EPA-600/2-76-155
June 1976

Environmental Protection Technology Series

ESTIMATION OF PERMISSIBLE CONCENTRATIONS OF POLLUTANTS FOR CONTINUOUS EXPOSURE

Industrial Environmental Research Laboratory
Office of Research and Development
U.S. Environmental Protection Agency
Research Triangle Park, North Carolina 27711

RESEARCH REPORTING SERIES

Research reports of the Office of Research and Development, U.S. Environmental Protection Agency, have been grouped into five series. These five broad categories were established to facilitate further development and application of environmental technology. Elimination of traditional grouping was consciously planned to foster technology transfer and a maximum interface in related fields. The five series are:

1. Environmental Health Effects Research
2. Environmental Protection Technology
3. Ecological Research
4. Environmental Monitoring
5. Socioeconomic Environmental Studies

This report has been assigned to the ENVIRONMENTAL PROTECTION TECHNOLOGY series. This series describes research performed to develop and demonstrate instrumentation, equipment, and methodology to repair or prevent environmental degradation from point and non-point sources of pollution. This work provides the new or improved technology required for the control and treatment of pollution sources to meet environmental quality standards.

EPA REVIEW NOTICE

This report has been reviewed by the U.S. Environmental Protection Agency, and approved for publication. Approval does not signify that the contents necessarily reflect the views and policy of the Agency, nor does mention of trade names or commercial products constitute endorsement or recommendation for use.

This document is available to the public through the National Technical Information Service, Springfield, Virginia 22161.

EPA-600/2-76-155
June 1976

ESTIMATION OF PERMISSIBLE CONCENTRATIONS OF POLLUTANTS FOR CONTINUOUS EXPOSURE

by

Robert Handy and Anton Schindler

Research Triangle Institute
P.O. Box 12194
Research Triangle Park, North Carolina 27709

Contract No. 68-02-1325, Tasks 34 and 46
Program Element No. EHE624

EPA Task Officer: Max Samfield

Industrial Environmental Research Laboratory
Office of Energy, Minerals, and Industry
Research Triangle Park, NC 27711

Prepared for

U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Research and Development
Washington, DC 20460

PREFACE

This report was prepared for the Industrial Environmental Research Laboratory - RTP, Environmental Protection Agency, to present results of the work carried out by RTI under Contract No. 68-02-1325 (Task 34). This work was performed in the Chemistry and Life Sciences Division of the Research Triangle Institute. The authors thank Dr. Max Samfield, EPA Task Officer, for many helpful discussions during the preparation of this document.

Approved for:

RESEARCH TRIANGLE INSTITUTE

Monroe E. Wall

Monroe E. Wall, Ph.D.
Vice President
Chemistry and Life Sciences Division

CONTENTS

		Page
List of Figures		vii
List of Tables		ix
Sections		
I	Introduction	1
II	Summary	3
	A. Ambient Air Concentrations	3
	B. Drinking Water Concentrations	4
	C. Carcinogens in Ambient Air	5
	D. Equations for Estimating Permissible Pollutant Concentrations	6
III	Permissible Ambient Air Concentrations	11
	A. Table of Symbols and Definitions	11
	B. Caveats	13
	C. Kinetics of Pollutant Accumulation in the Body	13
	D. Application of Kinetic Considerations	17
	E. Correlation Between TLV Standards and LD_{50} Values	21
	F. Estimation of Maximum Permissible Air Concentrations from Known LD_{50} Values	36
	G. Estimation of Air Quality Standards for Multicomponent Systems	42
	H. Estimation of Maximum Ground Level Concentrations from Stack Emission of Stationary Sources	43
IV	Permissible Drinking Water Concentrations	46
	A. Table of Symbols and Definitions	46
	B. Caveats	47
	C. Derivation of EPA Proposed Drinking Water Standards	47
	D. Stokinger-Woodward Treatment - Method I	49
	E. Estimation of Permissible Drinking Water Standards - Method II	52
	F. Estimation of Permissible Drinking Water Standards - Method III	60
	G. Estimation of Permissible Drinking Water Standards for Multicomponent Systems	63
	H. Comparison of Methods I, II, and III	66

CONTENTS (Continued)

Sections		Page
V	Carcinogens in Ambient Air	71
	A. Table of Symbols and Definitions	71
	B. Caveats	72
	C. Carcinogen Content in Cigarette Smoke and Intake by Smokers	72
	D. Lung Cancer Mortality as a Function of Individual Smoking Habits and Age	74
	E. Relationship of Lung Cancer Mortality and Age/Duration of Exposure	76
	F. Relationship of Lung Cancer Mortality and Carcinogen Concentration in Ambient Air	80
	G. Lung Cancer Mortality Estimates for the General Population	85
VI	References	94
VII	Appendices to Section III	96
	A. Effect of Age on the Build-Up of Body Concentration	96
	B. Average Accumulated Body Concentration During Intermittent Exposure	109
	C. Nomographic Correlation of Stack Emission Rates and Maximum Ground Level Concentrations	119

FIGURES

No.		Page
1	Accumulated Body Burden in mg/kg for Different Starting Times of Continuous Exposure to Polluted Air Containing 1 $\mu g/m^3$ Pollutant	22
2	Body Burden in mg/kg Accumulated During Continuous Exposure to Air Containing Different Concentrations of Pollutant	23
3	Plot of lg (TLV) versus lg (LD_{50}) for 30 Agricultural Chemicals	27
4	Plot of lg (TLV) versus lg (LD_{50}) for 50 Agricultural Chemicals	28
5	Plot of lg (TLV) versus lg (LD_{50}) for 191 Non-Agricultural Compounds	34
6	Plot of lg (TLV) versus lg (LD_{50}) for 191 Non-Agricultural and 50 Agricultural Compounds	35
7	Lung Cancer Mortality Versus Age and Cigarette Use	75
8	Nonsmoker Lung Cancer Mortality Versus Age	79
9	Lung Cancer Mortality Versus Duration of Exposure and Cigarette Use	81
10	Lung Cancer Mortality Versus Carcinogen Intake Rate	82
11	Lung Cancer Mortality Versus Carcinogen Air Concentration	84
12	Lung Cancer Mortality Versus Carcinogen Air Concentration - Dorn Study	88
13	Lung Cancer Mortality versus Carcinogen Air Concentration - General Population	90
14	Age Dependence of Breathing Frequency	102
15	Ratio of Body Concentration to Effective Pollutant Concentration in Air for Pollutants with Different Half-Life Times in the Body. Calculated for Age Dependent Breathing Frequency	103
16	Ratio of Body Concentration to Effective Pollutant Concentration in Air for Pollutants with Different Half-life Times in the Body Calculated for the Constant Breathing Frequency of an Adult	104
17	Effect of Age Dependent Breathing Frequency on the Body Concentration of Pollutants with Different Half-Life Times in the Body	105
18	Comparison of the Body Concentrations of Children and Adults Exposed to the Same Level of a Pollutant with a Half-Life Time in the Body of 36 Days	107

FIGURES (Continued)

No.		Page
19	Body Concentration Versus Time During Intermittent Exposure to p-Nitrophenol With a Known Biological Half-life Time in Man of 0.99 Hrs. Weekends not Considered	113
20	Body Concentration Versus Time During Intermittent Exposure to Dinitro-o-cresol With a Known Biological Half-Life Time in Man of 139 Hrs. Weekends not Considered	114
21	Effect of Weekends on the Body Concentration During Intermittent Exposure to p-Nitrophenol With a Biological Half-Life Time in Man of 0.99 Hrs.	116
22	Effect of Weekends on the Body Concentration During Intermittent Exposure to a Pollutant With an Assumed Biological Half-Life Time of 72 Hrs.	117
23	Effect of Weekends on the Body Concentration During Intermittent Exposure to Dinitro-o-cresol With a Biological Half-Life Time in Man of 139 Hrs.	118
24	Nomographic Example for the Determination of Plume Rise Above Stack by Holland's Equation	123
25	Distance of Maximum Concentration and Maximum (xu/Q)-Value As a Function of Weather Condition and Effective Height of Emission	125
26	Horizontal Dispersion Coefficient As a Function of Downwind Distance From the Source	127
27	Vertical Dispersion Coefficient As a Function of Downwind Distance From the Source	128
28	Nomographic Example for the Calculation of Stack Emission Rate for Which the Maximum Ground Level Concentration Does not Exceed a Permissible Value	130
29	Nomographic Example for the Calculation of Maximum Ground Level Concentration Resulting from Given Stack Emission Rate	132
30	Nomograph for the Estimation of Plume Rise Above Stack by Holland's Equation	135
31	Nomograph for the Correlation of Stack Emission Rates and Maximum Ground Level Concentrations	136

TABLES

No.		Page
1	Comparison of Calculated Maximum Permissible Pollutant Concentrations with EPA Standards	9
2	Respiration Data as Dependent on Age and Weight	15
3	Biological Half-Life Times of Different Compounds	19
4	Maximum Body Concentration for Continuous Exposure Calculated from TLV and Half-Life Times Determined on Man	19
5	Maximum Body Concentration for 8 Working Hours Exposure Calculated From TLV and Half-Life Times Determined on Man	20
6	TLV Standards and LD_{50} Values for Different Agricultural Compounds	25
7	List of TLV Standards and LD_{50} Values for Different Chemical Compounds	29
8	Permissible Air Concentrations for Continuous Exposure Estimated by Different Methods	40
9	Maximum Stationary Body Concentration Accumulated During Working Conditions (40 Hour Workweek) for Selected Inorganic Compounds	41
10	Analysis of a Multicomponent System (Selected Values for Los Angeles Air)	44
11	Derivation of EPA Proposed Drinking Water Standards for Pesticides	48
12	Derivation of EPA Proposed Drinking Water Standards for Inorganic Chemicals	50
13	Calculated Water Standards - Inorganic, Method I	51
14	Estimated Water Standards - Inorganic, Method II	55
15	Comparison of Proposed and Estimated Standards - Inorganic, Method III	56
16	Estimated Standards - Pesticides, Method II	57
17	Toxicity Data - Inorganic	59

TABLES (Continued)

No.		Page
18	Estimated Water Standards Using Assumed Half-Life - Inorganics, Method III B	64
19	Estimated Water Standards Using Assumed Half-Life - Pesticides, Method III C	65
20	Analysis of a Multicomponent System - Inorganics (Method III B)	67
21	Analysis of a Multicomponent System - Pesticides (Method III C)	68
22	Comparison of Methods I, II, III A, III B	69
23	Carcinogen Hydrocarbons Isolated from Cigarette Smoke	73
24	Carcinogen Intake for Smokers as a Function of Number of Cigarettes Smoked per Day	73
25	Lung Cancer Mortality as a Function of Smoking Pattern and Age	77
26	Estimated Lung Cancer Mortality of 45-54 Year Old Cigarette Smokers	78
27	Carcinogen Intake and Equivalent Air Concentration for Nonsmokers	78
28	Carcinogen Concentration in Ambient Air Equivalence to Carcinogen Intake	78
29	Estimated Nonsmoker Lung Cancer Death Rate as a Function of Carcinogen Concentration in Ambient Air	86
30	Lung Cancer Mortality versus Carcinogen Intake for Dorn Study Group Age 45-84	87
31	Estimated Nonsmoker Lung Cancer Mortality as a Function of Carcinogen Air Concentration	92
32	Carcinogen Concentrations Found in Ambient Air	93
33	Respiration Data as Dependent on Age and Weight	98

SECTION I

INTRODUCTION

The EPA has set several maximum concentration exposure levels for environmental pollutants in both air and water. However, there are many known toxic materials for which no safe concentration levels have been established. The main objective of this report was to derive pollutant hazard criteria for this group of compounds in order that safe, permissible concentrations in the environment might be estimated. The proposed permissible pollutant levels derived in this report were not intended to challenge present EPA standards. The mention of EPA standards in this report is for comparison purposes only. In their present form these estimated values serve only as a guide in assessing potential pollution hazards in lieu of official standards.

This report discusses the basis of estimating permissible pollutant levels in ambient air (Section III) and drinking water (Section IV). In addition a correlation between carcinogen exposure and lung cancer deaths was developed and presented as a guide for estimating the effect of carcinogen emissions in ambient air on the risk of lung cancer mortality (Section V).

The hazard criterion expressions were developed in the form of a ratio (actual pollutant concentration/permissible pollutant concentration). When this quotient was equal to or greater than one, a pollution hazard was judged to exist.

Several approaches were used to estimate safe concentration values. Expressions were derived using TLV and/or LD_{50} animal data, employing known or assumed biological half-lives.

Estimates for air pollution were based on episodes of continuous exposure and the use of the tidal volume to body weight relationship of infants. This model system took into account the higher pulmonary intake per unit weight characteristic of younger children.

The effect of source emission rates on ground level concentrations were assessed. The results were presented in the form of a nomograph which provides a simple means of correlating stack emission rates and ground level concentrations as a function of weather and source characteristics.

Permissible pollutant concentrations in drinking water were developed along the same lines. The first treatment employed derived TLV levels calculated from reported LD_{50} data by a method described in Section III. The second approach was based on fundamental biological concepts. Pollutant hazard criteria were derived using animal LD_{50}, human half-life data and an assumed safe maximum pollutant body concentration.

The final expressions were also used to treat multipollutant systems in both air and drinking water.

A means for estimating lung cancer mortality risk as a function of carcinogen concentrations in ambient air was presented in Section V. Since lung cancer mortality data for smokers was the best human dose response data available, this information was used to correlate carcinogen exposure and lung cancer death rate. This was accomplished by first determining the carcinogen intake by individuals smoking different number of cigarettes over varying time periods. Lung cancer mortality data for nonsmokers and different categories of cigarette smokers at different ages were used to correlate lung cancer death rate with carcinogen intake. Finally, a carcinogen content in ambient air equivalent to cigarette carcinogen intake was calculated and related to years of exposure.

This treatment allowed one to determine carcinogen air levels to which nonsmokers are exposed and to estimate the lung cancer mortality for nonsmokers exposed to any given carcinogen ambient air concentration. Since no threshold limit has been established for carcinogenic materials, the results must be expressed as <u>risk</u> versus carcinogen concentration.

The results of this treatment will be used by IERL for developing guidelines for estimating the effect of carcinogen emissions in ambient air on lung cancer mortality risk.

SECTION II
SUMMARY

A. Ambient Air Concentrations

Assessment of health hazards associated with air pollutants from process industries was complicated by the lack of established TLV standards for many pollutants. In cases where TLV standards had not been set, two different approaches were followed: (1) A method was developed for obtaining safe estimates of the TLV. (2) A different method based on pollutant accumulation in the body was established.

The first approach was based on the correlation between TLV standards and LD_{50} values of different compounds. This approach represented an extension of work started by Monsanto Research Corp. on 30 selected agricultural chemicals.[1] Increasing the sample size by 20 additional agricultural chemicals and 191 compounds for which both the TLV standards and the LD_{50} values could be retrieved from literature, a regression analysis yielded an equation of the form:

$$(TLV) = 0.029\ (LD_{50})^{0.983}$$

The lower 95% confidence limit of the above given regression line was then given to a very good approximation by:

$$(TLV)_{low} = 4.5 \times 10^{-4}\ (LD_{50})$$

Based on this relationship, an equation was derived which permitted estimation of safe ambient air concentrations of pollutants for which LD_{50} data was available. Since a one year old infant has approximately twice the respiratory frequency as an adult, a safety factor of two was introduced into the decision criterion. This expression differed from one proposed by the Chemical Process Section of EPA on the following points: (1) The criteria was based on LD_{50} values rather than TLV, making it applicable to a greater number of pollutants. (2) The factor

for converting intermittent exposures to continuous exposure has been adjusted to a weekly basis. The TLV is multiplied by 40/168, the fraction of time one is exposed to a working place environment. (3) The safety factor of (1/100) has been omitted because of the use of the low estimate of TLV from LD_{50}. (4) The relative susceptibility of young children has been taken into account.

The second approach was based on biological considerations. Data on biological half-lifes of different compounds in combination with their presently used TLV standards indicated that a stationary maximum body concentration corresponding to about 0.05% of the LD_{50} value of the compound can be considered safe. Assuming a half-life of 30 days, a maximum permissible air concentration for continuous exposure can be calculated for which the accumulation of pollutant in the body will never exceed 0.05% of its LD_{50} value. Results of both approaches were very similar, the criteria values differing by only approximately 10%.

When two or more hazardous substances are present, their combined effect, rather than that of either individually, should be considered as proposed by the American Conference of Governmental Industrial Hygienists.[2]

B. Drinking Water Concentrations

Stokinger and Woodward derived an expression for estimating safe pollutant drinking water limits.[3] They assumed that the amount of pollutant contained in 10 m^3 of air at the TLV concentration may be safely ingested daily in drinking water. Knowledge of pollutant respiratory and gastrointestinal absorption efficiencies was required and the daily consumption of 2 liters of drinking water was assumed. The limited number of compounds for which TLVs have been assigned and the still fewer substances with known abosrption efficiencies restricts the general applicability of this method.

Applying the $(TLV)_{low}$ concept developed in Section III to this problem yielded a pollutant hazard criterion expression of much greater utility. Estimated drinking water standards were then calculated by

substituting $(TLV)_{low}$ for TLV in the Stokinger-Woodward equation[3] and assuming complete respiratory and gastrointestinal absorption.

Another approach based on kinetic considerations is summarized below. The assumption made in this treatment were as follows:

a) Human disposition of a foreign substance was approximated by a single compartment system with first order kinetics.

b) A maximum body pollutant concentration equal to 0.05% of its LD_{50} can be considered safe.

The estimated safe drinking water concentration of a pollutant was expressed as a function of its LD_{50} and biological half-life. When the half-life of the compound was not known, a value for this parameter was assumed.

a) A thirty (30) day half-life is asusmed for all compounds excepting those known to be retained in the body for prolonged periods of time (e.g., chlorinated pesticides storage in adipose tissue).

b) A one year (365 day) half-life is assumed for those exceptions noted above.

C. Carcinogens in Ambient Air

The content of eight carcinogenic hydrocarbons in cigarette smoke has been determined (10.8 μg/100 cigarettes).[4] This information was used to calculate the rate of carcinogen intake for individuals smoking different numbers of cigarettes/day. Lung cancer mortality figures for nonsmokers and smokers (use of 1-9, 10-19, 20-39 and more than 39 cigarettes/day) at different ages (35-44, 45-54, 55-64, 65-74 and 75-84 years old) were available[5] and used to correlate carcinogen intake with lung cancer death rates. Plotting these data on a log-log scale indicated a linear relationship between these parameters and permitted extrapolation to low carcinogen intake values.

A linear relationship also existed between lung cancer mortality and age (or years of exposure) when plotted on a log-log scale. This relationship held for nonsmokers and individuals smoking different numbers of cigarettes/day.

Plotting lung cancer death rate against ambient air carcinogen concentration on a log-log scale gave a linear relationship which allowed ready estimation of mortality risk as a function of carcinogen air level. This treatment indicated that urban air concentration of 20 ng/m^3 would result in a lung cancer death risk of approximately 40/100,000, an increase of 150 percent over the reported nonsmoker rate. This level of contamination corresponds to smoking approximately 3 cigarettes/day.

D. Equations for Estimating Permissible Pollutant Concentrations

The expressions for the estimation of permissible pollutant concentrations are listed below. As shown, the particular form of the equation will depend on the data available for the pollutant under evaluation.

Ambient Air

Case I - TLV unknown, LD_{50} known

This case will be encountered most often. The oral LD_{50} (mg/kg) for rats should be used if known. It may be necessary to use the oral LD_{50} for mice. If the oral LD_{50} is not known, one should use the LD_{50} obtained by intraperitoneal injections. Avoid the use of intramuscular LD_{50} data. The permissible ambient air concentration, x_p (mg/m^3), is given by the following equation:

$$x_p = 4.77 \times 10^{-5} (LD_{50})$$

Case II - TLV known, LD_{50} unknown

This is a less common situation. A derived LD_{50} is computed from the equation,

$$LD_{50} = 34.5 \text{ TLV},$$

and used directly in the expression given in Case I.

Alternatively, the following equivalent equation may be used:

$$x_p = 1.65 \times 10^{-3} \text{ (TLV)}$$

Case III - TLV and LD_{50} known

Use the TLV and proceed as in Case II.

Case IV - TLV unknown, LD_{50} and biological half-life for man are known.

This case will not be encountered often, since the half-lives of most compounds in man are not known. However, the equations do provide for taking this into consideration if the information is available:

$$x_p = \frac{(14.2 \times 10^{-4})\ (LD_{50})}{\tau}$$

where τ is the biological half-life in days.

Drinking Water

Case I - TLV unknown, LD_{50} known

For inorganic compounds, the ionic LD_{50} for ion consideration is computed from the LD_{50} for the compound. The ionic LD_{50} is defined as:

$$\text{Ionic } LD_{50} = \frac{(\text{Compound } LD_{50})\ (\%\text{ content of metal or anion})}{100}$$

a) For most organic and inorganic compounds, excluding those that are known to be retained in the body for prolonged periods of time (e.g., chlorinated pesticides which are stored in adipose concentration, x_e (mg/l), compute from the following equation:

$$x_e = 4.0 \times 10^{-4}\ (LD_{50})$$

b) For those compounds that are known to be retained by the body for long periods of time, use the equation:

$$x_e = 3.3 \times 10^{-5}\ (LD_{50})$$

Case II - TLV known, LD_{50} unknown

A derived LD_{50} is computed from the equation,

$$LD_{50} = 34.5 \text{ TLV},$$

and used directly in the appropriate expression given in Case I. The equivalent equations for relating TLV directly to x_e are shown below.

a) $x_e = 1.38 \times 10^{-2}$ (TLV)

b) $x_e = 1.14 \times 10^{-3}$ (TLV)

Case III - TLV and LD_{50} known

Use the TLV and proceed as in Case II.

Case IV - TLV unknown, LD_{50} and biological half-life for man are known.

When the LD_{50} and biological half-life, τ, is known, the following equation should be used.

$$x_e = \frac{.012\ (LD_{50})}{\tau}$$

The ionic LD_{50} is used for inorganic compounds.

Carcinogens in Ambient Air

Since threshold values for carcinogenic substances have not been established, an attempt was made to relate cancer risk versus ambient air concentrations. Data on carcinogen intake for smokers, and lung cancer mortality figures for smokers and non-smokers, were used in relating lung cancer mortality and equivalent ambient air levels of carcinogens. The results seem to indicate that the "lowest concentration of concern" (equivalent to 1 ng/m^3 in ambient air) represents a practical limit of risk, and therefore a reasonable "permissible" concentration for establishing control technology R&D priorities.

Comparison of Air and Water Pollutant Standards With Calculated Safe Continuous Exposure Levels

Table 1 shows the comparison for 23 substances for which standards have either been set or proposed. The permissible exposure levels were calculated as outlined above.

Table 1. COMPARISON OF CALCULATED MAXIMUM PERMISSIBLE POLLUTANT CONCENTRATIONS WITH EPA STANDARDS

Continuous 24 hr. Exposure

A. Air ($\mu g/m^3$)

Substance	EPA Standard	Calculated	Ratio Stnd./Calc.
NO_2	100	15	6.66
SO_2	80	22	3.64
*Be	0.01	0.003	3.33
*Hg	1.0	0.082	12.2

*EPA emission rate standards based on indicated 24 hr. exposure

B. Water (mg/l)

Substance	EPA Standard	Calculated	Ratio Stnd./Calc.
Chlordane	0.003	0.009	0.33
Endrin	0.0002	0.0001	2.00
Heptachlor	0.001	0.0013	0.77
Lindane	0.004	0.003	1.33
Methoxychlor	0.10	0.165	0.61
Toxaphene	0.005	0.002	2.50
2, 4-D	0.10	0.012	8.4
2, 4, 5-TP (Silvex)	0.01	0.021	0.47
Ag	0.05	0.013	3.84
As	0.05	0.002	25
Ba	1.0	0.040	25
Cd	0.01	0.022	0.46
CN	0.20	0.001	200 (!!)
Cr	0.05	0.011	4.55
F	1.4-2.4	0.032	43.6-75
Hg*	0.002	0.046	0.435
NO_3 (as N)	10.0	0.092	109 (!!)
Pb	0.05	0.068	0.74
Se	0.01	0.001	10

* Based on MeHg (τ = 70 days)

The following observations were noted:

(1) For 16 of the 23 substances, calculated levels were on the "safe" side.

