 min
Nitrobenzene	Methemoglobinemia, headache, vertigo	1	-	-	10	-	1	10	0.1	1 hr
Chronic Toxicants										
Carbon disulfide	cardiovascular effects	10 ppm	-	4	10	2	2	160	0.062 ppm	24 hr
Toluene	narcosis, headaches, lassitude, nausea, anorexia, decreased erythrocyte count, liver enlargement	100	150	4	10	2	1	80	1.25	24 hr

SAMPLE AIR GUIDELINES

(Continued)

Carcinogens	Action Level	Averaging Time
Group A: (10^{-6} risk level)		
Arsenic	2×10^{-7} mg/m^3	Annual
Benzene	1.4×10^{-4}	"
Bischloromethyl ether	2.9×10^{-6}	"
Group B: (10^{-5} risk level)		
Acrylonitrile	1.4×10^{-4}	"
Cadmium	4×10^{-6}	"
Carbon tetrachloride	7×10^{-4}	"
Epichlorohydrin	4.5×10^{-2}	"
EDB	2×10^{-5}	"