(2) Only seven of the 23 calculated permissible levels differed by more than an order of magnitude.

(3) All of the seven that differed by more than an order of magnitude were among the metals and anions (Hg, As, Ba, CN, F, NO_3 and Se). The worst agreement was noted with cyanide, fluoride and nitrate.

The use of a 30 day half-life in the case of cyanide and fluoride certainly overestimates the residence time of these pollutants in the body. Use of more realistic half-lives and the Case IV equations given above would better reflect potential pollutant hazards. Nitrate toxicity mainly affects small children. It is significant that a drinking water limit of 1 mg NO_3 - N/l has been suggested for infant feeding.[6]

SECTION III

PERMISSIBLE AMBIENT AIR CONCENTRATIONS

A. Table of Symbols and Definitions

a	ordinate intercept of the regression line lg(TLV) on $lg(LD_{50})$
b	slope of regression line lg(TLV) on lg (LD_{50})
B	rate constant for pollutant uptake by respiration (m^3/kg day)
c	instantaneous pollutant concentration in the body (mg/kg)
c_m	maximum stationary body concentration (mg/kg)
C_o	initial pollutant concentration in the body (mg/kg)
C_{70}	final pollutant concentration in the body after 70 years accumulation without excretion
f	respiratory frequency (day^{-1})
F (t)	breathing frequency as function of age
gpg	guinea pig
imp	implant
ims	intramuscular
ipr	intraperitoneal
itr	intratracheal
k	first order rate constant of excretion (hr^{-1})
LD_{50}	lethal dose 50% kill (mg/kg)
LDL_o	lowest published lethal dose (mg/kg)
mus	mouse
orl	oral
Q	constant ratio of tidal volume to body weight (ml/kg)
rbt	rabbit
R_{uptake}	rate of pollutant uptake (mg/kg.day)
t	time (hours or days as stated)
TDL_o	lowest published toxic dose (mg/kg)
TLV	threshold limit value (mg/m^3)
$(TLV)_{low}$	lower 95% confidence limit for TLV estimated from LD_{50} (mg/m^3)
V_T	tidal respiratory volume (ml)
W	body weight (kg)
x	pollutant concentration in air (mg/m^3)

Table of Symbols and Definitions (Continued)

x_m	maximum ground level concentration (mg/m^3)
$(x_m)_i$	maximum ground level concentration of the i-th pollutant (mg/m^3)
x_p	maximum permissible air concentration (mg/m^3)
$(x_p)_i$	maximum permissible air concentration of the i-th pollutant (mg/m^3)
α	absorption factor for respiratory uptake of pollutant
τ	biological half-life time of pollutant in the body (hours or days as stated)

B. Caveats

The treatment described in this section was based, in part, on the following assumptions and limitations.

(1) The presented method of estimating permissible air concentrations is not applicable to pollutants with known carcinogenic, teratogenic, or mutagenic effects. A treatment of of carcinogens in ambient air is presented in Section V.

(2) The biological treatment was based on a one-compartment model with a single, first order excretion rate.

(3) It was assumed that all pollutants entering the respiratory system were retained by the body.

(4) The treatment was based on the assumption that LD_{50} values for animals were applicable to man.

(5) No allowance was made for synergism of pollutants in multicomponent systems.

(6) The derived equations are directly applicable only when the half-life of the pollutant is relatively short compared to the assumed life of the individual.

C. Kinetics of Pollutant Accumulation in the Body

Estimation of maximum permissible air concentrations of pollutants, x_p in mg/m^3, depends on the model used. In order to make the proper choice, some general kinetic considerations seem to be appropriate.

The simplest mathematical model describing the accumulation of inhaled pollutant in the body is derived from a one-compartment model. In this system, all of the pollutant entering the body through the respiratory system is evenly distributed over the whole body. Consequently, the amount of absorbed pollutant can be related to the total body weight. It is obvious that this model does not apply for particulates which remain trapped in the lung and exhibit only localized effects.

The rate of pollutant uptake per unit of body mass is given by

$$R_{uptake} = V_T f \alpha x / W$$

where V_T ..... tidal respiratory volume (m^3),
f ..... respiratory frequency (day^{-1}),
α ..... absorption factor determining the fraction of the inhaled compound entering the body; $1-\alpha$ is equal to the exhaled fraction of the pollutant,
x ..... air concentration of pollutant (mg/m^3),
W ..... body weight (kg.).

Three of the variables determining the rate of pollutant uptake change considerably with age. Table 2 gives values of W, f, and V_T for different ages. Ratios of V_T/W calculated for different ages are presented in column 5 of Table 2. These values reveal that for all practical purposes the ratio of V_T/W can be considered constant and independent of age.

$$V_T/W = Q = (6.36 \pm 0.38) \times 10^{-6}\ m^3.kg^{-1} \qquad (2)$$

Equ. (1) then takes the form

$$R_{uptake} = Q\alpha x F(t) \qquad (3)$$

where F(t) is a function which describes the age dependence of the average breathing frequency.

The effect of changes in breathing frquency with age on the uptake of pollutant is dealt with explicitly in the Appendix, Section VII-A. From this treatment a correction factor is derived which is applied to the decision criteria for adults to provide the same level of protection for young children. This application will be discussed after the mechanism of respiratory pollutant uptake has been developed for adults.

The breathing frequency of adults over the age of 18 can be considered constant as shown by respiratory data of Table 2. Assuming $\alpha = 1$, equ. (3) can be simplified by setting

$$B = QF(t) = \text{const.} \qquad (4)$$

Table 2. RESPIRATION DATA AS DEPENDENT ON AGE AND WEIGHT

Age (Years)	Weight (kg) (Ref. 7)	Breathing Frequency (min^{-1}) (Ref. 8)	Tidal Volume (ml) (Ref. 9)	Tidal Vol./ Weight (ml/kg) (*)	Calculated Breathing Rate (ml/min)	(m^3/year)
0	3.4	38 ± 10[10]	13 ± 5[10]	(3.82)	480 ± 227 [10]	252
1	10.4	31	67	6.44	2,050	1,077
2	12.7	26	87	6.85	2,100	1,104
3	14.5	25	98	6.76	2,305	1,212
4	16.8	24	110	6.55	2,564	1,348
5	19.1	23	130	6.81	2,795	1,469
6	21.3	22	150	7.04	2,980	1,566
7	24.5	21	162	6.61	3,272	1,720
8	27.2	20	180	6.62	3,460	1,819
9	29.9	20	190	6.35	3,800	1,997
10	33.1	19	220	6.65	4,000	2,102
11	37.2	19	235	6.31	4,495	2,363
12	39.5	19	245	6.20	4,773	2,509
13	44.9	19	275	6.12	5,426	2,852
14	51.3	19	300	5.85	6,200	3,259
15	58.1	18	340	5.85	6,651	3,496
16	62.1	17	365	5.88	6,714	3,529
17	64.9	17	380	5.86	7,017	3,688
18	67.6	16	405	5.99	6,878	3,615
19	69.4	16	420	6.05	7,062	3,712
22	71.7				7,000	3,679
27	73.9				7,000	3,679
32	74.8				7,000	3.679
37	75.3				7,000	3,679
44	75.8				7,000	3,679
54	74.8				7,000	3,679
64	73.5				7,000	3,679
74	71.2				7,000	3,679

* Average value of 6.36 ± 0.38 (ml/kg) used for further calculations.

The rate of pollutant uptake in adults is given by equ. (5).

$$R_{uptake} = Bx \tag{5}$$

The value of B in m^3/kg-day is equal to the daily tidal respiratory volume per kg body weight assuming all of the inhaled pollutant is absorbed, $\alpha = 1$. For a 70 kg adult, the value of B is 0.143 m^3/kg day, according to the respiratory data presented in Table 2.

The pollutant accumulating in the body is metabolized and excreted either unchanged or in form of metabolites. The rate of excretion can be assumed to be proportional to the instantaneous pollutant concentration in the body, c, i.e., the excretion proceeds according to a first order rate law given either by

$$-dc/dt = kc \tag{6}$$

or in its integrated form by

$$c = c_0 \exp(-kt). \tag{7}$$

From equ. (7) one obtains the biological half-life time, τ, which is equal to the time interval during which the body concentration decreases to half its value provided there is no uptake during this interval.

$$\tau = \ln 2/k. \tag{8}$$

The actual change of the concentration of the pollutant in the body is then generally described by combining equs. (5) and (6), and is given by

$$dc/dt = Bx - kc. \tag{9}$$

Equation (9) indicates that after a prolonged time the body concentration approaches a steady state with a constant value c_m corresponding to the maximum body concentration under given conditions which is given by

$$c_m = Bx/k \tag{10}$$

or, after substituting the half-life time of the pollutant from equ. (8), by

$$c_m = Bx\tau/\ln 2. \tag{11}$$

The integrated equ. (9), assuming B is constant, describes the accumulation of pollutant in the body with time provided the air concentration remains constant.

$$c = (Bx/k)\ [1 - \exp(-kt)] + C_0 \exp(-kt) \tag{12}$$

The value C_0 corresponds to the initial body concentration at the start of the exposure. If there was no previous exposure to the pollutant under consideration equ. (12) simplifies to

$$c = (Bx/k)\ [1 - \exp(-kt)]. \tag{13}$$

From equ. (13) one can calculate the time necessary to accumulate half the stationary maximum body concentration c_m. This value is also given by the biological half-life time of the pollutant, τ. Provided the pollutant concentration in the air remains constant, it takes about 7 half-lifes for the pollutant to approach a steady state concentration within 1%.

D. Application of Kinetic Considerations

Utilization of Biological Half-Life

The basic equation, equ. (11), describing the stationary maximum body concentration, was simplified by substituting numerical values for the constants, B = 0.143 and ln2 = 0.693. This was approximated by equ. (14),

$$c_m = x\tau/5. \tag{14}$$

Equation (14) provides a good estimate for permissible air concentrations of pollutants as a function of the biological half-life of the pollutant, τ, and the maximum body concentration, c_m, which does not cause adverse health effects over extended periods of time. Unfortunately, both values are not known for the majority of compounds.

In Table 3, biological half-lifes for a very small number of compounds are presented which could be retrieved from the literature. Most of the values were determined on man and cover a range from about 17 min to nearly 6 days.

By means of the half-life it was possible to calculate the stationary body concentration which builds up in an individual exposed to the presently permitted pollutant concentration in working room air (TLV). Data were calculated for continuous 24 hour exposure (Table 4) and for 8 working hour exposure followed by 16 hour and weekend recovery periods in unpolluted surroundings (Table 5).

The latter values are only 23.8% of the former ones. It can be shown (see Appendix B) that repeated 8 hour exposures followed by 16 hour recovery intervals decrease the average stationary body concentration to one-third of the value for continuous 24 hour exposure. By including weekends for recovery (40 hour workweek) the body concentration averaged over one week is further reduced to 23.8% of the maximum value obtained during continuous exposure.

In both Table 4 and 5, LD_{50} values (in mg/kg determined orally on rats) were included and related to the maximum body concentrations. At TLV concentration levels an individual accumulates less than 1% of the LD_{50} of the compound. Indeed, most of the C_m values were below 0.1% of the LD_{50} values. Although biological data were extremely sparse, a permissible maximum body concentration being equal to 0.05% of the LD_{50} value might be used as a guide in further estimations of permissible air concentrations.

Utilization of LD_{50} Values

Although in equ. (14) the maximum body concentration, c_m, might be replaced by 0.0005 x LD_{50} there remains still one unknown, the biological half-life time of the pollutant, in order to calculate permissible air concentrations.

It follows from equ. (14) that at constant c_m, the permissible air concentration becomes smaller with increasing values of τ. Consequently, the safest assumption would be to assume τ to be equal to infinity, i.e.,

Table 3. BIOLOGICAL HALF-LIFE TIMES OF DIFFERENT COMPOUNDS[11]

Compound	Animal	Medium or Metabolite	Coefficient of Loss (hr^{-1})	Half-Life Time (days)
Methylchloride	dog	blood	2.5	0.012
p-Nitrophenol	man	urine	0.7	0.041
Carbondisulfide	mam	expired air	0.8	0.036
"	man	metabolite	0.5	0.058
Benzene	man	blood	0.23	0.126
Toluene	man	benzoic acid	0.35	0.083
Aniline	man	p-aminophenol	0.24	0.120
Dinitro-o-cresol	man	blood	0.005	5.78
"	rat	blood	0.04	0.722
"	rbt	blood	0.1	0.289
Methanol	man	urine	0.1	0.289
"	man	formate	0.3	0.096

Table 4. MAXIMUM BODY CONCENTRATIONS FOR CONTINUOUS EXPOSURE CALCULATED FROM TLV AND HALF-LIFE TIMES DETERMINED ON MAN

Compound	Half-Life Time (days)	TLV (mg/m^3)	c_m (mg/kg)	LD_{50} (mg/kg)	$(c_m/LD_{50}) \times 100$ (%)
Methylchloride *	0.012	210	0.50	1800	0.03
Carbondisulfide	0.047	60	0.56	400	0.14
Benzene	0.126	80	2.02	3400	0.06
Toluene	0.083	750	12.45	3000	0.42
Aniline	0.120	19	0.46	440	0.10
Dinitro-o-cresol	5.78	0.2	0.23	30	0.77
Methanol	0.193	260	10.04	420	2.38

$c_m = B(TLV)\tau/\ln 2 = 0.2(TLV)\tau$ calculated for an inhalation volume of 10 m^3 per day and 70 kg body weight with the assumption of 100% absorption of the inhaled compound.

*) half-life time determined on dogs

Table 5. MAXIMUM BODY CONCENTRATION FOR 8 WORKING HOURS EXPOSURE AND 40 HOUR WORK WEEK CALCULATED FROM TLV STANDARDS AND HALF-LIFE TIMES DETERMINED ON MAN

Compound	Half-Life Time (Days)	TLV (mg/m^3)	c_m (mg/kg)	LD_{50} (mg/kg)	(c_m/LD_{50}) x 100
Methylchloride*	0.012	210	0.12	1,800	0.007
Carbondisulfide	0.047	60	0.13	400	0.033
Benzene	0.126	80	0.48	3,400	0.014
Toluene	0.083	750	2.96	3,000	0.100
Aniline	0.120	19	0.11	440	0.025
Dinitro-o-cresol	5.78	0.2	0.06	30	0.182
Methanol	0.193	260	2.39	420	0.569

$c_m = B \times (TLV) \times 0.238 \times \tau/\ln 2 = 0.0476 \times (TLV) \times \tau$

inhalation volume of 10 m^3 per day and 70 kg weight with the assumption of 100% absorption of the inhaled pollutant.

* Half-life time determined on dogs.

to make k = 0. This assumption means that there is no excretion of the absorbed pollutant and that all of the inhaled pollutant accumulates indefinitely in the body. Under this condition the body concentration c in mg/kg accumulated during the time period $t_2 - t_1$ is then given by

$$c = [x/W(t_2)] \int_{t_1}^{t_2} F(V_T f, t)\, dt \qquad (15)$$

where
- t_1 ..... age at the start of exposure
- t_2 ..... age at the end of exposure
- $W(t_2)$ ..... body weight (kg) at the end of exposure
- $F(V_T f, t)$ ..... breathing rate (tidal volume times breathing frequency) as a function of age (t)
- x ..... pollutant concentration (mg/m^3) assumed to remain constant during the time period t_2-t_1

Pertinent respiratory data for the evaluation of equ. (15) are summarized in Table 2. A graphical representation of equ. (15) is shown in Fig. 1. where final body concentrations in mg/kg are plotted versus age for an air concentration of pollutant equal to 1 $\mu g/m^3$. If the air concentration differs from 1 $\mu g/m^3$ the body concentrations have to be prorated, e.g., with an air concentration of 1 mg/m^3 all body concentrations are in g/kg. Figure 1 depicts several curves representing different starting ages with respect to exposure to polluted air (0, 5, 10, 22, 27, and 44 years of age).

In Fig. 2 a similar plot is presented demonstrating body concentrations (mg/kg) accumulated from birth (t_1 = 0 in equ. (15)) for different air concentrations of 1, 2, 5, 10, and 20 microgram/m^3.

E. Correlation Between TLV and LD_{50} Values

In order to establish safe TLV estimates one has to be guided primarily by the toxicity of the compound, and consequently, one might expect a correlation to exist between TLVs and LD_{50} values. The possibility of such a correlation was investigated by Monsanto[1] for 30 selected agricultural chemicals. In compiling the data no distinction was made between inhalation and skin TLV, and the acute oral LD_{50} was taken for male rats.

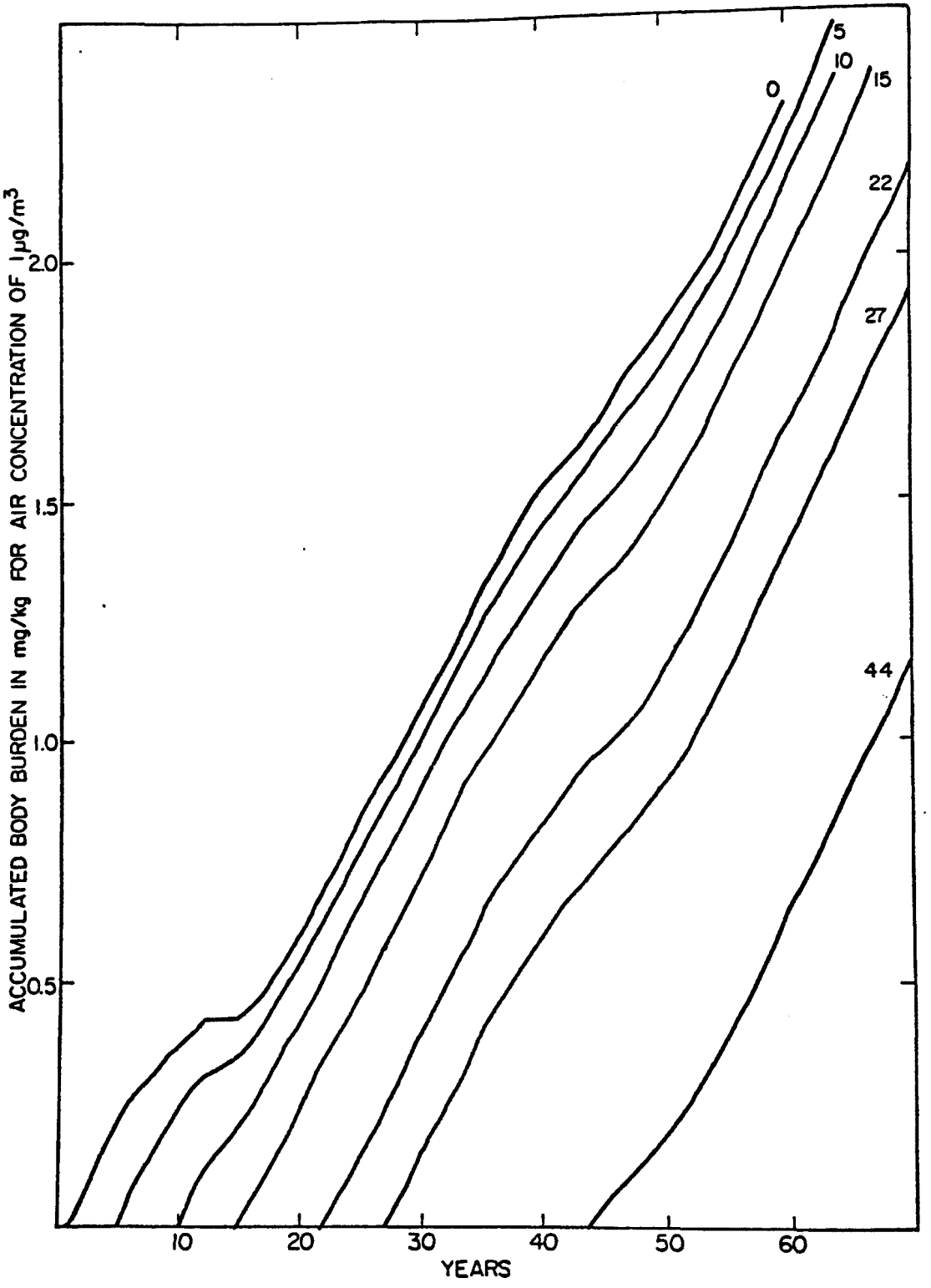


Figure 1. Accumulated body burden in mg/kg for different starting times of continuous exposure to polluted air containing 1 $\mu g/m^3$ pollutant. Curves calculated with the assumption of an infinite biological life-time of the pollutant in the body. Accompanying numbers correspond to the starting age with respect to exposure.

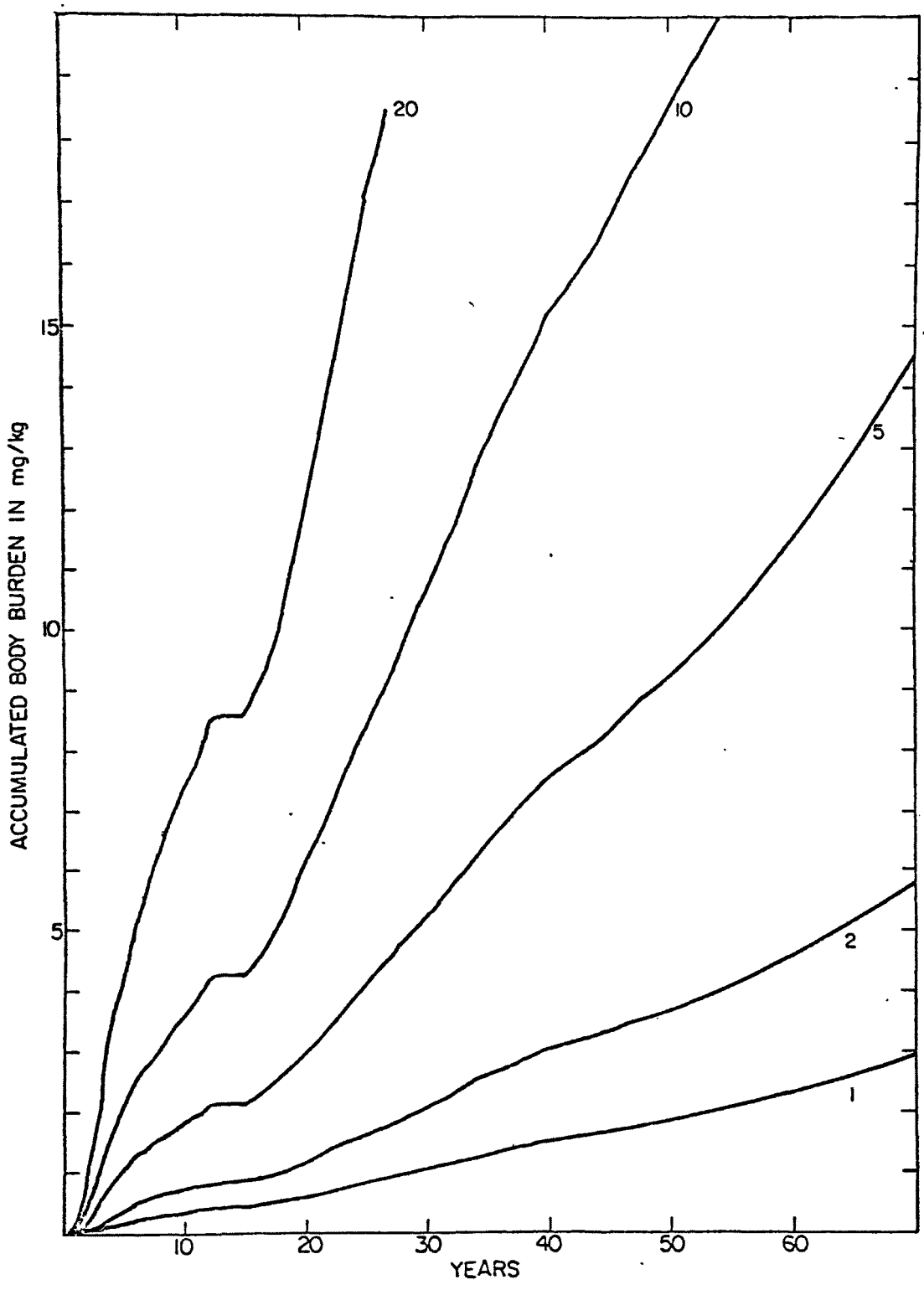


Figure 2. Body burden in mg/kg accumulated during continuous exposure to air containing different concentrations of pollutant. Curves calculated with the assumption of an infinite biological life-time of the pollutant in the body. Accompanying numbers correspond to the pollutant concentration in $\mu g/m^3$.

The best regression fit was on an equation of the type

$$(TLV) = a\ (LD_{50})^b \tag{16}$$

after logarithmic transformation to

$$\lg(TLV) = \lg a + b\ \lg(LD_{50}) \tag{17}$$

The linear regression according to equ. (17) yielded a correlation coefficient of 0.89, and the values of the constants were found to be

$$a = (0.00916 < 0.00198 < 0.0429) = 95\% \tag{18}$$

$$b = (0.629 < 0.774 < 0.920) = 95\% \tag{19}$$

Data are summarized in Table 6 and are shown graphically in Fig. 3 together with the calculated regression line and its 95% confidence range for a predicted TLV.

With additional 20 agricultural chemicals the correlation coefficient did not change. In this evaluation the lowest reported LD_{50} values were used which correspond to the underlined values in Table 6. The new constants for the enlarged sample number were

$$a = (0.0292 < 0.0483 < 0.0797) = 95\% \tag{20}$$

$$b = (0.574 < 0.675 < 0.776) = 95\% \tag{21}$$

Graphical representation of the sample of 50 agricultural chemicals is shown in Fig. 4 together with the calculated regression line and its 95% confidence interval for predicted TLVs.

Because all the compounds are related agricultural chemicals, some bias might exist in their correlation thus making the results doubtful for general application. A list was established (Table 7) for 191 compounds for which TLVs and LD_{50} values were available. The TLVs were taken from "Documentation of the TLVs for Substances in Workingroom Air", Am. Soc. Govern. Ind. Hygienists, 3rd Ed., 1971, 2nd Printing 1974.[12] The LD_{50}

Table 6. TLV AND LD_{50} FOR DIFFERENT AGRICULTURAL CHEMICALS

Compound	TLV[12] (mg/m^3)	LD_{50} Values (mg/kg) from Different Sources: Monsanto[1]	ACGIH[12]	TSL[13]
1. Abate	10	2000	4000	2000
2. Aldrin	0.25	55	60	39
3. Allyl alcohol	3	95	--	69
4. Ammate	10	3900	--	3900
5. Arsenic acid	0.5	48	--	--
6. Carbaryl (Sevin)	5	500	500	89
7. Chlordane	0.5	570	590	283
8. Toxaphene	0.5	69	73	60
9. 2,4-D	10	1200	--	375
10. DDT	1	113	250	113
11. DDVP	1	56	--	56
12. Demeton (Systox)	0.1	9	4	1.7
13. Diazinon	0.1	134	34	76
14. Dibrom (Naled)	3	430	250	--
15. Dieldrin	0.25	60	--	46
16. Dinitro-o-cresol	0.2	50	31	30
17. Diquat	0.5	300	--	231
18. Endrin	0.1	5	--	3
19. EPN	0.5	50	--	8
20. Heptachlor	0.5	90	--	40
21. Malathion	10	1375	2100	599
22. Methoxychlor	10	5000	6000	5000
23. Methylparathion	0.2	25	14	4
24. Paraquat	0.5	145	127	57
25. Parathion	0.1	15	3	2
26. Phosdrin	0.1	7	6.5	4
27. Ronnel	10	1740	1250	906
28. 2,4,5-T	10	500	300	300
29. TEPP	0.05	1.2	3	0.5
30. Thiram	5	860	1300	560
31. Lindane	0.5		125	76
32. TEDP	0.2		5	5
33. Rotenone	5		132	132
34. Pyrethrum	5		820	--
35. Baygon (Propoxur)	0.5		83	83
36. Captan	5		9000	480
37. Carbofuran (Furadan)	0.05		8	8
38. Chlorpyrifos (Dursban)	0.2		120	145
39. Clopidol (Coyden)	10		8000	--
40. Crufomate (Ruelene)	5		490	660
41. Disulfoton	0.1		2.3	10
42. Phorate (Thimet)	0.05		1.1	1

Table 6 (Continued). TLV AND LD_{50} FOR DIFFERENT AGRICULTURAL CHEMICALS

Compound	TLV (mg/m^3)	LD_{50} Values from Different Sources		
		Monsanto	ACGIH	TSL
43. Picloram (Tordon)	10		8000	3750
44. Plictran	5		540	--
45. Antu	0.3		30	6
46. Azinphos-Methyl	0.2		16.4	11
47. Crag (Sesone)	10		1500	730
48. Endosulfane (Thiodan)	0.1		20	28
49. Ferbam	10		17,000	4000
50. Methyldemeton	0.5		40	15

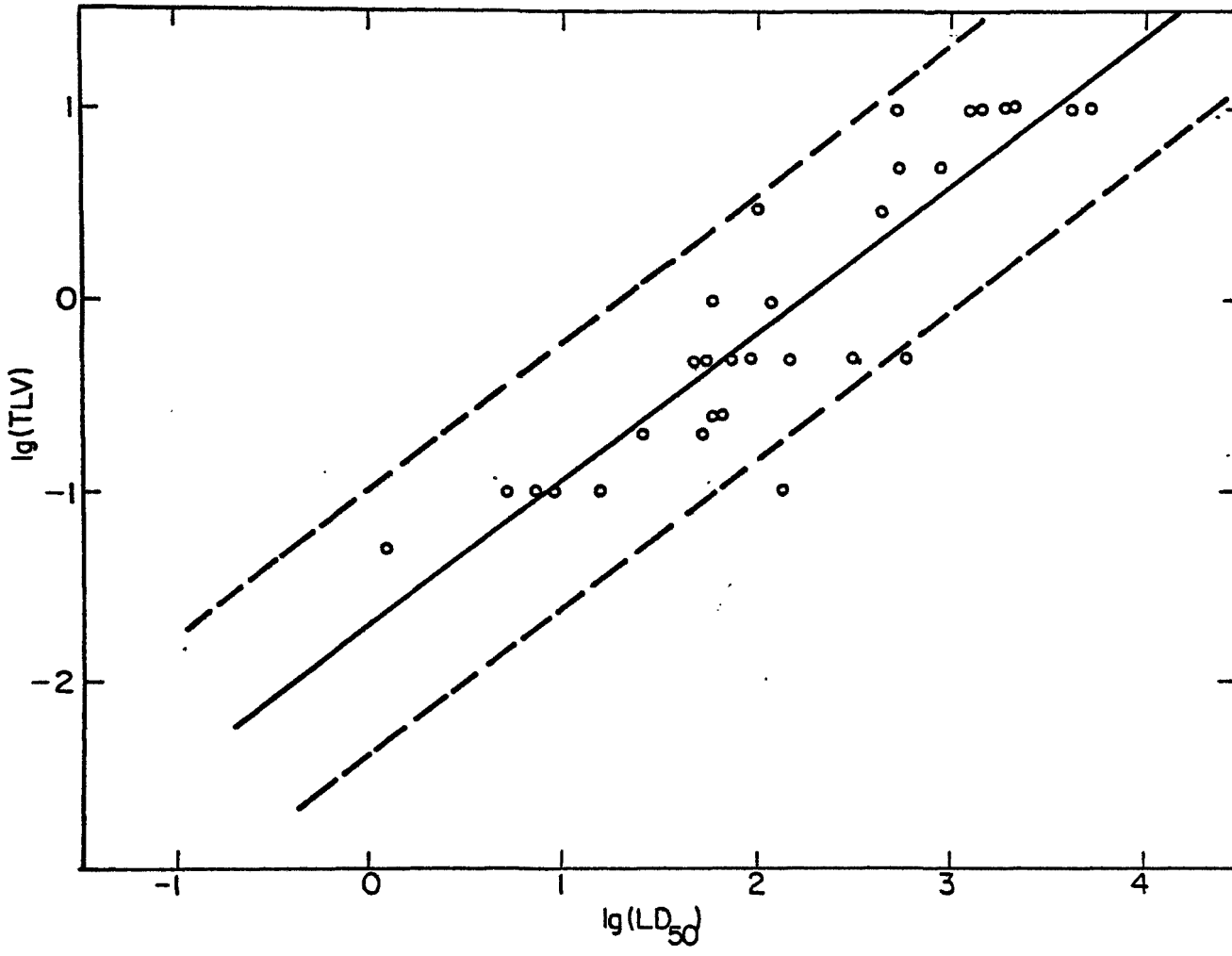


Figure 3. Plot of lg (TLV) versus lg (LD_{50}) for 30 agricultural chemicals selected by Monsanto Research Corporation.[1]

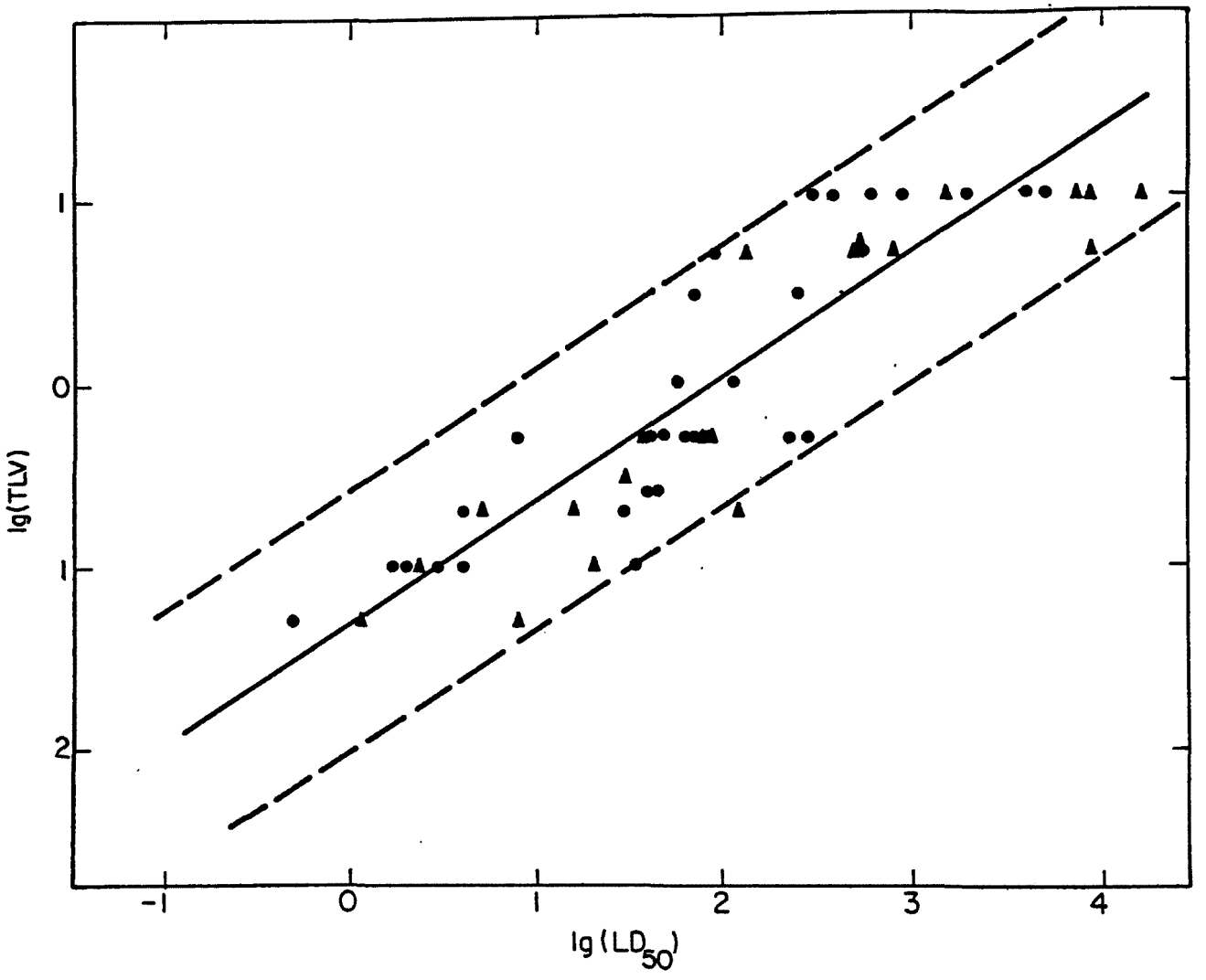


Figure 4. Plot of lg (TLV) versus lg (LD_{50}) for 50 agricultural chemicals. (o) compounds of Fig. 3, (Δ) additional compounds.

Table 7. LIST OF TLV[12] AND LD_{50}[13] FOR DIFFERENT CHEMICAL COMPOUNDS

Compound	TLV (mg/m^3)	LD_{50} (mg/kg)	Remarks
1. Acetaldehyde	180	1930	
2. Acetic acid	25	3310	
3. Acetic anhydride	20	1780	
4. Acetonitrile	70	160	
5. Acrolein	0.25	46	
6. Acrylamide	0.3	170	
7. Acrylonitrile	45	93	
8. Allylchloride	3	64	
9. Allylglycidyl ether	22	922	
10. Ammonium chloride	10	1650	
11. Ammoniumsulfamate	10	3900	
12. Aniline	19	440	
13. Antimony dust	0.5	100	
14. Benzene	80	3400	
15. Benzylchloride	5	1231	
16. Berryllium oxide	0.002	54	itr-rat TDL_o
17. Bromoform	5	1820	
18. 2-Butanone	590	3100	
19. 2-Butoxyethanol	240	1480	
20. Butanol	300	2510	
21. t-Butanol	300	3500	
22. Butylamine	15	500	
23. Butylglycidyl ether	270	2050	
24. p-t-Butyltoluene	60	1500	
25. Cadmium oxide	0.2	72	
26. Calcium arsenate	1	298	
27. Camphor	12	900	
28. Carbondisulfide	60	400	ipr-rat LDL_o
29. Chloroacetaldehyde	3	23	
30. alpha-Chloroacetophenone	0.3	52	
31. Chlorobenzene	350	2910	
32. Chlorobenzylidene malononitrile	0.4	178	
33. Aroclor 1254	0.5	500	orl-rat LDL_o
34. Chloroform	250	300	
35. 1-Chloro-1-nitropropane	100	510	orl-mus LD50
36. Chloroprene	90	64	orl-rat LDL_o
37. o-Cresol	22	121	
38. Crotonaldehyde	56	300	
39. Cumene	250	1400	
40. Cyclohexane	1050	813	orl-mus LDL_o
41. Cyclohexanol	200	2060	
42. Cyclohexanone	200	1620	
43. Decaborane	0.3	64	
44. Diacetone alcohol	240	4000	
45. 1,2-Dibromoethane	190	140	
46. 2-N-Dibutylaminoethanol	14	1070	

Table 7 (Continued). LIST OF TLV[12] AND LD_{50}[13] FOR DIFFERENT CHEMICAL COMPOUNDS

Compound	TLV	LD_{50}	Remarks
47. Dibutylphosphate	5	3200	
48. o-Dichlorobenzene	300	500	
49. p-Dichlorobenzene	450	500	
50. Dichlorodimethyl hydantoin	0.2	542	
51. 1,1-Dichloroethane	400	725	
52. 1,2-Dichloroethane	200	680	
53. 1,1-Dichloro-1-nitroethane	60	150	
54. Dimethylamine	75	540	
55. Diethylamino ethanol	50	1300	
56. Diethylenetriamine	4	1080	
57. Diglycidyl ether	2.8	450	
58. Diisobutylketone	290	1416	orl-mus LD50
59. Diisopropylamine	20	700	
60. Dimethylamine	18	698	
61. Dimethylaniline	25	1410	orl-rat LDL_o
62. Dimethylforamide	30	1500	
63. 1-1-Dimethylhydrazine	1	122	
64. Dimethylnaphthalene	5	4400	orl-rbt LD50
65. Dimethylsulfate	5	440	
66. Dinitrobenzene	1	27	orl-cat LDL_o
67. Dinitro-o-cresol	0.2	30	
68. Dinitrotoluene	1.5	177	
69. Dioxane	360	3150	orl-gpg LD50
70. Diphenyl	1	2180	
71. Diphenylamine	10	464	
72. Dipropyleneglycol methylether	600	7500	orl-dog LD50
73. Epichlorhydrine	19	90	
74. Ethanolamine	6	2100	
75. 2-Ethoxyethanol	740	3000	
76. 2-Ethoxyethyl acetate	540	1910	orl-gpg LD50
77. Ethylacrylate	100	830	
78. Ethanol	1900	5560	orl-gpg LD50
79. Ethylamine	18	400	orl-rat LDL_o
80. Ethyl-sec-amyl ketone	130	2800	
81. Ethylbenzene	435	3500	
82. Ethylbutyl ketone	230	2760	
83. Ethyl ether	1200	2200	
84. Ethyl formate	300	1850	
85. Ethylene chlorhydrine	16	71	
86. Ethylenediamine	25	1160	
87. Ethyleneglycol dinitrate	1.2	616	
88. Ethyleneimine	1	15	
89. Ethyleneoxide	90	330	
90. N-Ethylmorpholine	94	1780	
91. Formaldehyde	2.5	800	
92. Formic acid	9	1210	
93. Furfural	20	127	
94. Furfurol	200	275	
95. Glycidol	150	850	

Table 7 (Continued). LIST OF TLV[12] AND LD_{50}[13] FOR DIFFERENT CHEMICAL COMPOUNDS

Compound	TLV	LD_{50}	Remarks
96. 2-Hexanone	410	2590	
97. Hexane	410	1620	
98. Hydrazine	1.3	60	
99. Hydrocyanic acid	11	0.37	orl-mus LD50
100. Hydroquinone	2	370	
101. Ironpentacarbonyl	0.08	18	orl-rbt LDL_o
102. i-Amylalcohol	360	3380	
103. Isobutanol	300	3500	
104. Isophorone	140	2330	
105. Isopropylacetate	950	3200	orl-rat LDL_o
106. Isopropanol	980	192	orl-mus LDL_o
107. Isopropylamine	12	820	
108. Isopropylglycidyl ether	240	4200	
109. Ketene	0.9	1300	
110. Lead arsenate	0.15	100	
111. Maleic anhydride	1	850	orl-rat LDL_o
112. Methylacetate	610	4800	orl-rat LDL_o
113. Methylacrylate	35	300	
114. Methanol	260	420	orl-mus LDL_o
115. Methyl-i-amylketone	460	4760	
116. Methyl-n-amylketone	465	1670	
117. Methylcellosolve	80	3000	
118. Methylcellosolve acetate	120	1910	orl-gpg LD50
119. Methylchloride	210	1800	
120. Trichloroethane	1900	5660	orl-rbt LD50
121. Methylcyclohexane	2000	4000	orl-rbt LDL_o
122. o-Methylcyclohexanone	460	2140	
123. 2-Methylcyclopentadienyl-manganese tricarbonyl	0.2	23	
124. Methyliodide	28	50	orl-rat LDL_o
125. Methyl-i-butylcarbinol	100	2600	
126. Methylisocyanate	0.05	71	
127. alpha-Methylstyrene	480	4900	
128. Methylene chloride	1750	3000	orl-dog LDL_o
129. Methylaniline	9	280	orl-rbt LDL_o
130. Monomethyl hydrazine	0.35	32	
131. Morpholin	70	1050	
132. Naphthalene	50	1780	
133. Nicotine	0.5	70	
134. p-Nitroaniline	6	3249	
135. Nitrobenzene	5	640	
136. p-Nitrochlorobenzene	1	420	
137. Nitroethane	310	1100	
138. Nitromethane	250	940	
139. 1-Nitropropane	90	1000	orl-rat LDL_o
140. 2-Nitropropane	90	500	orl-rat LDL_o
141. o-Nitrotoluene	30	891	
142. Nitroglycerine	1.2	80	orl-rat LDL_o

Table 7 (Continued). LIST OF TLV[12] AND LD_{50}[13] FOR DIFFERENT CHEMICAL COMPOUNDS

Compound	TLV	LD_{50}	Remarks
143. Oxalic acid	1	700	orl-hmn LDL_o
144. Pentachlorophenol	0.5	27	
145. 2-Pentanone	700	3730	
146. Perchloromethyl mercaptane	0.8	83	
147. Phenol	19	414	
148. Phenothiazine	5	5000	
149. p-Phenylenediamine	0.1	100	orl-rat LDL_o
150. Phenyl ether	7	4000	orl-rat LDL_o
151. Phenylglycidyl ether	62	3850	
152. Phenylhydrazine	22	188	
153. Phosphoric acid	1	1530	
154. Phosphorus	0.1	1.4	orl-hmn LDL_o
155. Phosphorpentasulfide	1	389	
156. Phthalic anhydride	12	4020	
157. Pival	0.1	150	orl-rat LDL_o
158. Propargyl alcohol	2	70	
159. n-Propanol	490	1870	
160. Propylenedichloride	350	1900	
161. Propylene imine	5	19	
162. Propylene oxide	240	1140	
163. Pyridine	15	891	
164. Quinone	0.4	130	
165. RDX	1.5	200	
166. Sodium fluoroacetate	0.05	1.7	
167. Sodium hydroxide	2	500	orl-rbt LDL_o
168. Strychnine	0.15	16	
169. Styrene	420	4920	
170. Sulfuric acid	1	2140	
171. Sulfuryl fluoride	20	100	orl-rat LDL_o
172. Tetrabromoethane	14	1000	orl-rat LDL_o
173. Tetrachloroethane	35	30	orl-hmn TDL_o
174. Tetraethyl lead	0.1	17	orl-rat LDL_o
175. Tetrahydrofuran	590	3000	orl-rat LDL_o
176. Tetramethyl lead	0.15	109	
177. Toluene	750	3000	
178. o-Toluidine	22	900	
179. Tributylphosphate	5	3000	
180. Trichloroethane	45	580	
181. Trichloroethylene	535	4920	
182. Trichloropropane	300	320	
183. Triethylamine	100	460	
184. Trinitrotoluene	1.5	700	orl-rat LDL_o
185. Tri-o-cresylphosphate	0.1	4680	orl-rat LDL_o
186. Triphenylphosphate	3	3000	orl-rat LDL_o
187. Vinyl acetate	30	2920	
188. Vinyl toluene	480	4000	
189. Worfarin	0.1	325	
190. Xylene	440	4300	
191. Xylidine	25	610	orl-rat LDL_o

values were taken from "The Toxic Substances List", HEW, 1974.[13] As far as available LD_{50} values (oral-rat) were used. In several cases oral LD_{50} values for other animals (mouse, guinea pig, dog, cat, etc.) had to be used. If LD_{50} values were not reported at all LDL_o values were taken again with preference of rats.

The graphic representation of this group of 191 compounds is shown in Figure 5. Linear regression yielded a correlation coefficient of 0.61. The values of the constants of equ. (17) were found to be

$$a = (0.00971 < 0.0343 < 0.121) = 95\% \quad (22a)$$

$$b = (0.800 < 0.991 < 1.182) = 95\% \quad (22b)$$

After inclusion of the previous 50 agricultural chemicals (total of 241 compounds) the correlation coefficient improved slightly to 0.70. The values of the constants in this case were

$$a = (0.0125 < 0.0291 < 0.0678) = 95\% \quad (23)$$

$$b = (0.849 < 0.983 < 1.117) = 95\% \quad (24)$$

A graphic representation of the 241 compounds is shown in Figure 6.

It might be pointed out that the 95% confidence limits given in equs. (18) to (24) refer to the estimates of the mean and not to the estimate of an individual prediction, i.e., the values represent confidence limits for the constants of the regression line and not for the prediction of an individual TLV from a given LD_{50} value. Confidence ranges inside which 95% of the TLVs predicted from the regression equation might fall on repeated trials are shown by the dashed lines in Figures 3 to 6.

The poor correlation between TLVs and LD_{50} values is not surprising if one considers the spread in TLVs for a fixed LD_{50} value. The ratio of TLV maximum to TLV minimum for a given LD_{50} value is generally in the range of 1,000 to 10,000. There exists also a distinct cut-off at LD_{50} values around 5-6 g/kg. In this range the lowest reported TLV is 0.1 mg/m^3 whereas the highest reported TLV is 1,800 mg/m^3.

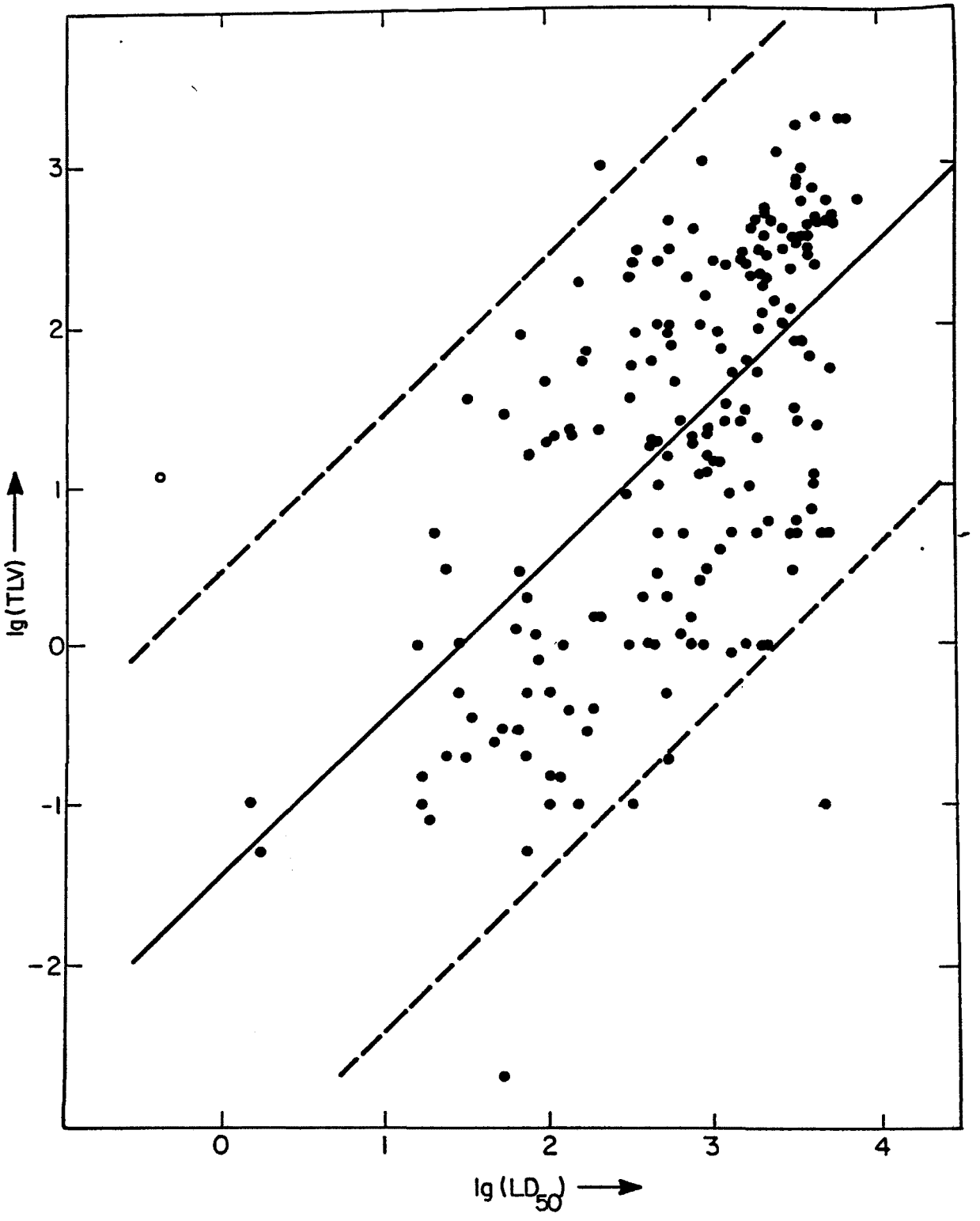


Figure 5. Plot of lg (TLV) versus lg (LD_{50}) for 191 non-agricultural compounds.

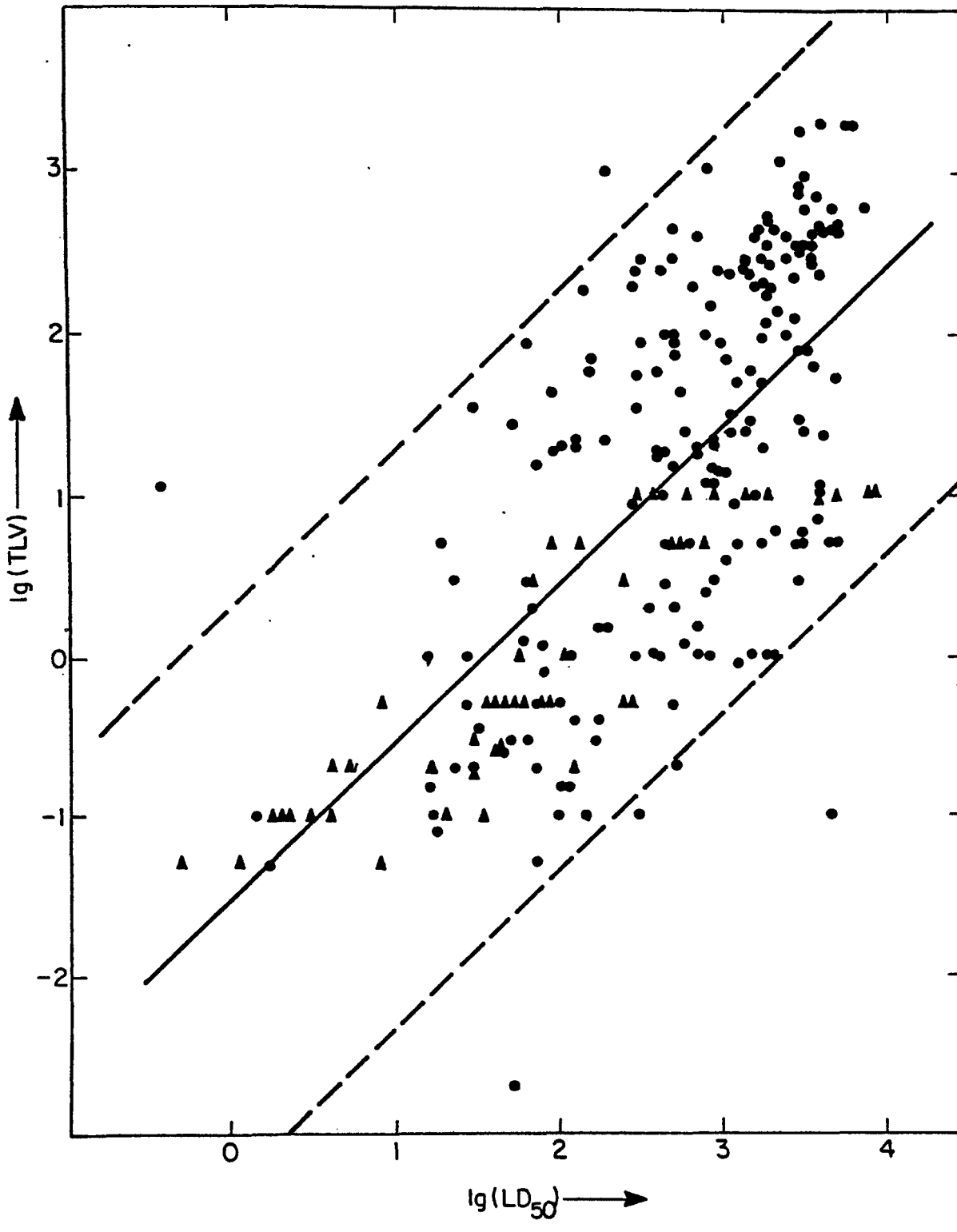


Figure 6. Plot of lg (TLV) versus lg (LD_{50}) for 191 non-agricultural (o) and 50 agricultural (Δ) compounds.

F. Estimation of Maximum Permissible Air Concentrations from Known LD_{50} Values

Safe estimates of permissible air concentrations have to be based on two assumptions, one concerning the accumulation of pollutant in the body and the other one concerning the highest permissible body concentration which does not create adverse health effects.

If one assumes that all of the pollutant inhaled remains in the body and accumulates from birth for a life span of 70 years, a final body concentration results which is unrealistic by several orders of magnitude. According to equ. (15) or Figures 1 and 2, the body concentration accumulated during 70 years of exposure, C_{70}, is given by

$$C_{70} = 2.9 \times 10^3 \, x \tag{25}$$

where C_{70} and x are in mg/kg and mg/m^3, respectively.

Biological data presented in Table 5 allow us to draw two conclusions, (1) according to the presently suggested TLV standards a stationary maximum body concentration corresponding to 0.05% of the LD_{50} value can be considered as a safe limit, (2) the assumption of a biological half-life of 30 days far exceeds the residence time in the human body for most compounds. By combining both assumptions permissible air concentrations can be calculated from equ. (11). The maximum permissible air concentration is then defined by the pollutant concentration (mg/m^3) for which continuous exposure with 100% absorption gives rise to a stationary maximum body concentration equal to 0.05% of the LD_{50} value of the compound, assuming a biological half-life time of 30 days.

From equ. (11) the maximum permissible air concentration, subjected to the above postulated conditions, is given by

$$x_p = 0.0005 \, (LD_{50}) \, (\ln 2/B\tau) \tag{26}$$

or, after inserting numerical values by

$$x_p = (0.0005 \times 0.693/0.143 \times 30) \, (LD_{50}) = 8.1 \times 10^{-5} \, (LD_{50}) \tag{27}$$

where x_p and LD_{50} are expressed in mg/m^3 and mg/kg, respectively. The numerical value of B = 0.143 m^3/kg.day corresponds to a 70 kg adult and a tidal breathing rate of 10.0 m^3/day.

Regression analysis of 241 compounds according to equ. (17) yielded the values of the constants presented in equs. (23) and (24). The slope of the regression line in the double-logarithmic plot of (TLV) versus (LD_{50}) was found to be b = 0.983, and therefore, a direct proportionality between (TLV) and LD_{50}) can be assumed without introducing any substantial error.

$$(TLV) = 0.029\ (LD_{50}) \tag{28}$$

For the lower 95% confidence limit the (TLV) is then obtained from (LD_{50}) values by

$$(TLV)_{low} = 4.5 \times 10^{-4}\ (LD_{50}) \tag{29}$$

Since intermittent exposure (40 hour work week of 5 days with 8 hour exposure) gave rise to a weekly body concentration buildup only 23.8% of that experienced during continuous exposure, the factor 0.238 has to be included into equ. (29). The maximum permissible air concentration of a compound is then related to its LD_{50} value by

$$x_p = 1.07 \times 10^{-4}\ (LD_{50}) \tag{30}$$

Comparison of equs. (27) and (30) shows close correspondence thus indicating that both equations are based on similar ratios of maximum stationary body concentration to biological half-life time of the component.

For the determination of a pollutant hazard to exist during continuous exposure the following inequality was proposed by Monsanto:

$$\frac{x_m}{(TLV)\ (8/24)\ (1/100)} \geq 1.0 \tag{31}$$

where TLV is the presently suggested standard for working room air. The factor (8/24) considers the intermittent exposure under working conditions, but does not consider weekends. The factor (1/100) is a safety factor. If for any pollutant the left side of equ. (31) is equal or greater than 1.0, then a hazard is judged to exist.

The maximum permissible pollutant concentration not to be exceeded during continuous exposure is given by equ. (30). Consequently, the air quality criteria corresponding to equ. (31) but based on LD_{50} values is given by

$$\frac{x_m}{1.07 \times 10^{-4} \, (LD_{50})} \geq 1.0 \qquad (32)$$

Comparing equ. (32) with equ. (31) the following changes have been applied. The TLV of equ. (31) was replaced by $(TLV)_{low}$ as calculated from LD_{50} by regression analysis. The factor (8/24) has been replaced by (40/168) to take into account normal working patterns during a calendar week. The safety factor (1/100) was omitted because of the use of the lower 95% confidence limit in the calculation of $(TLV)_{low}$ from LD_{50} values.

Equation (32) should be applied in all cases where LD_{50} values are known. It is now possible that for some pollutants TLV standards are given although the LD_{50} value of the component is not known. In this case equ. (32) would not be directly applicable and in a multicomponent system two sets of equations would have to be used, one based on LD_{50} values, equ. (32), the other one on TLV standards, equ. (31). In order to overcome this complication the unknown LD_{50} value is estimated from the given TLV standard by solving the regression equation, equ. (28) for LD_{50}

$$(LD_{50}) = 34.5 \, (TLV) \qquad (33)$$

This estimated LD_{50} value is then substituted into equ. (32).

The expression for permissible air concentrations given by equs. (27) and (30) were calculated for the respiratory conditions of adults, i.e., for an average breathing frequency of 16 per min. In the Appendix, Section VII-A, the effect of the higher breathing frequencies is discussed.

Considering that the respiratory frequency of an infant of one year of age is about twice that of adults, a factor of 0.5 has to be applied to equ. (30) in order to make the permissible air concentration safe for all age groups. The corrected equ. (30) is then given by equ. (34).

$$x_p = 5.35 \times 10^{-5} (LD_{50}) \tag{34}$$

Considering the variation in the respiratory frequency during growth of an infant through adolescence it could be shown that during this time interval the body concentration never exceed that of an adult by more than a factor of 1.7. Consequently, equ. (27) has to be modified correspondingly, the corrected permissible air concentration being now given by

$$x_p = 4.77 \times 10^{-5} (LD_{50}) \tag{35}$$

Estimates of x_p values for 5 compounds were obtained by three different methods (Table 8). In Method I, the current TLV standards and equ. (31) were used to compute x_p estimates.

In Method II, the TLVs were estimated from LD_{50} values by means of equ. (29). Equation (34) was applied for the determination of x_p values.

Method III utilized equ. (35). The maximum stationary body concentration does not exceed a concentration corresponding to 0.05% of the LD_{50} value, assuming a pollutant half-life of 30 days.

The close correspondence of x_p values estimated either by Method II or by Method III demonstrates that a correlation between TLV and LD_{50} is unnecessary. Values of x_p for compounds with unknown TLV and a known LD_{50} can be directly obtained from equ. (35).

So far mainly organic compounds were considered, inorganic compounds presenting considerable problems due to lack of sufficient data. In Table 9 four metals are compared for which data could be retrieved. According to the presently used TLV standards a rather high percentage of the LD_{50} value accumulates during normal working exposure.

Table 8. PERMISSIBLE AIR CONCENTRATIONS FOR CONTINUOUS EXPOSURE ESTIMATED BY DIFFERENT METHODS

Compound	Clopidol	Methylcyclohexane	Tetrachloroethane	TEPP	Methylisocyanate
Table/Number	I/39	II/121	II/173	I/29	II/126
LD_{50} (mg/kg)	8,000	4,000	30	0.5	71
Presently Proposed TLV (mg/m^3)	10	2,000	35	0.05	0.05
Estimated $(TLV)_{low}$ (mg/m^3)	3.6	1.8	0.014	0.0002	0.032
Permissible Air Concentration x_p in mg/m^3 Estimated by:					
Method I	0.033	6.6	0.12	0.00016	0.00016
Method II	0.43	0.22	0.0016	0.000027	0.0038
Method III	0.38	0.19	0.0014	0.000024	0.0034

Method I: Eq. (31) applied to presently proposed TLV. $x_p = 0.0033$ (TLV)

Method II: Eq. (34) applied to $(TLV)_{low}$ estimated from LD_{50}. $x_p = 5.35 \times 10^{-5}$ (LD_{50})

Method III: Eq. (35) applied to LD_{50} value. $x_p = 4.77 \times 10^{-5}$ (LD_{50})

Table 9. MAXIMUM STATIONARY BODY CONCENTRATION ACCUMULATED DURING DURING WORKING CONDITIONS (40 HOUR WORKWEEK) FOR SELECTED INORGANIC COMPOUNDS

Compound	Half-Life (Days)	TLV (mg/m^3)	c_m (mg/kg)	LD_{50} (mg/kg)	$(c_m/LD_{50}) \times 100$
$PbMe_4$	2920	0.15	20.8	109 (a)	19.1
$PbEt_4$	2920	0.1	13.9	17 (a)	81.8
Cr	83	1.0	4.0	400 (b)	1.0
Hg-Alkyls	120	0.01	0.057	8 (c)	0.7
Cd	5475	0.1	26.1	15 (d)	173.7

(a) orl-rat LD_{50} (b) imp-rat TDL$_o$ (c) ipr-mus LDL$_o$ (d) ims-rat LDL$_o$

Permissible Air Concentrations, mg/m^3, for Continuous Exposure Estimated by Different Methods

Compound	Method I $x_p = 0.0033$ (TLV)	Method II $x_p = 5.35 \times 10^{-5} (LD_{50})$	Method III $x_p = 4.77 \times 10^{-5} (LD_{50})$
$PbMe_4$	0.00050 (0.3)	0.0059 (3.1)	0.0049 (2.7)
$PbEt_4$	0.00033 (1.1)	0.0009 (3.1)	0.0008 (2.7)
Cr	0.0033 (0.01)	0.022 (0.1)	0.0181 (0.06)
Hg-Alkyls	0.00003 (0.01)	0.0004 (0.1)	0.0003 (0.1)
Cd	0.00033 (2.4)	0.0008 (5.9)	0.0007 (5.0)

Values in parenthesis indicate the maximum stationary body concentration in percentage of LD_{50} values which accumulate during continuous exposure.

In the lower part of Table 9 permissible air concentrations for continuous exposure are estimated by the three different methods discussed previously. For each estimated air concentration the maximum stationary body concentration expressed as percentage of LD_{50} is given in parenthesis. Comparing these values with those resulting from presently set TLV standards demonstrates that the estimates obtained by Methods II or III can be considered safe.

G. Estimation of Air Quality Standards For Multicomponent Systems

When two or more pollutants are present, their combined effect, rather than that of either individually, should be given primary consideration. In the absence of information to the contrary, the effects of the different pollutants should be considered as additive.[2] That is, if the sum of the following fractions

$$\sum_{1}^{n} [(x_m)_i/(x_p)_i] \geq 1 \tag{36}$$

exceeds unity, a health hazard should be judged to exist. In equ. (36) $(x_m)_i$ indicates the observed maximum ground level concentration of the i-th pollutant and $(x_p)_i$ corresponds to its estimated maximum permissible air concentration.

Equation (36) can be evaluated by the three previously discussed methods by substituting for x_p the proper value given by equs. (31), (34), or (35), respectively. The air quality standards according to the three methods are then given as follows.

Method I
$$\sum_{i}^{n} \frac{(x_m)_i}{0.0033\ (TLV)_i} \geq 1 \tag{37}$$

Method II
$$\sum_{i}^{n} \frac{(x_m)_i}{5.35 \times 10^{-5}\ (LD_{50})_i} \geq 1 \tag{38}$$

Method III
$$\sum_{i}^{n} \frac{(x_m)_i}{4.77 \times 10^{-5}\ (LD_{50})_i} \geq 1 \tag{39}$$

As an example, data of Table 10 show the evaluation of selected Los Angeles air data by three different methods. In all three evaluations the absolute prorated and the percentage prorated contribution of each individual pollutant are shown.

The evaluation by Method I was performed according to the presently used standard procedure which is based on presently set TLV standards, equ. (37). For the evaluation by Method II the TLVs were assumed to be unknown and the evaluation was based on LD_{50} values, equ. (38). In the evaluation by Method III equ. (39) was utilized.

Data of Table 10 indicate that in order to qualify for the Air Quality Standard the average air concentration of each compound would have to be reduced by a factor of 0.44 or 0.39 provided the relative amounts of each compound remained unchanged, and either Method II, equ. (38), or Method III, equ. (39), is applied, respectively.

H. Estimation of Maximum Ground Level Concentrations From Stack Emission Data of Stationary Sources

Assessments of health hazards associated with air pollutants from process industries require the knowledge of the maximum ground level concentration, x_m, of pollutants during a 24 hour period. According to the first decision criterion for possible health hazards expressed in equ. (36), the value of x_m must not exceed the permissible ground level concentration, x_p. In the preceding sections three methods were outlined for the determination of x_p which resulted in equs. (37-38). The present section deals with the estimation of x_m generated by stationary sources.

The maximum ground level concentration generated by a stationary source is affected by both the operation conditions of the source and the ambient weather conditions. Consequently, operation conditions have to be adjusted according to the current weather conditions in order not to generate maximum ground level concentrations in excess of the permissible ones.

In the Appendix, Section VII-C, two nomographs are presented as aids for obtaining first estimates of the effects of changes in both the emission rate of the source and the prevailing weather conditions on the maximum ground level concentration of the pollutant. These

Table 10. ANALYSIS OF A MULTICOMPONENT SYSTEM (SELECTED VALUES FOR LA AIR)

Compound	TLV (mg/m^3)	LD_{50} (mg/kg)	Reported Average Air Concentration (mg/m^3)	Absolute (percent) Contribution to Air Quality Standard		
				Method I	Method II	Method III
Xylene	440	4,300	0.130	0.090 (23.1)	0.505 (24.6)	0.643 (24.6)
Toluene	750	3,000	0.140	0.057 (13.4)	0.872 (38.0)	0.479 (38.0)
Benzene	80	3,400	0.050	0.189 (44.6)	0.275 (12.0)	0.309 (12.0)
Naphthalene	50	1,780	0.008	0.048 (11.3)	0.084 (3.7)	0.094 (3.6)
Hexane	410	1,620	0.043	0.032 (7.5)	0.496 (21.6)	0.558 (21.7)
Air Quality Standard				0.424 (100)	2.292 (100)	2.574 (100)

Air Quality Standard calculated by:

Method I equ. (37)
$$\sum_{1}^{n} \frac{(x_m)_i}{0.0033\ (TLV)_i}$$

Method II equ. (38)
$$\sum_{1}^{n} \frac{(x_m)_i}{5.35 \times 10^{-5}\ (LD_{50})_i}$$

Method III equ. (39)
$$\sum_{1}^{n} \frac{(x_m)_i}{4.77 \times 10^{-5}\ (LD_{50})_i}$$

nomographs facilitate the determination of either one of two source criteria as a function of weather conditions, (1) the maximum source emission rate for which the ground level concentration will not exceed a given maximum permissible value, or (2) the maximum ground level concentration resulting from given operation conditions (emission rates) of the source.

The design of the nomographs is based on the mathematical treatment of atmospheric dispersion estimates presented by D. Bruce Turner.[14] In addition to five weather categories the following input variables are provided: ambient air temperature and windspeed, stack gas temperature and exit velocity, stack diameter and height. The application of the nomographs is demonstrated by several examples.

SECTION IV

PERMISSIBLE DRINKING WATER CONCENTRATIONS

A. Table of Symbols and Definitions

α	fraction of pollutant absorbed through respiratory system
β	fraction of pollutant absorbed through gastrointestinal tract
c_m	maximum stationary body concentration (mg/kg)
k	first order rate constant (1/hr)
LD_{50}	lethal dose 50% kill (mg/kg)
$(LD_{50})_i$	lethal dose 50% kill of ith pollutant (mg/kg)
R_{uptake}	rate of pollutant uptake (mg/kg/day)
rbt	rabbit
τ	biological half-life of pollutant (days)
TLV	threshold limit value (mg/m^3)
$(TLV)_{low}$	lower 95% confidence limit for TLV estimated from LD_{50} (mg/m^3)
x	actual pollutant drinking water conc. (mg/l)
x_i	actual drinking water conc. of ith pollutant (mg/l)
x_e	estimated safe drinking water conc. (mg/l)
$(x_e)_i$	estimated safe drinking water conc. of ith pollutant (mg/l)
V	volume of drinking water ingested (l/day)
W	body weight (kg)

B. Caveats

The treatment described in this section was based in part, on the following assumptions and limitations.

a) The proposed method of estimating permissible drinking water concentrations is not applicable to pollutants with carcinogenic, teratogenic or mutagenic effects. A treatment of carcinogens in ambient air is presented in Section V.

b) This method does not take into account other sources of environmental contamination. No allowance has been made for pollutant uptake in air or diet.

c) No allowance was made for synergistic or antagonistic effects of pollutants in multicomponent systems.

d) No allowance was made for metabolic inhibition or induction effects on pollutants in the body.

e) The treatment was based on the assumption that animal LD_{50} values were applicable to man.

f) The biological treatment was based on a simplified one compartment model with first order kinetics.

g) No allowance was made for factors such as odor and taste which may necessarily lower the standard below the maximum safe concentration limit.

C. Derivation of EPA Proposed Drinking Water Standards

Pesticides

The proposed drinking water standards for pesticides were established on the basis of animal feeding experiments.[6] The minimal or no-effect dose fed to the more susceptible specie was used to calculate a safe body burden (mg/kg). The proposed safe concentration limit was determined by applying a appropriate safety factor to the animal data. Table 11 summarizes the derivation of each pollutant standard. A constant safety factor of 2500 was applied to all the compounds, except for methoxychlor for which comparable human toxicity data was available. An additional safety factor was imposed on chlordane and toxaphene because of organoleptic effects and on heptachlor because of its presence in the diet.

Inorganics

The derivation of EPA proposed drinking water standards for inorganic chemicals was based mainly on observed human health effects. There

Table 11. DERIVATION OF EPA PROPOSED DRINKING WATER STANDARDS FOR PESTICIDES

Contaminant	(1) Animal safe level (mg/kg/day)	(2) Equivalent level for 70 kg man (mg/day)	(3) Equivalent derived water St'd (mg/l)*	(4) Proposed EPA water St'd (mg/l)*	(5) Safety factor, ratio (3)/(4)
Chlordane	.42	29.4	14.7	.003	4900
Endrin	.02	1.4	.7	.0002	3500
Heptachlor	.08	5.6	2.8	.0001	2800
Lindane	.3	21.	10.5	.004	2625
Methoxychlor	17.	1190.	59.5	.1	5950
Toxaphene	1.7	119.	59.5	.005	11900
2,4-D	8.0	560.	280.	.1	2800
2,4,5-TP (Silvex)	.9	63.	31.5	.01	3150

* Assume consumption of 2l/day.

has been no report of a consistent animal feeding experiment comparable to the pesticide studies. Table 12 indicates the more pertinent toxicity information for each contaminant and a 2l/day water concentration corresponding to the given dosage. The EPA proposed drinking water limit is given and the factor of safety separating it from the derived value. It is significant that the safety factors obtained in this manner are considerably lower than those associated with the pesticide drinking water limits.

D. Stokinger-Woodward Treatment - METHOD I

Stokinger and Woodward[3] used TLV in calculating safe drinking water standards. The assumption was made that an individual breathes 10 m^3 of air during an 8 hour working day and that the total pollutant uptake from air at the TLV concentration can be safely tolerated. It was then assumed that this safe quantity of pollutant/day can be similarly tolerated in drinking water. Consumption of two liters of drinking water/day was assumed. Correction for the efficiency of respiratory and gastrointestinal absorption for the specific compounds were included in this treatment. The corresponding safe drinking water concentration was calculated as shown below.

$$x_e = \frac{10\ \alpha\ (TLV)}{2\beta} \tag{40}$$

where

x_e = calculated safe drinking water concentration

α = fraction of pollutant absorbed through respiratory system

β = fraction of pollutant absorbed through gastrointestinal tract.

In general, the calculated values (x_e) for inorganics are 1-3 orders of magnitude higher than the limits proposed by EPA (see Table 13).

Based on this Method I, the criterion used to assess a pollutant hazard would be expressed as

$$\frac{x\beta}{5\alpha\ (TLV)} \geq 1.0 \tag{41}$$

x = actual pollutant drinking water concentration (mg/l).

If, for any pollutant, this quotient is equal to or greater than unity a hazard is judged to exist.

Table 12. DERIVATION OF EPA PROPOSED DRINKING WATER STANDARDS FOR INORGANIC CHEMICALS

Contaminant	Toxicity Data	Derived Water Conc. (mg/l)*	Proposed Water St'd (mg/l)*	Safety Factor
Ag	60μg/day-human intake 1940	.03	.05	-
As	12mg/l-human skin cancer	12.	.05	240
Ba	.5mg/m^3-TLV	2.	1.	2
Cd	352μg/day-human max. no-effect	.18	.01	18
CN	4.7mg/l-human no effect	4.7	.2	24
Cr	.45mg/l-human no effect (3 yr)	.45	.05	9
F	8mg/l-human fluorosis	8.	1.4-2.4	4-6
Hg	.3mg/day**-human lowest toxic	.15	.002	75
NO_3(as N)	10mg/l-adult no effect	10.	10.	-
Pb	600μg/l-human no effect	.3	.05	6
Se	.7mg/day-human toxic	.35	.01	35

*Assume consumption of 2l/day

**Based on MeHg

Table 13. CALCULATED WATER STANDARDS - INORGANIC

Method I*

Contaminant	TLV, ppm	α	β	x_e (mg/l)	Proposed St'd (mg/l)
As	0.5	0.20	0.80	0.6	.05
Ba	0.5	0.75	1.00	2.0	1.0
Cd	0.1	0.25	0.03	4.0	.01
CN	0.1	0.60	0.80	19.0	.02
Cr	5.0	0.75	0.06	6.0	.05
F	2.5	0.10	1.0	1.25	1.4-2.4
P6	0.2	0.20	0.20	1.0	.05
Se	0.1	0.80	0.80	0.5	.01

*Data taken from Reference (3)

$$x_e = \frac{10\alpha\ (TLV)}{2\beta}$$

x_e = calculated safe drinking water concentration

α = fraction of pollutant absorbed through respiratory system

β = fraction of pollutant absorbed through gastrointestinal tract.

TLV = threshold limiting value.

E. Estimation of Permissible Drinking Water Standars - METHOD II

Introduction

There are two common measures of a compound's toxicity and its effect on human health. The threshold limiting value (TLV) for several industrial compounds have been set by the American Conference of Governmental Industrial Hygienists.[2] Although these values are based in part on animal toxicity experiment, they have been extrapolated to define pollutant air concentrations safely tolerated by humans during a working day. Unfortunately, the TLV for only a comparatively few substances have been established.

The second measure is animal toxicity data. Several different toxicity parameters have been determined and reported in the literature. However, the most common of these is the oral LD_{50} value in the rat. Animal LD_{50} data, at best, reflects a relative measure of toxic potential in man. The most serious problem is the variability among different species and the relationship of the toxicity of a particular specie to man. In the present context, the value of LD_{50} data lies in the fact that the mode of administration, absorption into the body and routes of metabolism and excretion, are comparable to the ingestion of drinking water.

Thus, oral LD_{50} is important because the phenomena in operation parallel human drinking water consumption, although such data may correlate poorly with toxicology in man. On the other hand, the limited TLV information is directly applicable to the effects of air pollutant concentrations on human health, but is not related in any way to the chemical form which compounds are likely to exist in drinking water nor the gastrointestinal absorption behavior of these compounds. In addition, organic compounds contained in drinking water and absorbed through the intestines may result in a lower body burden compared to the same amount taken into the body through the respiratory system. This is due to the first pass liver effect, which action may detoxify some portion of an oral dose before it is delivered to the rest of the body.

Application of $(TLV)_{low}$ Concept in Estimating Drinking Water Standards

Ideally, the best of both parameters should be combined to give an indicator which could be directly related to absolute toxic or no-effect levels in man. An approximation to this end was developed in

Section III of this report. TLV and the LD_{50} values for 241 different organic and inorganic compounds were plotted on a log-log scale. TLV data were obtained from the American Conference of Governmental Industrial Hygienists 1974 Adopted Values and the LD_{50} values were taken, when available, from oral rat experiments. A regression analysis of these data yielded the following relationship:

$$TLV = 0.029\ (LD_{50}) \tag{28}$$

The lower 95% confidence limit of this regression line was derived and shown to be described by the following expression:

$$(TLV)_{low} = 4.5 \times 10^{-4}\ (LD_{50}) \tag{29}$$

The treatment described below is a modification of the approach used by Stokinger and Woodward.[3] The major difference is the use of the $(TLV)_{low}$ value of the pollutant in place of the reported TLV.

By definition, the $(TLV)_{low}$ of a pollutant is that air concentration to which a normal individual may be safely exposed to any substance for an 8 hour working day at the 95% confidence level. In addition to using this basic parameter, the following assumptions are made:

a) Ten cubic meters of air are breathed/working day and all pollutants are completely absorbed in the body.
b) The total amount of pollutant in 10 cubic meters of $(TLV)_{low}$ air can be safely tolerated by man.
c) This total amount would also be safely tolerated daily if contained in drinking water.
d) Two liters of drinking water are consumed per day and all of the soluble contaminants are completely absorbed into the body.

Thus, ten times the number of mg contained in one m^3 of $(TLV)_{air}$ may be safely distributed in 2 liters of drinking water. The estimate of safe pollutant concentration (x_e) may be expressed as follows:

$$x_e = \frac{10\ m^3\ (TLV)_{low}\ mg/m^3}{2l} \tag{42}$$

$$= 5\ (TLV)_{low}\ mg/l$$

Since, $$(TLV)_{low} = 4.5 \times 10^{-4}\ LD_{50} \quad (43)$$

$$x_e = 2.25 \times 10^{-3}\ LD_{50}$$

This expression was used directly to generate derived estimated data for selected inorganic cations and anions. The calculated values were compared to the EPA proposed values and showed generally good agreement (Tables 14 and 15). The pesticides for which values have been proposed were treated similarly and the method was not found to be applicable. The derived values were 100 times higher than EPA proposed values (Table 16).

An alternative form of this equation is available for use when evaluating a pollutant with an established TLV and no LD_{50} data. It was shown that

$$LD_{50} = 34.5\ TLV. \quad (33)$$

Substitution then yields the desired expression:

$$x_e = 7.76 \times 10^{-2}\ TLV \quad (44)$$

There are three practical advantages in utilizing the $(TLV)_{low}$ - LD_{50} concept over the Stokinger-Woodward TLV approach.

(1) LD_{50} have been determined for a much larger number of compounds and hence, the $(TLV)_{low}$ treatment is applicable to a greater number of pollutants.

(2) Knowledge of the respiratory and gastrointestinal absorption factors for specific compounds, which Stokinger and Woodward used in their treatment, is not required.

(3) The $(TLV)_{low}$ has a built-in safety factor making additional corrections unnecessary.

Based on Method II, the criterion used to assess a pollutant hazard would be expressed as

$$\frac{x}{2.25 \times 10^{-3}\ LD_{50}} \geq 1.0; \qquad \frac{x}{7.76 \times 10^{-2}\ TLV} \geq 1.0 \quad (45;46)$$

x = actual pollutant drinking water concentration (mg/l).

If, for any pollutant, this quotient is equal to or greater than unit a hazard is judged to exist.

Table 14. ESTIMATED WATER STANDARDS - INORGANIC

Method II

Contaminant	Proposed St'd (mg/l)	Ionic LD_{50} (mg/kg)	x_e (mg/l)
Ag	0.05	32	0.072
As	0.05	5	0.011
Ba	1.0	99	0.223
Cd	0.010	54	0.122
CN	0.02	3.4	0.008
Cr	0.05	28	0.063
F	1.4-2.4	80	0.180
Hg	0.002	27	0.061
NO_3(as N)	10.0	231	0.520
Pb	0.05	169	0.380
Se	0.01	3	0.007

$$x_e = 2.25 \times 10^{-3} \text{ (Ionic } LD_{50})$$

$$x_e = \frac{10(TLV)_{low}}{2} = 5 \ (TLV)_{low}$$

$$(TLV)_{low} = 4.5 \times 10^{-4} \ (LD_{50})$$

$$x_e = 2.25 \times 10^{-3} \ (LD_{50})$$

Table 15. COMPARISON OF PROPOSED AND ESTIMATED STANDARDS - INORGANIC

Method II

Contaminant	Proposed Standard (mg/l)	x_e	x_e/Proposed Standard
Ag	.05	.072	1.44
As	.05	.011	.22
Ba	1.	.223	.22
Cd	.01	.122	12.2
CN	.20	.008	.04
Cr	.05	.0063	1.26
F	1.4-2.4	.180	.10
Hg	.002	.061	30.5
NO_3 (as N)	10.	.520	.05
Pb	.05	.380	7.6
Se	.01	.007	.7

Table 16. ESTIMATED STANDARDS - PESTICIDES

Method II

Contaminant	LD_{50}	x_e (mg/ml)*	Proposed St'd (mg/ml)
Chlordane	283	.64	.003
Endrin	3	.007	.0002
Heptachlor	40	.09	.0001
Lindane	76	.17	.004
Methoxychlor	5000	11.25	.10
Toxaphene	60	.14	.005
2,4-D	375	.84	.10
2,4,5-TP (Silvex)	650	1.5	.01

*$x_e = 2.25 \times 10^{-3}\ LD_{50}$

$$x_e = \frac{10\ (TLV)_{low}}{} = 5\ (TLV)_{low}$$

$$(TLV)_{low} = 4.5 \times 10^{-4}\ LD_{50}$$

$$x_e = 2.25 \times 10^{-3}\ LD_{50}$$

Selection of Appropriate Toxicity Data

A workable pollution criteria statement should involve the use of toxicity and pharmacological data already compiled. Information such as maximum no-effect body burden levels, percent gastrointestinal absorption, biological or elimination half-lives, although extremely pertinent, would normally not be known. Whenever possible, oral rat LD_{50} data was used in this treatment. Although in some cases the proposed EPA drinking water standards were estimated using other species, the more available oral rat information was used to provide greater scope of application.

1. Inorganic Chemicals

Any metal in drinking water must be present as a stable soluble compound. Selection of an appropriate LD_{50} value for a particular metal is by no means a straightforward task. Different compounds of the same metal have widely different oral rat LD_{50} values.[13] In this treatment, the following criteria were used.

(1) The compound must be stable and be at least slightly soluble in water.

(2) Since LD_{50} data is available only for molecular species, the reported toxicity represents a contribution of both anion and cation moieties. In an attempt to relate molecular toxicity to the ion under study, the toxicity of the associated ion must be minimal. Cation LD_{50} data was obtained from toxicity data of metal salts containing relatively inocuous anions, e.g., chlorides, nitrates, oxides. In a similar way anion LD_{50} data was obtained from toxicity data of salts of relatively inocuous metals, e.g., sodium potassium.

(3) The most toxic (lowest LD_{50} - preferably oral rat) compound meeting the above criteria was selected for use.

Since LD_{50} values are expressed in terms of weight of compound under test, the cation (or anion) content was calculated and the LD_{50} reported as mg of cation or anion/kg. This value is defined as ionic LD_{50} (Table 17).

$$\text{Ionic } LD_{50} = \frac{(\text{Compound } LD_{50}) \times (\text{Percent Content of Metal or Anion})}{100} \qquad (47)$$

Table 17. TOXICITY DATA - INORGANICS

Contaminant	Compound - LD_{50} (mg/kg)	Ionic LD_{50} (mg/kg)
Ag	$AgNO_3$ - 50 (oral, mouse)	32
As	As_2O_5 - 8 (oral, rat)	5
Ba	$BaCl_2$ - 150 (oral, rat)	99
Cd	$CdCl_2$ - 88 (oral, rat)	54
CN	NaCN - 6.4 (oral, rat)	3.4
Cr	$Na_2Cr_2O_7$ - 140 (TDL_o-im, rat)	28
F	KF - 245 (oral, rat)	80
Hg	$HgCl_2$ - 37 (oral, rat)	27
NO_3(as N)	$Ca(NO_3)_2$ - 3900 (oral, rat)	231
Pb	$Pb(NO_3)_2$ - 270 (LDL_o, ip, rat)	169
Se	Na_2SeO_3 - 7 (oral, rat)	3

2. Pesticides

All of the pesticides treated in this analysis had oral rat LD_{50} values reported in the literature.[13]

F. Estimation of Permissible Drinking Water Standards - Method III Application of Kinetic Method

In Section III of this report an air quality criteria based on a one compartment biological model was developed. The following derivation is based on similar considerations.

The rate of pollutant uptake per unit body mass per day is given by

$$R_{uptake} = V\beta x/W \tag{1}$$

where

V = volume drinking water ingested/day (liters)

β = fraction of ingested compound absorbed through gastrointestinal tract

x = drinking water concentration of pollutant (mg/l)

W = body weight (kg)

If $V = 2$, $\beta = 1$, $W = 70$ then the expression reduces to the following form:

$$R_{uptake} = 2x/70 = .029x \tag{48}$$

The maximum daily uptake of a pollutant by a 70 kg man drinking 2 liters of water/day is .029 times the pollutant water concentration. This amount would accumulate indefinitely unless the compound was metabolized or excreted.

Assuming first order metabolism and excretion processes from this one compartment model, a maximum body concentration (cm) of the pollutant would be given by

$$c_m = \frac{V\ x}{Wk} = \frac{R_{uptake}}{k} \tag{49}$$

where k = first order elimination rate constant (hr^{-1}).

The rate constant k is related to the biological half-life τ.

$$k = \ln 2/\tau. \tag{50}$$

Substituting,

$$c_m = \frac{R_{uptake}\ \tau}{1r2} \tag{51}$$

Assuming a 70 kg body weight and a drinking water volume of 2l, the expression simplifies to

$$c_m = .042x\tau. \tag{52}$$

If the safe maximum body concentration and the biological half-life of a pollutant are known, the safe drinking water concentration is readily calculated. As shown in Section III, a survey of compounds with known half-life and LD_{50} values indicated that a safe maximum body concentration may be estimated as 0.05% of the LD_{50}.

$$c_m = .0005\ LD_{50} \tag{53}$$

therefore,

$$x_e = \frac{.012\ LD_{50}}{\tau} \tag{54}$$

Unfortunately, the biological half-life for most compounds is not known. To apply Method III in these cases, a half-life must be assumed.

Derivation of Method III, A, B, C

A list of heavy industrial chemicals was compiled in Section III (Table 3). With the exception of dinitro-o-cresol (τ = 5.78 days), the half-life of these compounds is less than one day. Based on this data, a 30-day half-life was assumed for compounds where this parameter was not known. This provided an additional safety factor for substances with half-life periods less than 30 days. Compounds retained in the body for prolonged periods of time cannot be treated in this manner; a longer assumed half-life must be incorporated into the Method III calculation. An assumed value of 365 days (1 yr) is reasonable in such cases.

Thus, three different τ values may be used in the basic equation (the known value or the assumed 30 day or 1 year value). The following listing gives the alternative forms of Method III estimation and their area of application.

Method III A (known half-life)

$$x_e = \frac{.012\ LD_{50}}{\tau} \tag{54}$$

Method III B (assumed 30 day half-life)

$$x_e = 4.0 \times 10^4 \ LD_{50} \tag{55}$$

Method III C (assumed 1 year half-life)

$$x_e = 3.3 \times 10^{-5} \ LD_{50} \tag{56}$$

In cases where the TLV is known and the LD_{50} is not available, the above equations take the following form

$$LD_{50} = 34.5 \ TLV \tag{33}$$

$$\text{Method III A} \quad x_e = \frac{.414 \ TLV}{\tau} \tag{57}$$

$$\text{Method III B} \quad x_e = 1.38 \times 10^{-2} \ TLV \tag{58}$$

$$\text{Method III C} \quad x_e = 1.14 \times 10^{-3} \ TLV \tag{59}$$

These equations expressed as assessment criteria for pollutant hazard are shown below.

$$\text{Method III A} \quad \frac{x\tau}{.012 \ LD_{50}} \geq 1.0; \ \frac{x\tau}{.414 \ TLV} \geq 1.0 \tag{60;61}$$

$$\text{Method III B} \quad \frac{x}{4.0 \times 10^{-4} \ LD_{50}} \geq 1.0; \ \frac{x}{1.38 \times 10^{-2} \ TLV} \geq 1.0 \tag{62;63}$$

$$\text{Method III C} \quad \frac{x}{3.3 \times 10^{-5} \ LD_{50}} \geq 1.0; \ \frac{x}{1.14 \times 10^{-3} \ TLV} \geq 1.0 \tag{64;65}$$

x = actual pollutant water concentration (mg/l)

τ = biological half-life (days)

LD_{50} = animal (oral rat) LD_{50} (mg/kg)

If, for any pollutant these quotients are equal to or greater than unit a hazard is judged to exist.

The recommended treatment for compounds with a known half-life is Method III A. However, the value of parameter will not be available for most pollutants. In these cases, Method III B should be used except for those compounds with known prolonged body retention times for which Method III C is appropriate.

A 30-day half-life was assumed for the group of inorganics and the corresponding estimated water standards were calculated (Table 18) (Method III B). Only the derived standard water value for mercury was appreciably higher (x 5.5) than the proposed limit. However, the proposed value was based on the reported toxicity of methylmercury which has a half-life of 70 days. If this value is used in the original expression, the estimated water concentration limit is .0046 mg/l (proposed, .002 mg/l).

Chlorinated pesticides and other lipid soluble organic compounds are stored in human adipose tissue for prolonged periods of time. Pollution criteria should be assessed with this is mind. Thus, the longer half-life assumption is applicable in these cases (Method III C). Table 19 lists the estimated and proposed water standards for a series of pesticides. Only two compounds, chlordane and heptachlor, gave estimated values appreciably higher (x9-13) than those proposed. It is significant that an additional safety factor was applied to the proposed standards of these substances because of organoleptic effects or presence in the diet.

G. Estimation of Permissible Drinking Water Standards for Multicomponent Systems

When two or more pollutants are present, the effect of each should be considered additive and their combined action should be given primary consideration. This treatment is recommended by the ACGIH[2] and is shown below.

$$\sum_{1}^{n} \frac{x_i}{(x_e)_i} \geq 1.0 \qquad (66)$$

x_i = actual drinking water concentration of ith pollutant (mg/l)

x_e = estimated drinking water concentration of ith pollutant (mg/l)

If the above summation equals or exceeds unity a hazard is judged to exist.

This expression can be evaluated in terms of the general estimation methods previously discussed by appropriate substitution of x_e. The water quality standards according to these methods are given below.

Table 18. ESTIMATED WATER STANDARDS USING ASSUMED HALF-LIFE - INORGANICS

Method IIIB

Contaminant	Ionic LD_{50}	x_e (τ 30 days) (mg/l)	Proposed St'd (mg/l)
Ag	32	.013	.05
As	5	.002	.05
Ba	99	.040	1.0
Cd	54	.022	.01
CN	3.4	.001	.20
Cr	28	.011	.05
F	80	.032	1.4-2.4
Hg	27	.011	.002
NO_3 (as N)	231	.092	10.0
Pb	169	.068	.05
Se	2	.001	.01

$$x_e = \frac{.0005 \times .693}{.0286 \times \tau} (LD_{50})$$

$$x_e = \frac{.012 \ (LD_{50})}{\tau}$$

$$x_e \ (\tau \ 30 \text{ days}) = 4 \times 10^{-4} \ (LD_{50})$$

Table 19. ESTIMATED WATER STANDARDS USING ASSUMED HALF-LIFE - PESTICIDES

Method IIIC

Contaminant	LD_{50}	x_e (τ 365 days) (mg/l)	Proposed St'd (mg/l)
Chlordane	283	.0093	.003
Endrin	3	.0001	.0002
Heptachlor	40	.0013	.0001
Lindane	76	.0025	.004
Methoxychlor	5000	.1650	.10
Toxaphene	60	.0020	.005
2,4-D	375	.0124	.10
2,4,5-TP (Silvex)	650	.0215	.01

$$x_e = \frac{.0005 \times .693}{.0286 \times \tau} (LD_{50})$$

$$x_e = \frac{.012 \ (LD_{50})}{\tau}$$

$$x_e \ (\tau \ 365 \text{ days}) = 3.3 \times 10^{-5} \ (LD_{50})$$

Method I $$\sum_{i}^{n} \frac{x_i \beta_i}{(5\alpha\ TLV)_i} \geq 1.0 \quad (67)$$

Method II $$\sum_{i}^{n} \frac{x_i}{(2.25 \times 10^{-3}\ LD_{50})_i} \geq \quad (68)$$

Method III A $$\sum_{i}^{n} \frac{x_i \tau_i}{(.012\ LD_{50})_i} \geq 1.0 \quad (69)$$

Method III B $$\sum_{i}^{n} \frac{x_i}{(4.0 \times 10^{-4}\ LD_{50})_i} \geq 1.0 \quad (70)$$

Method III C $$\sum_{i}^{n} \frac{x_i}{(3.3 \times 10^{-5}\ LD_{50})_i} \geq 1.0 \quad (71)$$

These equations may be written in terms of TLV by substituting the value 34.5 TLV for LD_{50} as shown in previous sections.

Concentrations of selected pesticide and inorganic pollutants were taken from the literature[15] and a water quality standard calculated using the above equations. The pollutant concentration represents a purely hypothetical situation and does not refer to the analysis at a particular river site. Moreover, the medium being evaluated in this example is river water and not drinking water.

The inorganic profile (Table 20) showed a borderline water quality standard (0.92) based on the EPA proposed standards and a distinctly polluted situation using Method III B (τ = 30 days) estimated standards. It is significant that the greatest contribution to the inorganic river contamination according to Method III B (97%) and the EPA standards (79%) is due to the anions; cyanide, nitrate and fluoride.

A comparable pesticide profile is shown in Table 21. Water quality standards were calculated based on EPA proposed standards and Method III C (τ = 1 year) estimated standards. The values calculated by both techniques differed by only approximately 25% with the Method III C approach indicating the greater pollution hazard.

H. Comparison of Methods I, II, and III

A group of heavy industrial chemicals is listed in Table 22 and an estimated drinking water standard calculated by Methods I, II, III A

Table 20. ANALYSIS OF A MULTICOMPONENT SYSTEM - INORGANICS (METHOD IIIB)

(SELECTED CONCENTRATIONS IN RIVER WATER)

Contaminant	Proposed St'd (mg/l)	Estimated St'd (mg/l)	Typ. River Conc. (mg/l)*	Absolute (percent) Contribution to Air Quality Standard: Proposed St'd	Absolute (percent) Contribution to Air Quality Standard: Method IIIB
Ag	.05	.013	.001	.02 (2.2)	.08 (.2)
As	.05	.002	ND	---	---
Ba	1.0	.04	.04	.04 (4.4)	1.0 (2.2)
Cd	.01	.022	ND	---	---
CN	.05	.001	.015	.30 (32.6)	15.0 (33.7)
Cr	.20	.011	.002	.01 (1.1)	.18 (.4)
F	1.9 (average)	.032	.70	.37 (40.2)	21.9 (49.2)
NO_3	10.0	.092	.58	.06 (6.5)	6.3 (14.1)
Pb	.05	.068	.006	.12 (13.0)	.09 (.2)
			Water Quality Standard	.92 (100)	44.6 (100)

* Data taken from Reference 14.

Estimated St'd $x_e = 4.0 \times 10^{-4}\ LD_{50}$ (τ = 30 days assumed) - METHOD IIIB

ND - not detected

Air quality standard calculated by: Proposed St'd $\sum_{1}^{n} \frac{x_i}{(\text{EPA Proposed St'd})_i}$

Method IIIB $\sum_{1}^{n} \frac{x_i}{(4.0 \times 10^{-4}\ LD_{50})_i}$

where x_i = conc. (mg/l) of ith component

Table 21. ANALYSIS OF A MULTICOMPONENT SYSTEM - PESTICIDES (METHOD IIIC)

(SELECTED CONCENTRATIONS IN RIVER WATER)

Contaminant	Proposed St'd (mg/l)	Estimated (St'd (mg/l)	Typ. River Conc. (μg/l)*	Absolute (percent) Contribution to Air Quality Standard: Proposed St'd	Absolute (percent) Contribution to Air Quality Standard: Method IIIC
Chlordane	.003	.0093	.02	.007 (1.4)	.002 (.4)
Endrin	.0002	.0001	.03	.15 (30.9)	.30 (47.5)
Heptachlor	.0001	.0013	.02	.20 (41.2)	.015 (2.4)
Lindane	.004	.0025	.01	.003 (.5)	.004 (.6)
Toxaphene	.005	.002	.60	.12 (24.7)	.30 (47.5)
2,4-D	.10	.0124	.10	.001 (.2)	.008 (1.3)
2,4,5-TP (Silvex)	.01	.0215	.05	.005 (1.0)	.002 (.3)
		Water Quality Standard		.485 (100)	.631 (100)

* Data taken from Reference 14.

Estimated St'd, $x_e = 3.3 \times 10^{-5}\ LD_{50}$ (τ = 365 days assumed) - METHOD IIIC

Air quality standard calculated by: Proposed St'd $\sum_{1}^{n} \frac{x_i}{(\text{EPA Proposed St'd})_i}$

Method IIIC $\sum_{1}^{n} \frac{x_i}{(3.3 \times 10^{-5}\ LD_{50})_i}$

where x_i = conc (mg/l) of ith component

Table 22. COMPARISON OF METHODS I, II, IIIA, IIIB

Contaminant	Industrial Organics		x_e, Estimated Water Quality Standards (mg/l)			
	LD_{50} (mg/kg)	τ (days)	Method I	Method II	Method IIIA	Method IIIB
Acrylonitrile	93	---	240	.21	---	.037
Aniline	440	.120	47	.99	44	.176
Benzene	3400	.126	340	7.65	324	1.36
Carbon disulfide	400	.047	---	.9	102	.16
Dinitro-o-cresol	30	5.78	---	---	---	---
Ethylenediamine	1160	---	140	2.61	---	.464
Formaldehyde	800	---	30	1.80	---	.320
Methanol	420	.193	---	.95	26	.168
Methyl chloride	1800	.012	---	4.05	1800	.72
Phenol	414	---	95	.93	---	.166
Pyrindine	891	---	30	2.0	---	.356
Toluene	3000	.083	---	6.75	434	1.20

Method I: taken from Ref. 3.

Method II: $x_e = 2.25 \times 10^{-3}\ LD_{50}$

Method IIIA: $x_e = .012\ LD_{50}/\tau$

Method IIIB: $x_e = 4.0 \times 10^{-4}\ LD_{50}$

(known half-life) and III B (assume τ = 30 days). Compounds with known half-life by the recommended method, Method III A. Because of the relatively short half-life of these compounds, the estimated standards are appreciably higher than those found using Method II or Method III B. It must be borne in mind that these values represent levels at which these compounds can be safely tolerated in drinking water without regard to factors such as odor, taste, carcinogenicity, tetratogenicity or mutagenicity.

SECTION V

CARCINOGENS IN AMBIENT AIR

A. Table of Symbols and Definitions

a	age (years since birth)
B	breathing rate (3700 m^3/yr)
D_N	number of nonsmoker lung cancer deaths/year
C	carcinogen intake (μg/yr)
M	annual lung cancer mortality/100,000, based on Dorn study
M_{DN}	annual nonsmoker lung cancer mortality/100,000, based on Dorn study (equal to M_{NWM})
M_N	annual nonsmoker lung cancer mortality/100,000, based on general population
M_{NB}	annual black nonsmoker lung cancer mortality/100,000, based on general population
M_{NW}	annual white nonsmoker lung cancer mortality/100,000, based on general population
M_{NWF}	annual white female nonsmoker lung cancer mortality/100,000, based on general population
M_{NWM}	annual white male nonsmoker lung cancer mortality/100,000, based on general population (equal to M_{DN})
N	number of cigarettes smoked/day
ND	cigarette nonsmoker
P_N	nonsmoking population
x	carcinogen concentration in ambient air (ng/m^3), annual mean

B. Caveats

The reader should be aware of the following limitations of the methodology used in this report.

(1) The term carcinogen refers only to agents responsible for the initiation and development of lung and bronchial cancers.

(2) It is assumed that a major contributing factor in the incidence of lung cancer death of cigarette smokers and nonsmokers alike is the inhalation of certain carcinogenic hydrocarbons.

(3) The exposure level of eight (8) hydrocarbon carcinogens, identified and quantitated in cigarette smoke, is assumed to be a major contributing factor in lung cancer incidence and a valid measure of lung cancer mortality of smokers and nonsmokers.

(4) The 8-component hydrocarbon mixture, present in cigarette smoke, possesses a total carcinogenic potency equal to a mixture of the same materials in ambient air.

(5) A number of lung cancer deaths are due to carcinogens in the ambient air and this is reflected in the lung cancer mortality of nonsmokers.

(6) Any linear relationship between carcinogen intake by smokers and the lung cancer death rate corresponding to these smokers may be extrapolated to yield valid mortality data for low carcinogen intake values.

(7) Ambient air concentrations have been calculated assuming a total breathing volume of 3700 m^3/year for the average adult.

C. Carcinogen Content in Cigarette Smoke and Intake by Smokers

Cigarette smoke has been analyzed for carcinogenic components by several investigators. The amounts of eight (8) hydrocarbon carcinogens present in cigarette smoke have been reported by Wynder and Hoffman and are listed in Table 23 with a ranking of their relative carcinogenicity.[4]

Knowing the carcinogen content in cigarette smoke, a carcinogen intake rate is readily determined for individuals smoking different number of cigarettes/day for varying lengths of time.

$$C = \frac{10.8\ (N)\ 365}{100}$$

$$C = 39.4\ N$$

Table 23. CARCINOGENIC HYDROCARBONS ISOLATED FROM CIGARETTE SMOKE

Hydrocarbon	Relative carcinogenicity*	Micrograms** per 100 cigarettes
Benzo-a-pyrene	+++	2.5
Dibenz-a,h anthracene	+++	0.4
Benzo-b-fluoranthene	++	0.3
Benzo-j-fluoranthene	++	0.6
Benz-a-anthracene	+	0.3
Chrysene	+	6.0
Benzo-e-pyrene	+	0.3
Indeno - 1,2,3,c,d - pyrene	+	0.4
	TOTAL µg/100 cigts.	10.8

* Carcinogenicity as determined on mouse skin.

** Isolated from cigarette smoke.

Table 24. CARCINOGEN INTAKE FOR SMOKERS AS A FUNCTION OF NUMBER OF CIGARETTES SMOKER PER DAY

Cigarettes smoked/day (N)	Carcinogen intake from cigarettes only, µg/yr (C)
5	197
15	591
30	1182
50	1970

where C = carcinogen intake (μg/yr)

N = number of cigarettes smoked/day

Values of C for different groups of cigarette smokers is shown in Table 24.

D. Lung Cancer Mortality as a Function of Individual Smoking Habits and Age

Lung cancer death rates as a function of age and individual smoking patterns have been reported in the Dorn Study of Smoking and Mortality Among U.S. Veterans.[5] This study was conducted over an eight one-half year period with a population of over 293,000 military veterans holding Government Life Insurance policies. The study group was composed of practically all white males drawn from the middle and upper socioeconomic classes.

The Dorn study gives the cause of death for individuals classified into ten-year age brackets (45-54, 55-64, 65-74 and 75-84). In correlating age and lung cancer mortality (see Figure 7) these groupings are identified by their median age (50,60, 70 and 80). Dorn classified smoking patterns as never or occasionally smoked, 1-9, 10-20, 21-39 and more than 39 cigarettes/day. These groupings are indicated in the present report as follows: nonsmokers, 5, 15, 30, and 50 cigarettes/day.

The data used in this evaluation was taken from the Dorn study as presented in a paper by Kahn on pages 30, 38, 40, 42, and 44 under the cause of death listing of cancer of lung and brochus.[5]. The death rate in each category was determined by dividing the number of deaths by person-years of observation and relating this value to a rate per 100,000.

Supplemental data was taken from a similar study conducted by Hammond.[16] This study was carried out over a 40-year period and consisted of over one million men and women. The study results were reported separately by sex. The male cohort of nonsmokers under age 55 was much larger than the comparable Dorn group and, as a result, provided a more reliable estimate of lung cancer risk for that category.

The lung cancer mortality figures from both studies have dubious significance for age groups under 45 years. The reported number of

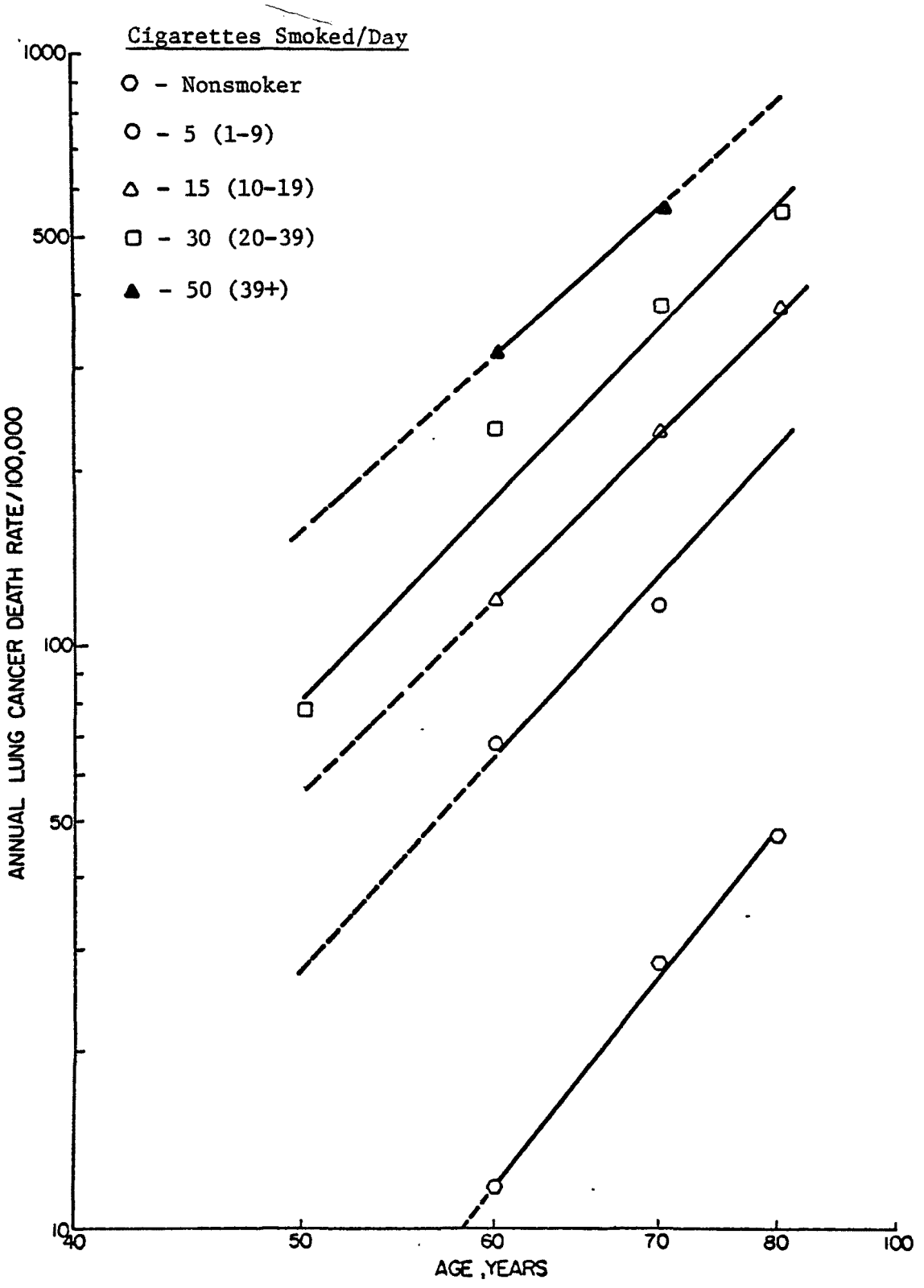


Figure 7. Lung cancer mortality versus age and cigarette use.

deaths in these study subgroups was too low (less than 5) to warrant use in this report. Any age-smoking mortality rates derived from less than 5 reported deaths were considered invalid. These values were established by alternative means as described below. Hammond set a similar criterion in evaluating his study results.[16]

The annual death rates used in this treatment for the different age-smoking categories is shown in Table 25.

E. Relationship of Lung Cancer Mortality and Age/Duration of Exposure

It has been shown that the incidence rate of many different epithelial cancers show a linear relationship with age when both parameters are plotted on logarithmic scales. Doll demonstrated this behavior by showing a linear relationship of this type between the incidence of bronchial carcinoma in cigarette smokers and nonsmokers with age.[17]

A similar treatment was performed on the data obtained from the Dorn study (see Figure 7). The plots show a closely linear lung cancer death rate and age relationship.

Extrapolation of the 5, 15 and 50 cigarettes/day lines to age 50 (45-54 years old) yielded estimated smoker mortality data for this age group. These risk values were used in subsequent steps of this evaluation and are given in Table 26.

Dorn did not report any nonsmoker lung cancer deaths between the ages of 35 and 54. The total number of person-years of observation for subjects between the ages of 35 and 55 in the Hammond study was nearly 4 times that used by Dorn. Hammond's data was examined and used to derive a more valid death rate for these younger nonsmokers. Hammond reported no male nonsmoker lung cancer deaths in the 35-39 age group and only two in the 40-44 year old category. Nine lung cancer deaths were reported for male nonsmokers, 45 to 54 years old. The average annual mortality risk over this ten-year period was shown to be 6.4. Graphic representation of three Dorn and one Hammond nonsmoker points on a risk versus age log-log plot was reasonably linear (Figure 8). The nonsmoker lung cancer risk-age relationship may be expressed by the following equation:

$$M = 1.7 \times 10^{-7} a^{4.42}$$

Table 25. LUNG CANCER MORTALITY AS A FUNCTION OF SMOKING PATTERN AND AGE (FROM DORN STUDY UNLESS INDICATED OTHERWISE)

Age	Cigarettes smoked/day	Lung cancer deaths	Person-years of observation	Lung cancer death rate/100,000
45-54	NS	1	15,134	6.4*
	5	(1)	3,129	28.0
	15	(9)	16,392	57.0
	30	10	12,839	77.9
	50	(3)	1,928	160.0
55-64	NS	25	213,858	11.7
	5	31	45,217	68.6
	15	183	151,664	120.7
	30	245	103,020	237.8
	50	63	19,649	320.6
65-74	NS	49	171,211	28.6
	5	44	37,130	118.5
	15	239	101,731	234.9
	30	194	50,045	387.7
	50	50	8,937	559.9
75-84	NS	4	8,489	47.1
	5	5	1,923	260.0
	15	15	3,867	387.9
	30	7	1,273	549.9
	50	(2)	232	890.0

* From Hammond Study (ref. 16).
Deaths in parenthesis were calculated from a death rate obtained by extrapolation (Fig. 7).

Table 26. ESTIMATED LUNG CANCER MORTALITY OF 45-54 YEAR OLD CIGARETTE SMOKERS

Cigarettes smoked/day	Lung cancer mortality/100,000
5	28.0[a]
15	57.0[a]
30	77.9
50	160.0[a]

[a] Extrapolated values from Figure 7.

Table 27. CARCINOGEN INTAKE AND EQUIVALENT AIR CONCENTRATION FOR NONSMOKERS

Age	Carcinogen intake (μg/yr)	Equiv. carcinogen air conc. (ng/m^3)	Equiv. number of cigarettes smoked/day
45-54	4.7	1.3	.12
55-64	23.0	6.2	.59
65-74	16.0	4.3	.41
75-84	30.0	8.1	.77

Table 28. CARCINOGEN CONCENTRATION IN AMBIENT AIR EQUIVALENCE TO CARCINOGEN INTAKE

Carcinogen intake (μg/yr)	Carcinogen concentration in ambient air (ng/m^3)	Equiv. number of cigarettes/day
197	53.2	5
591	159.7	15
1182	319.5	30
1970	532.4	50

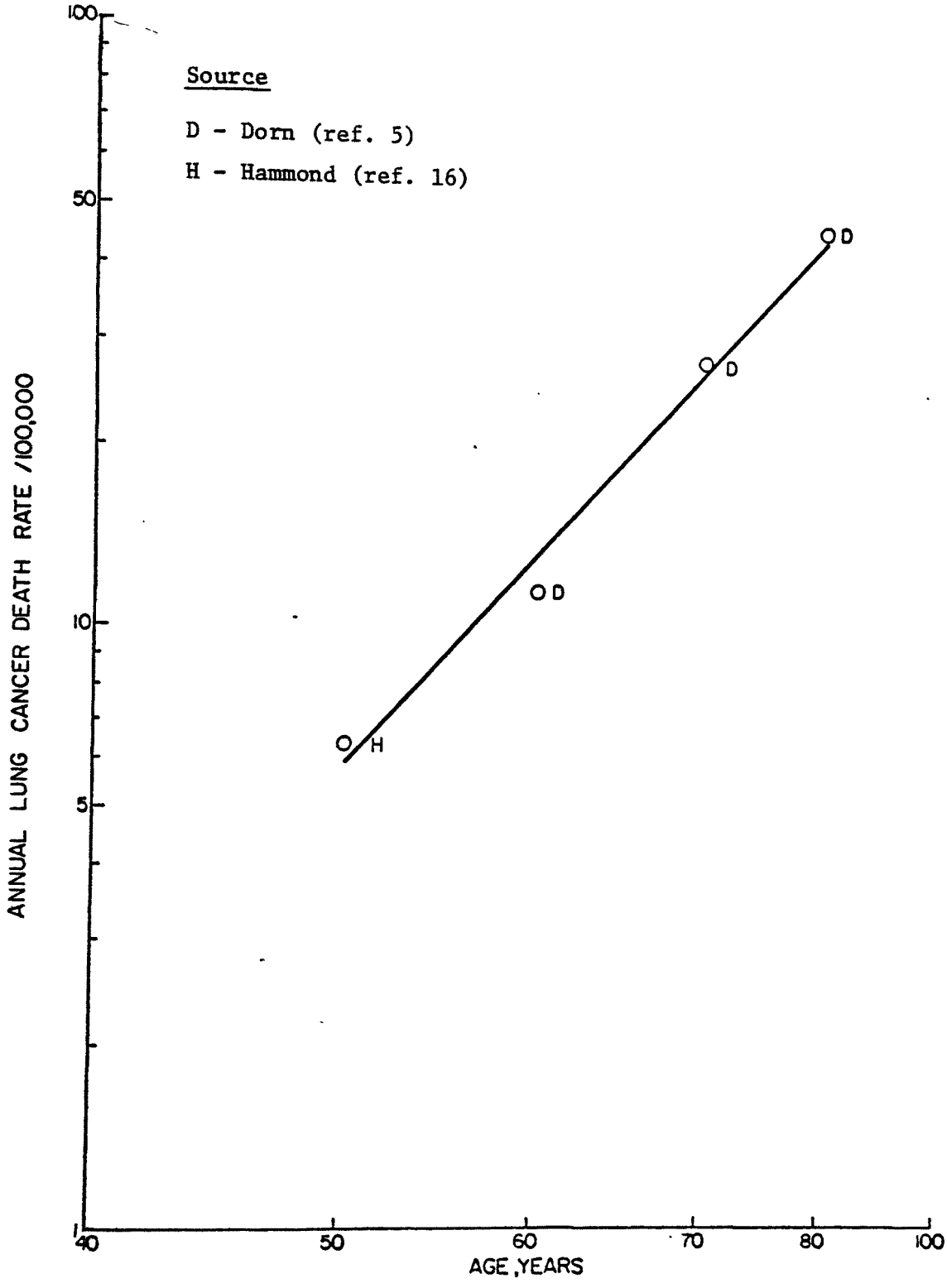


Figure 8. Nonsmoker lung cancer maortality versus age.

where M = annual nonsmoker lung cancer mortality/100,000, based on Dorn and Hammond studies, age 45-84.

a = age (years since birth)

The smoker lines had similar slopes, ranging from 3.7 to 4.7.

A similar British study in which 34,000 male doctors were observed over 17 years showed that smoker incidence of bronchial cancer varied with the seven and one-half power of the age.[17] However, when Doll plotted the same incidence data against nonsmoker age and duration of smoking for cigarette users, he found that both groups were represented by lines with slopes between 4 and 5.

When the Dorn mortality data was plotted in a similar fashion (Figure 9), the slopes of the smoker lines were lowered to 2.5-3.2 (cigarette smoking was assumed to start at age 20). Unlike the incidence rate data reported by Doll, Dorn mortality figures for both nonsmokers and smokers varied uniformly with age and not duration of exposure.

F. Relationship of Lung Cancer Mortality and Carcinogen Concentration in Ambient Air

Since the lung cancer death rates of individuals exposed to different carcinogen levels (i.e., nonsmokers and smokers) are related to age by closely parallel lines (see Figure 7), it is assumed that the mortality - cancer intake relationship, for all individuals of a given age group, may be represented by a single line (see Caveat #6).

Carcinogen intake (μg/yr) for different groups of smokers has been calculated and noted earlier in this report (see Table 2). These data were graphed on a log-log plot against the lung cancer death rate for each age group (Figure 10). This graph shows the same data plotted in Figure 10 except the cigarettes smoked/day variable is replaced by the corresponding carcinogen intake rate.

Figure 10 shows several interesting features:

(1) The points graphed for the 55-64 and 65-74 year old groups lie on parallel straight lines.

(2) The data for the 75-84 year old group falls on a straight line which has a somewhat flatter slope than the others.

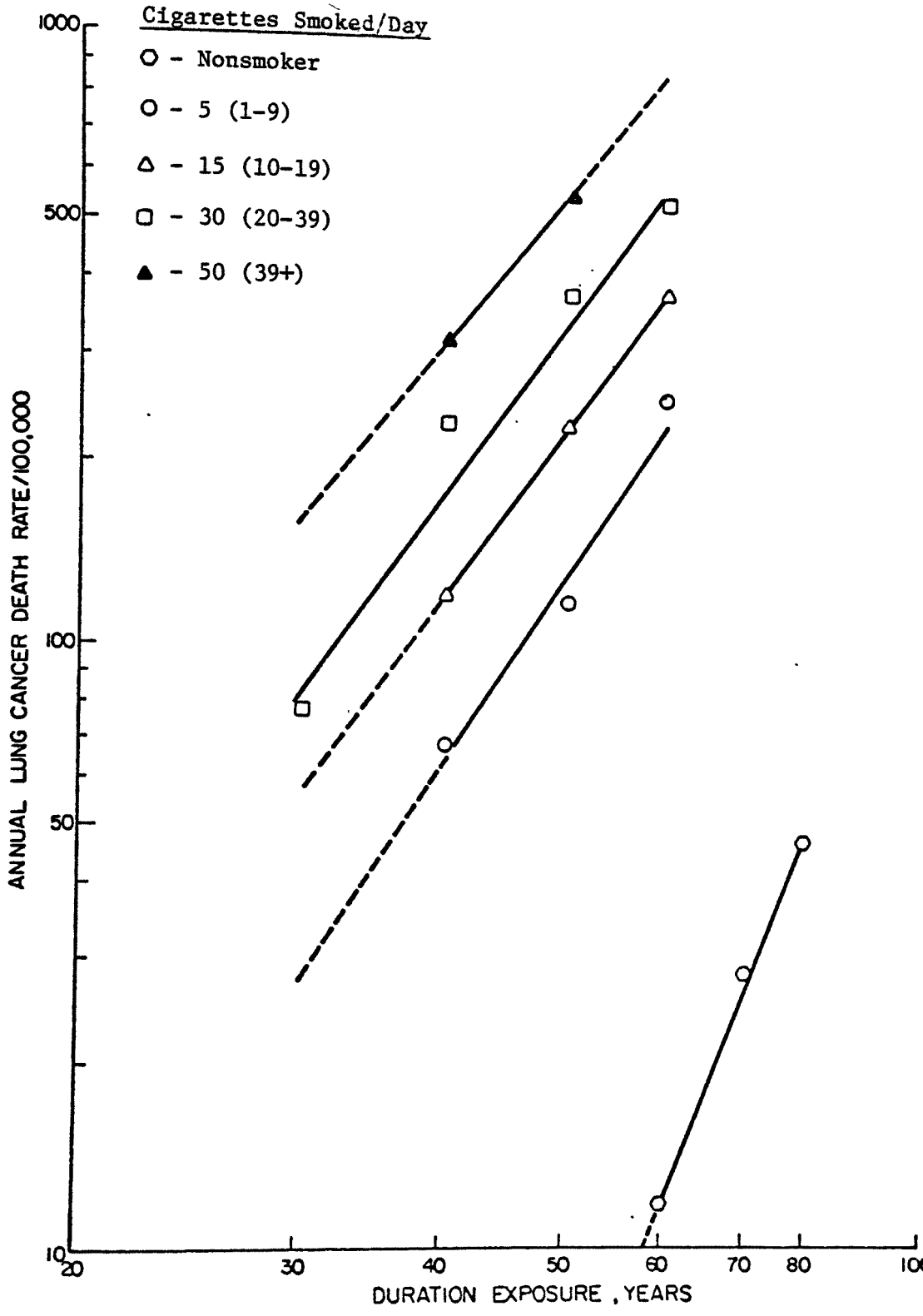


Figure 9. Lung cancer mortality versus duration of exposure and cigarette use.

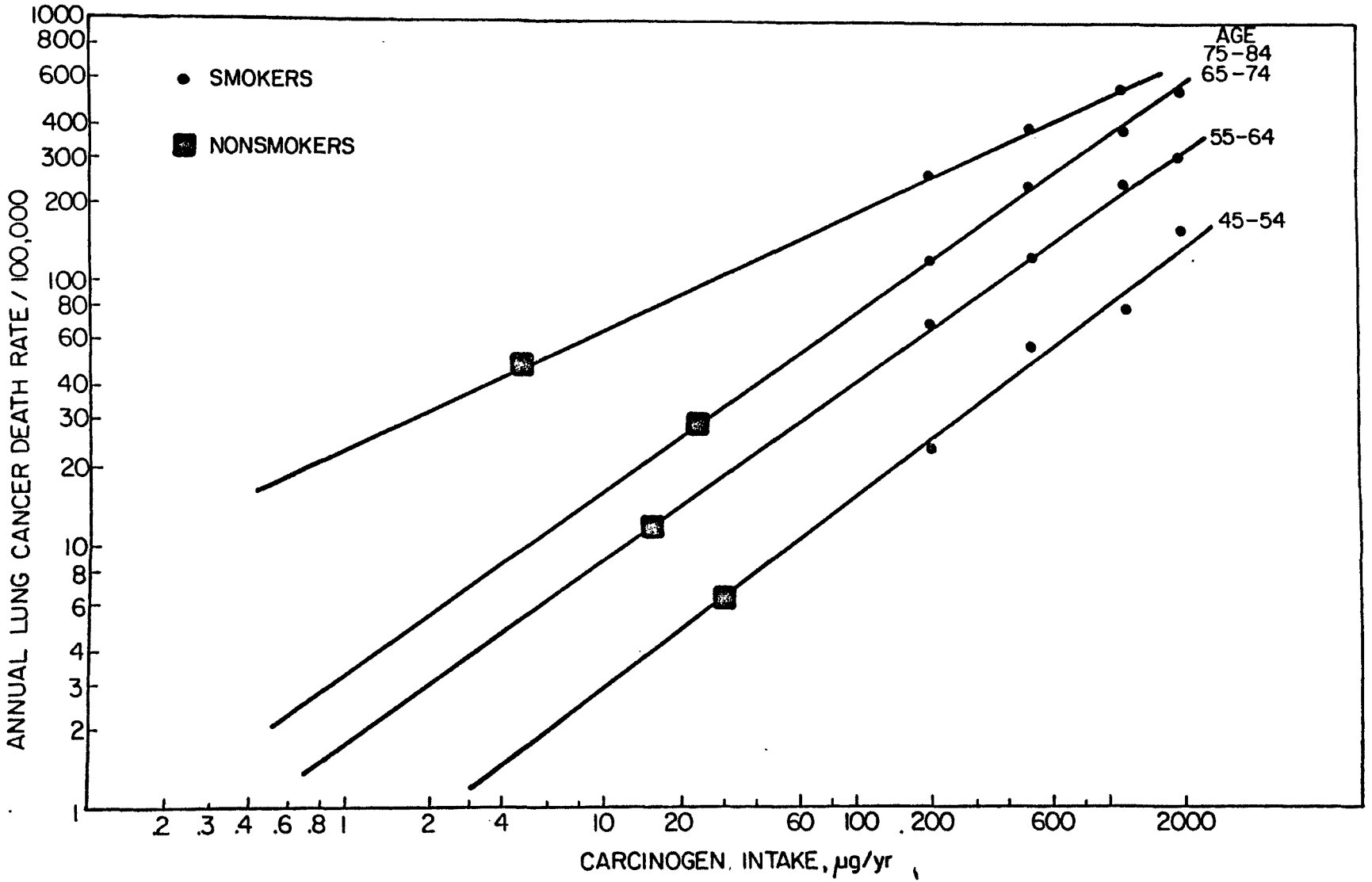


Figure 10. Lung cancer mortality versus carcinogen intake rate.

(3) Three of the four points representing the 45-54 age group were obtained by extrapolation in Figure 7. The slope of this line was somewhat steeper than the other.

The lines connecting the points representing different rates of carcinogen uptake (i.e., number of cigarettes smoked/day) for each age group were extrapolated to low carcinogen intake values. The known nonsmoker (NS) lung cancer mortality rates (Table 25) were positioned on the appropriate age line. This treatment permits one to read an equivalent carcinogen intake rate for nonsmokers from the X-axis in Figure 9. These data is shown in Table 27.

The data shown in Figure 10 were replotted in a form where the carcinogen intake rate was expressed as a carcinogen concentration in ambient air (Figure 11). The breathing rate for all age groups was rounded off to 3700 m^3/year (see Table 2). The carcinogen ambient air concentration equivalent to carcinogen intake was calculated as follows:

$$x\ (ng/m^3) = \frac{C\ (\mu g/yr)}{B\ (m^3/yr)} \times 10^3 \qquad (73)$$

where x = carcinogen concentration in ambient air (mg/m^3), annual mean

C = carcinogen intake ($\mu g/yr$)

B = breathing rate (3700 m^3/yr).

The results are presented in Table 28 and graphed in Figure 11 for smokers of different ages.

The lung cancer death rate for nonsmokers was located on each extrapolated age line in Figure 11. An equivalent air carcinogen concentration to which nonsmokers of different ages were exposed was read off the X-axis and given in Table 27.

The equations which express the linear lung cancer mortality-ambient air concentration relationships shown in Figure 11 have been determined as follows:

Age		
75-84	$M = 42.5\ x^{.419}$	(74)
65-74	$M = 8.2\ x^{.675}$	(75)
55-64	$M = 4.5\ x^{.675}$	(76)
45-54	$M = 1.3\ x^{.727}$	(77)

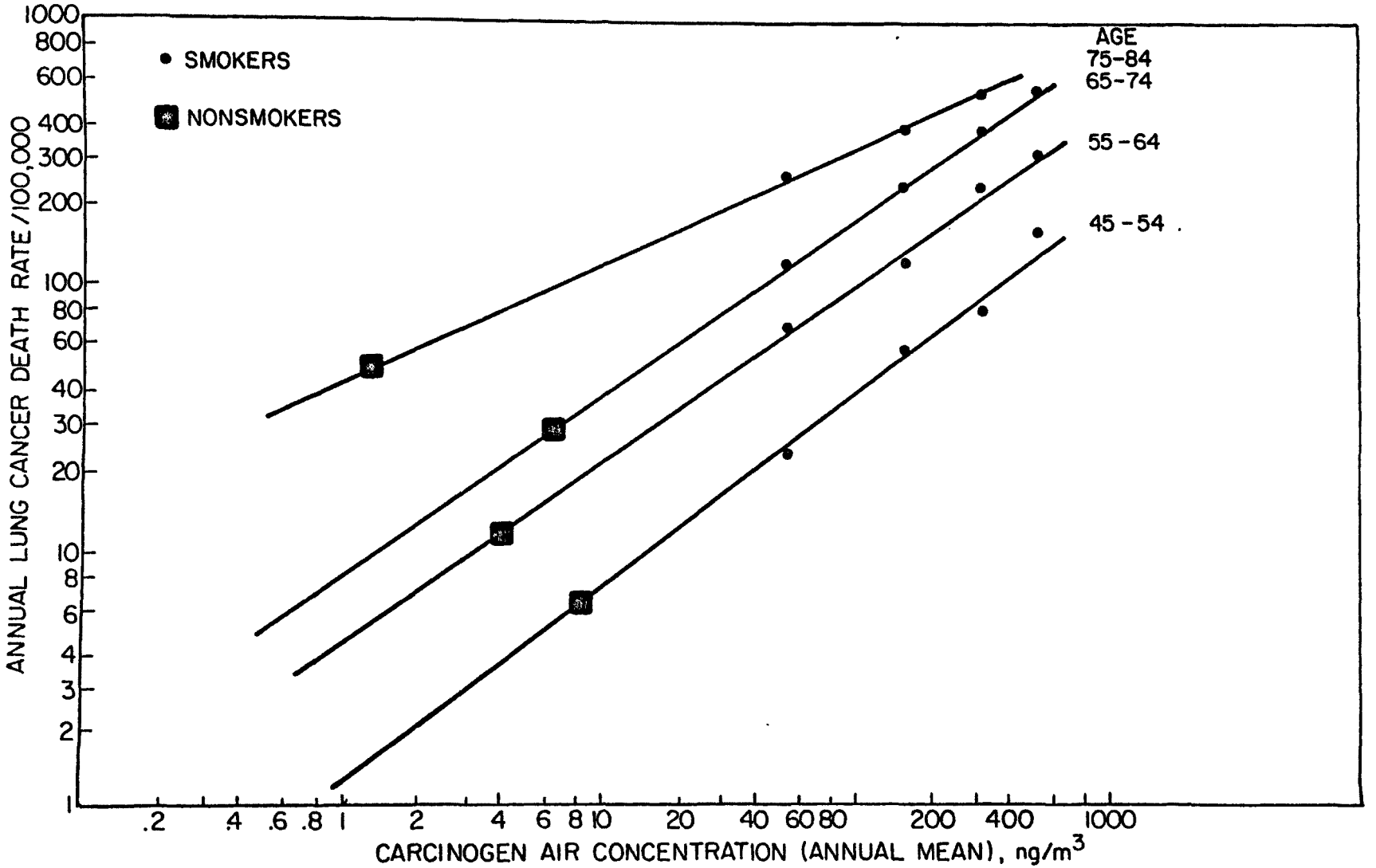


Figure 11. Lung cancer mortality versus carcinogen air concentration.

where M = annual lung cancer death rate/100,000

x = carcinogen air concentration (ng/m^3)

The effect of lowering the carcinogen concentration in ambient air on lung cancer mortality risk for different age groups is shown in Table 29.

All the Dorn study subjects from age 45 to 84 were combined and an overall death rate calculated for each smoking category (Table 30). The lung cancer mortality versus carcinogen air concentration plot for this composite age group is shown in Figure 12. The line best representing these data points is given by the following equation:

$$M = 6.7\ x^{.657} \tag{78}$$

The overall Dorn nonsmoker mortality (M_{DN}) is 19.1/100,000 (Table 30) and the carcinogen air concentration (x) corresponding to this rate is 4.9 ng/m^3 (equivalent to smoking one-half cigarette/day).

G. Lung Cancer Mortality Estimates for the General Population

An expression relating lung cancer mortality (M_N) and carcinogen air concentration (x) was derived for 45-84 year old individuals in the general population. Since the Dorn study was used as a model in this treatment, the general population data were fit to an equation of the same form, $M_N = Ax^Y$.

The exponent Y is a measure of the relative effect of variations in ambient air concentration on lung cancer mortality. It was assumed that all segments of the population over 45 years old possessed a carcinogen intake - lung cancer mortality correspondence represented by lines parallel to those shown in Figures 9 and 10. Thus, the exponent or slope, Y, was assigned the same value as the age 45-84 Dorn group (Y = .657).

The value of A (y-intercept at x = 1) is a measure of the susceptibility to lung cancer death of the population under examination. This constant was readily determined from the nonsmoker lung cancer death rate, the ambient air carcinogen concentration and the slope (Y).

$$A = M_N/x^Y. \tag{79}$$

The Dorn study group consisted of adult white males. As a result, data derived from this study cannot be directly applied to any geographical segment of the general population. Females show lower lung cancer mortality and blacks of both sexes exhibit higher rates. The Dorn nonsmoking death rate (19.1/100,000 at x = 4.9 ng/m^3) was adjusted for an

Table 29. ESTIMATED NONSMOKER LUNG CANCER DEATH RATE AS A FUNCTION OF CARCINOGEN CONCENTRATION IN AMBIENT AIR

Age	Nonsmoker lung cancer death rate/ 100,000*	Carcinogen conc. in ambient air (ng/m^3)	Estimated nonsmoker lung cancer death rate/ 100,000	% Decrease in death rate
75-84	47.1	1.0	42.5	9.8
		0.5	31.8	32.5
		0.1	16.2	65.6
65-74	28.6	1.0	8.2	71.3
		0.5	5.1	82.2
		0.1	1.7	94.1
55-64	11.7	1.0	4.5	61.5
		0.5	2.8	76.1
		0.1	1.0	91.5
45-54	6.4	1.0	1.3	79.7
		0.5	.79	87.5
		0.1	.24	96.3

* See H. A. Kahn (ref. 5) and E. C. Hammond (ref. 16).

Table 30. LUNG CANCER MORTALITY VERSUS CARCINOGEN INTAKE FOR DORN STUDY GROUP AGE 45-84

Cigarettes smoked/day	Smoker carcinogen intake (μg/yr)	Equivalent carcinogen air concentration (ng/m^3)	Total lung cancer deaths	Total person-years	Lung cancer death rate/100,000
NS	(17.9)	(4.9)	78	408,692	19.1
5	197	54	81	87,399	92.7
15	591	157	446	273,554	163.0
30	1182	319	456	167,177	272.8
50	1970	532	118	30,746	383.8

Values in parenthesis were derived graphically.

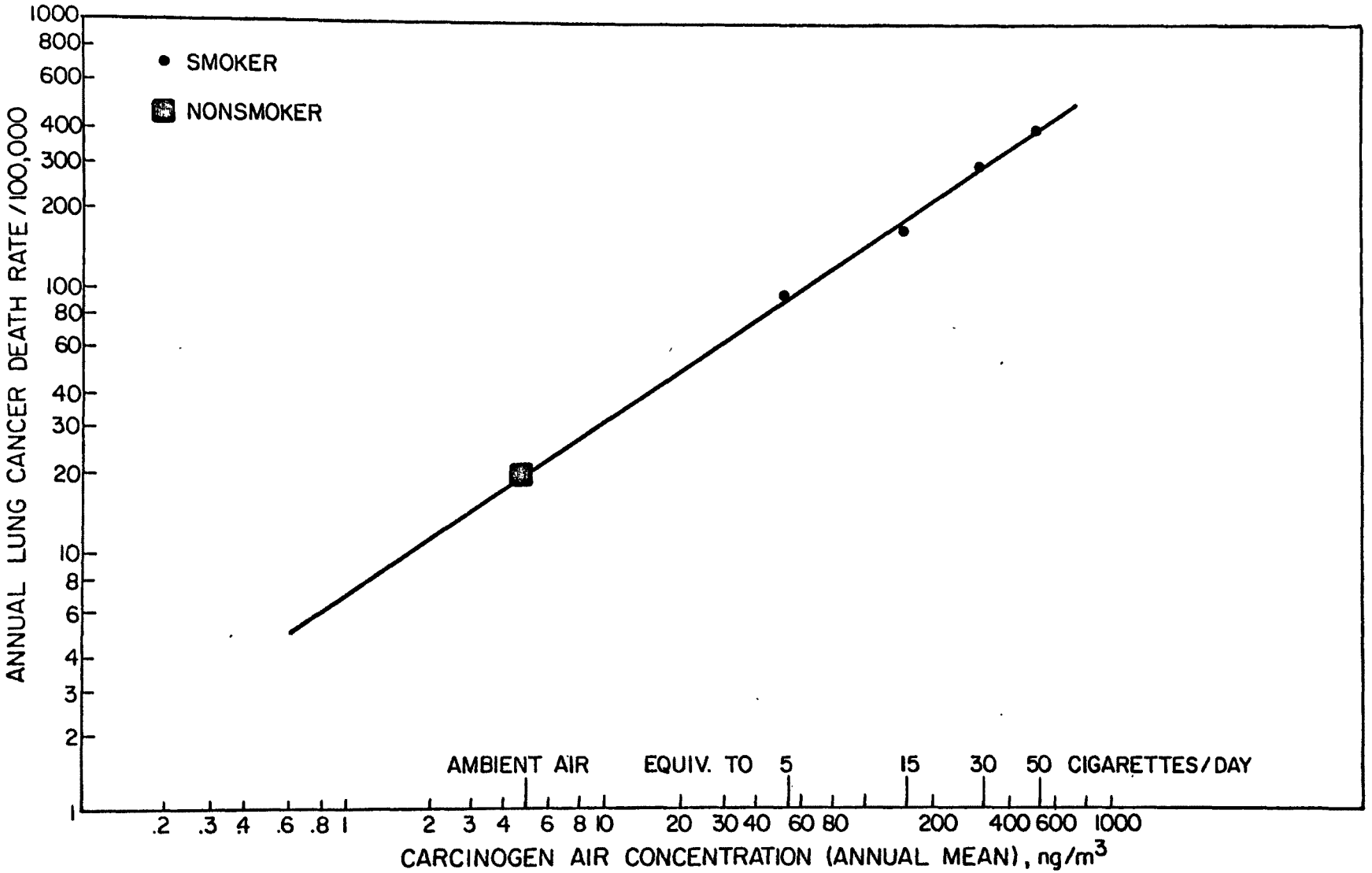


Figure 12. Lung cancer mortality versus carcinogen air concentration - Dorn Study

equal number of females in the population. Hammond has presented data which indicates that the nonsmoker lung cancer mortality rate is 1.5 times higher for men than women.[16] Blacks make up approximately 15% of the population and exhibit an approximately 20% higher lung cancer death rate than whites.[18] Adjustment for these factors gives a nonsmoking lung cancer mortality rate (M_N) of 16.6.

$$M_{DN} = M_{NWM} = 19.1 \tag{80}$$

$$M_{NWM} = 1.5\ M_{NWF};\ M_{NWF} = 12.7 \tag{81}$$

$$M_{NW} = \frac{M_{NWM} + M_{NWF}}{2} \tag{82}$$

$$M_{NW} = 15.9 \tag{83}$$

$$M_N = .85\ M_{NW} + .15\ M_{NB} \tag{84}$$

$$M_{NB} = 1.2\ M_{NW};\ M_{NB} = 19.1 \tag{85}$$

$$M_N = 16.4 \tag{86}$$

where M_{NWM} = annual white male nonsmoker lung cancer mortality/100,000 (equal to M_{DN}).

M_{NWF} = annual white female nonsmoker lung cancer mortality/100,000,

M_{NW} = annual white nonsmoker lung cancer mortality/100,000,

M_{NB} = annual black nonsmoker lung cancer mortality/100,000,

M_N = annual nonsmoker lung cancer mortality/100,000,

Since this derivation was based on Dorn study nonsmokers, the carcinogen air concentration (x) associated with M_N is 4.9 ng/m^3.

The constant A was calculated and the desired lung cancer mortality relationship, shown below, is graphed in Figure 13.

$$A = M_N/x^Y;\ A = 5.77 \tag{79}$$

$$M_N = 5.77\ x^{.657}. \tag{87}$$

This expression has practical application only for nonsmokers. Since cigarette smokers were found to inhale 10 to 100 times more carcinogens than nonsmokers, modest changes in carcinogen air levels would not appreciably effect their lung cancer mortality risk. Moreover, moderate changes in cigarette use patterns would probably correspond to a greater change in carcinogen intake than variations in ambient air quality.

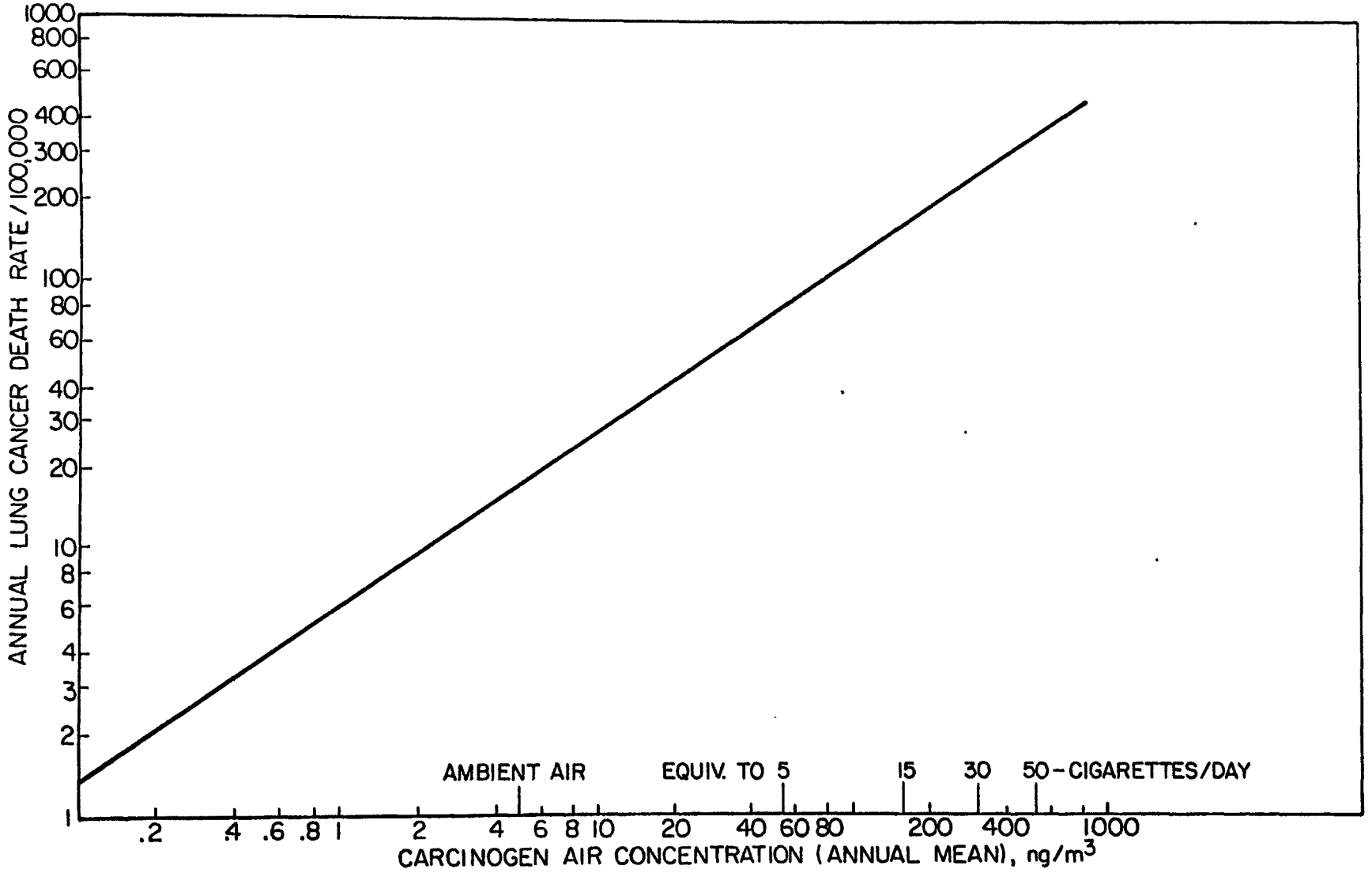


Figure 13. Lung cancer mortality versus carcinogen air concentration - General Population

No adjustment was made for the younger segment of the population. Use of this approach to estimate lung cancer mortality is intended to reflect a potential death risk not only for the adult population but also for younger age groups who will eventually reach the age of 45-84. For this reason, the predicted number of deaths in a year of increased carcinogen air levels may be higher than observed. The additional deaths would result as the exposed individuals aged into 45-84 year old group, under conditions of constant ambient air carcinogen content. Conversely, a marked improvement in air quality may indicate a death rate lower than observed. Higher past exposure levels would be responsible for this difference; the predicted relief would be realized at a later time.

In a nonsmoking population of 150 million, the lung cancer mortality and the number of deaths/year is given in Table 31.

$$M_N = \frac{10^{-5} D_N}{P_N} \tag{88}$$

$$D_N = 1500 M_N \tag{89}$$

$$D_N = 8655 x^{.657} \tag{90}$$

where, P_N = nonsmoking population (1.5×10^8)

D_N = number of nonsmoker lung cancer deaths/year

Sawicki has analyzed ambient air samples and has reported the carcinogen concentrations found at several different locations.[19] A listing of some of his data is given in Table 32. Levels as high as 20 ng/m^3 are indicated at some sampling sites. Reference to Figure 13 shows that continued exposure to these levels will lead to a nonsmoker lung cancer mortality risk of 41.3, an increase of approximately 150% over Dorn study basal rate of 16.4.

Table 31. ESTIMATED NONSMOKER LUNG CANCER MORTALITY AS A FUNCTION OF CARCINOGEN AIR CONCENTRATION

Based on General Population

Carcinogen air concentration, ng/m^3 (x)	Death rate/100,000 (M_N)*	Deaths (D_N)**
100	118.9	178,350
80	102.7	154 050
60	85.0	127,500
40	65.1	97,650
20	41.3	61,950
10	26.2	39,300
5	16.6	24,900
2	9.1	13,650
1	5.8	8 700
.5	3.7	5,550
.1	1.3	1,950

* $M_N = 5.77\ x^{.657}$

** $D_N = 8655\ x^{.657}$

Table 32. CARCINOGEN CONCENTRATIONS FOUND IN AMBIENT AIR[19]

a) United States

Benzo[a]pyrene	6 ng/m^3	(average U.S. urban air)
Dibenzo[a,h]anthracene	.4 ng/m^3	
Benzo[b]fluoranthene	1.6 ng/m^3	(LA, 1971-2, max.)
Benzo[j]fluoranthene	.8 ng/m^3	(LA, 1971-2, max.)
Benz[a]anthracene	4 ng/m^3	(average U.S. urban air)
Chrysene	0.5 ng/m^3	(average U.S. urban air)
Benzo[e]pyrene	5 ng/m^3	(average U.S. urban air)
Indeno [1,2,3,c,d]pyrene	1.2 ng/m^3	(LA, 1971-2, max.)
	Σ 20 ng/m^3	

b) Outside United States

Chrysene	71.5 ng/m^3	(average Budapest)
Benz[a]pyrene	40-415 ng/m^3	(German cities)
Benz[a]pyrene	10-150 ng/m^3	(typical, worldwide)
Benz[e]pyrene	36-362 ng/m^3	(German cities)
Dibenzo[a,h]anthracene	3-32 ng/m^3	(German cities)
	22 ng/m^3	(Budapest, 1971-2)
Benz[a]pyrene	3-7 ng/m^3	(urban survey)

SECTION VI
REFERENCES

1. T. R. Blackwood, "A Method for Estimating TLV Values for Compounds Where None Exists," Letter Report from Monsanto Research Corporation, Dayton, Ohio, to Chemical Process Section of EPA, 15 April 1975.
2. "Threshold Limit Values for Chemical Substances in Workroom Air Adopted by ACGIH for 1974," American Conference of Governmental Industrial Hygienists, 1974.
3. H. E. Stokinger and R. L. Woodward, JAWWA 515 (1958).
4. Wynder and Hoffman, Tobacco and Tobacco Smoke, Academic Press, New York, N. Y., 1967.
5. H. A. Kahn, The Dorn Study of Smoking and Mortality Among U.S. Veterans: Report on Eight and One-Half Years of Observation, National Cancer Institute Monograph No. 19, 1966.
6. "Statement of Basis and Purpose for the Proposed National Interim Primary Drinking Water Standards," EPA, 1975.
7. P. L. Altman and D. S. Dittmer, "Biological Data Book," Vol. 1, 2nd Ed., Fed. Am. Soc. Exper. Biology, Bethesda, Md., 1972.
8. W. W. Waring, in "Pulmanory Disorders," E. L. Kending, Ed., Vol. 1, p. 78, W. B. Saunders, 1972.
9. E. P. Radford, J. Appl. Physiol., 7, 451 (1955); New England J. Med., 251, 877 (1954).
10. N. M. Nelson et al., Pediatrics, 30, 963 (1962).
11. J. Piotrowski, "The Application of Metabolic and Excretion Kinetics to Problems of Industrial Toxicology," HEW, 1971.
12. "Documentation of Threshold Limit Values for Substances in Working Room Air," American Society of Governmental Industrial Hygienists, 3rd Ed., 1971, 2nd Printing, 1974.
13. "The Toxic Substances List," HEW, 1974.
14. D. Bruce Turner, "Workbook of Atmospheric Dispersion Estimates," EPA, Office of Air Programs Publication No. AP-26, 7th Printing, January, 1974.
15. "Water Quality Criteria Data Book. Volume I Organic Chemical Pollution of Fresh Water and Volume II Inorganic Chemical Pollution of Fresh Water," EPA, 1970-1971.

16. E. C. Hammond, Smoking in Relation to the Death Rate of One Million Men and Women, National Cancer Institute Monograph No. 19, 1966.
17. R. Doll, Cancer and Aging: The Epidemiological Evidence, The Harold Dorn Memorial Lecture, 1970.
18. D. L. Levin, S. S. Devasa, J. D. Godwin, II and D. T. Silverman, Cancer Rates and Risks, 2nd Edition, U.S.D.H.E.W., U.S. Government Printing Office, 1974.
19. E. Sawicki, Analysis of a Carcinogen Conglomerate in the Environment and in Tissue, Presented at the Fifth Annual Symposium on Recent Advances in the Analytical Chemistry of Pollutants, Jekyll Island, Georgia, 1975.

SECTION VII

APPENDICES TO SECTION III

A. Effect of Age on the Build-up of Body Concentration

List of Symbols and Definitions

c	instantaneous pollutant concentration in the body (mg/kg)
$(c/\alpha x)_{f(t)}$	ratio of body concentration to effective pollutant concentration for time dependent breathing frequency
$(c/\alpha x)_{f=16}$	ratio of body concentration to effective pollutant concentration for constant breathing frequency of 16 (1/min)
f	respiratory frequency (day^{-1})
$F(t)$	breathing frequency as function of age
k	first order rate constant of excretion (hr^{-1})
LD_{50}	lethal dose 50% kill (mg/kg)
Q	constant ratio of tidal volume to body weight
R_{uptake}	rate of respiratory pollutant uptake (mg/kg day)
t	time (hours or days as stated)
V_T	tidal respiratory volume (ml)
W	body weight (kg)
x	pollutant concentration in air (mg/m^3)
x_m	maximum ground level concentration (mg/m^3)
$(x_m)_i$	maximum ground level concentration of the i-th pollutant (mg/m^3)
α	absorption factor for respiratory uptake of pollutant

Introduction

The objective of the present analysis is the determination of correction factors for pollutant criteria which take into account the effect of age on the rate of respiratory pollutant uptake.

Previously proposed pollutant criteria (Section III) were based on pollutant uptake by adults and did not consider higher uptake rates by children.

It is the purpose of this presentation to provide correction factors for previously proposed decision criteria in order to provide the same level of protection for all age groups.

General Considerations

The rate of pollutant uptake by the body from ambient air was given by

$$R_{uptake} = V_T f \alpha x / W \tag{1}$$

where R_{uptake} = rate of pollutant uptake (mg kg^{-1} $year^{-1}$)
V_T = tidal respiratory volume (m^3)
f = respiratory frequency ($year^{-1}$)
α = absorption factor determining the fraction of inhaled compound entering the body
x = air concentration of pollutant (mg m^{-3})
W = body weight (kg)

Three of the variables determining the rate of pollutant uptake change considerably with age as shown in Table 33 where values are presented of W, f, and V_T for different ages. Ratios of V_T/W calculated for different ages are presented in Column 5 of Table 33. These values reveal that for all practical purposes the ratio of V_T/W can be considered constant and independent of age.

$$V_T/W = Q = (6.36 \pm 0.38) \times 10^{-6}\ m^3\ kg^{-1} \tag{2}$$

Equation (1) then takes the form

$$R_{uptake} = Q \alpha x F(t) \tag{3}$$

Table 33. RESPIRATION DATA AS DEPENDENT ON AGE AND WEIGHT

Age (Years)	Weight (kg) (Ref. 7)	Breathing Frequency (min^{-1}) (Ref. 8)	Tidal Volume (ml) (Ref. 9)	Tidal Vol./ Weight (ml/kg) (*)	Relative Breat Frequencies w Respect to Adu
0	3.4	38 ± 10[10]	13 ± 5[10]	(3.82)	---
1	10.4	31	67	6.44	1.94
2	12.7	26	87	6.85	1.63
3	14.5	25	98	6.76	1.56
4	16.8	24	110	6.55	1.50
5	19.1	23	130	6.81	1.44
6	21.3	22	150	7.04	1.38
7	24.5	21	162	6.61	1.31
8	27.2	20	180	6.62	1.25
9	29.9	20	190	6.35	1.25
10	33.1	19	220	6.65	1.19
11	37.2	19	235	6.31	1.19
12	39.5	19	245	6.20	1.19
13	44.9	19	275	6.12	1.19
14	51.3	19	300	5.85	1.19
15	58.1	18	340	5.85	1.13
16	62.1	17	365	5.88	1.06
17	64.9	17	380	5.86	1.06
18	67.6	16	405	5.99	1.00
19	69.4	16	420	6.05	1.00
22	71.7				
27	73.9				
32	74.8				
37	75.3				
44	75.8				
54	74.8				
64	73.5				
74	71.2				

* Average value of 6.36 ± 0.38 (ml/kg) used for further calculations.

where F(t) is a function which describes the age dependence of the average breathing frequency.

Further, it is assumed that the absorption factor, α, is independent of age. This is very likely an oversimplification since one might expect α to be lower for children than for adults because of (1) a smaller surface area of the respiratory tract at early ages and (2) a shorter residence time of the inhaled air due to the increased breathing frequency. The assumption of a constant absorption factor thus introduces an additional safety factor in further considerations.

Decision Criteria Based on TLV Standards

Equation (3) indicates that pollutant criteria for ambient air which are based either directly or indirectly on TLV data should be corrected by considering the higher breathing frequency of young children. TLV data are established for adults for which an age-independent breathing frequency of 16 min^{-1} is assumed. In order to limit the pollutant uptake by a child at the same level the higher average breathing frequency of the child has to be taken into account. In the last column of Table 33 relative breathing frequencies are given for different ages with respect to the constant breathing frequency of adults. The highest value is about 2.0 for a child of one year of age. Consequently, for equivalent protection of all age groups from ambient pollutants the permissible pollutant concentration should be only one-half of that presently permissible for adults.

A decision criterion for possible health hazards of the form

$$\frac{x_m}{1.07 \times 10^{-4}\ (LD_{50})} \geq 1.0 \qquad (32)$$

was derived from a correlation between TLV and LD_{50} data and utilization of the lower 95% confidence limit of the regression interval. This criteria has to be modified in order to take into account the higher rate of pollutant uptake by small children. Consequently, the maximum permissible ambient air concentration should not exceed half the value given by Equ. (32), the latter now being postulated to be

$$\frac{x_m}{5.35 \times 10^{-5}\ (LD_{50})} \geq 1.0 \qquad (91, \text{ see } 34)$$

Again, if, for any pollutant, the parameter is equal or greater than unity a hazard is judged to exist.

Numerically the same criterion as given by Equ. (91) applies for a multicomponent system for which the sum over all pollutants has to be taken.

$$\sum_{1}^{n} \frac{(x_m)_i}{5.35 \times 10^{-5} \, (LD_{50})_i} \geq 1.0 \tag{38}$$

Decision Criteria Based on Biological Considerations

The change in body concentration of a compound, applying a one-compartment model, is given by the interaction of respiratory uptake and first order excretion of the pollutant,

$$dc/dt = R_{uptake} - kc \tag{92}$$

where k is the first order rate constant of excretion and c is the instantaneous body concentration. Substituting Equ. (3) into Equ. (92) one obtains

$$dc/dt = Q\alpha x F(t) - kc \tag{93}$$

where the first term on the right side is a function of time only because of the changing breathing frequency.

The general solution of Equ. (93) is given by

$$c/\alpha x = C_I \exp(-kt) + \exp(-kt) \int QF(t)\exp(kt)dt \tag{94}$$

where C_I is the integration constant defined by the initial conditions $c = 0$ at $t = 0$. With these initial conditions Equ. (94) yields after integration

$$c/\alpha x = (Q/k) \left[\sum_{0}^{\infty} k^{-n} F^{(n)}(t) - \exp(-kt) \sum_{0}^{\infty} k^{-n} F^{(n)}(0)\right] \tag{95}$$

where $F^{(n)}(t)$ and $F^{(n)}(0)$ are the n-th order derivatives of $F(t)$ for $t = t$ and $t = 0$, respectively.

For the evaluation of Equ. (95) the time dependence of the breathing frequency is approximated by a fourth order polynomial of the form

$$F(t) = \sum_{0}^{4} a_n t^n \tag{96}$$

Substituting Equ. (96) and its higher order derivatives into Equ. (95) yields after rearrangement

$$c/\alpha x = b_o[1 - \exp(-kt)] + b_1 t + b_2 t^2 + b_3 t^3 + b_4 t^4 \tag{97}$$

where the coefficients have the following meanings

$$b_o = k^{-5}(k^4 a_o - k^3 a_1 + 2k^2 a_2 - 6k a_3 + 24 a_4)\ Q \tag{98}$$

$$b_1 = k^{-4}(k^3 a_1 - 2k^2 a_2 + 6k a_3 - 24 a_4)\ Q \tag{99}$$

$$b_2 = k^{-3}(k^2 a_2 - 3k a_3 + 12 a_4)\ Q \tag{100}$$

$$b_3 = k^{-2}(k a_3 - 4 a_4)\ Q \tag{101}$$

$$b_4 = k^{-1} a_4\ Q \tag{102}$$

Breathing frequencies for different ages according to Table 33 and the approximation of their age dependence by Equ. (96) are shown in Figure 14. Equation (97) was evaluated by assuming different half-life times, τ, for pollutants in the range of one to 20 years. Results of these calculations are shown graphically in Figure 15 where values of $c/\alpha x$, the ratio of body concentration in mg/kg to the effective pollutant concentration in mg/m^3, were plotted versus age in years. For comparison, Figure 16 shows corresponding plots calculated with the assumption of a constant breathing frequency of $f = 16\ min^{-1}$ corresponding to an adult. In order to distinguish these $c/\alpha x$ values from the preceding ones they were designated by $(c/\alpha x)_{f=16}$.

$$(c/\alpha x)_{f=16} = (Q/k)\ [1 - \exp(-kt)] \tag{103}$$

In Figure 17 the effect of age on the ratio of body concentrations calculated by both methods (time dependent breathing frequency, $c_{f(t)}$, and constant breathing frequency, $c_{f=16}$) are shown for pollutants of different half-life times.

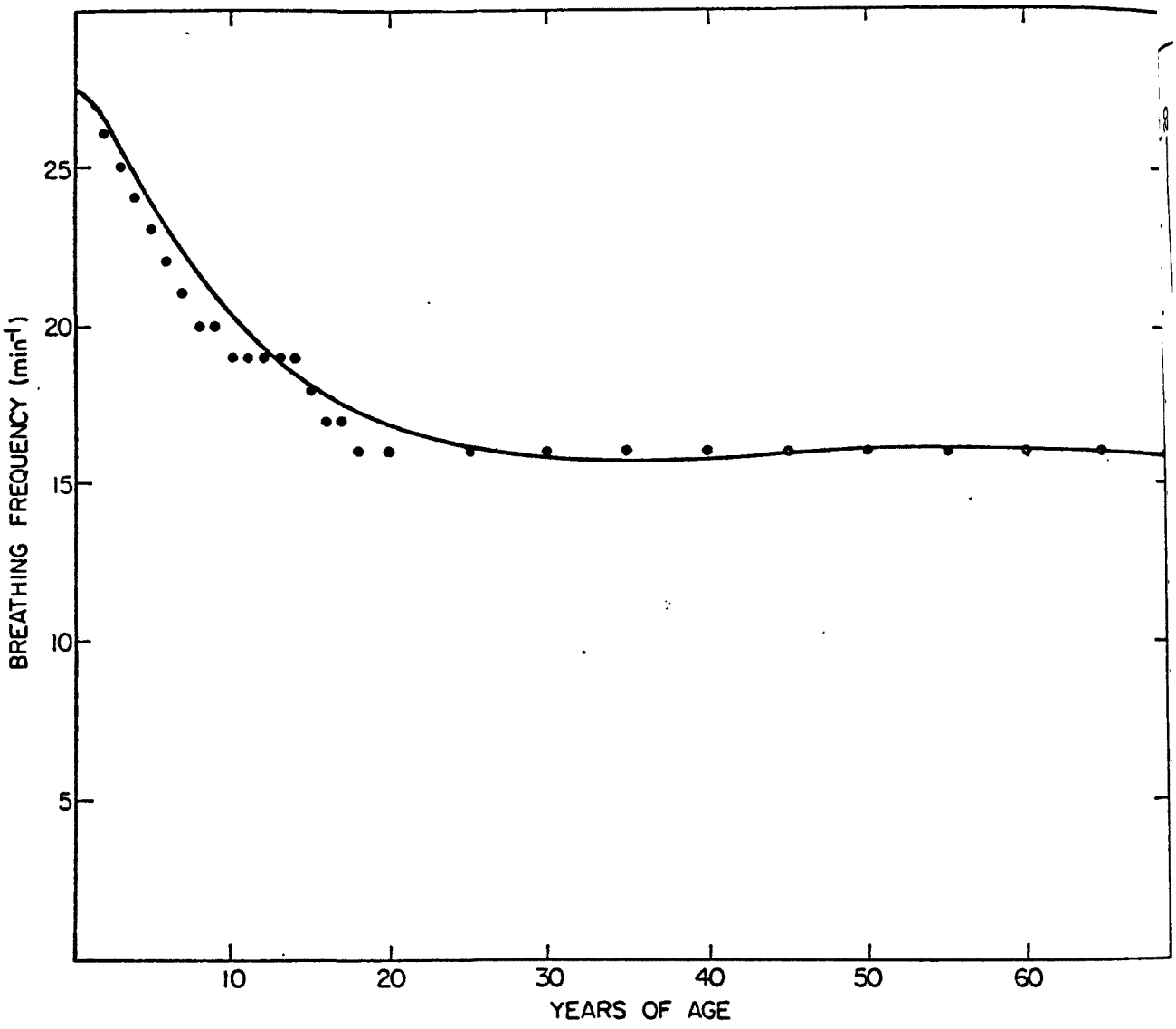


Figure 14. Age dependence of breathing frequency. Points from data of Table 1 are approximated by equ. (96).

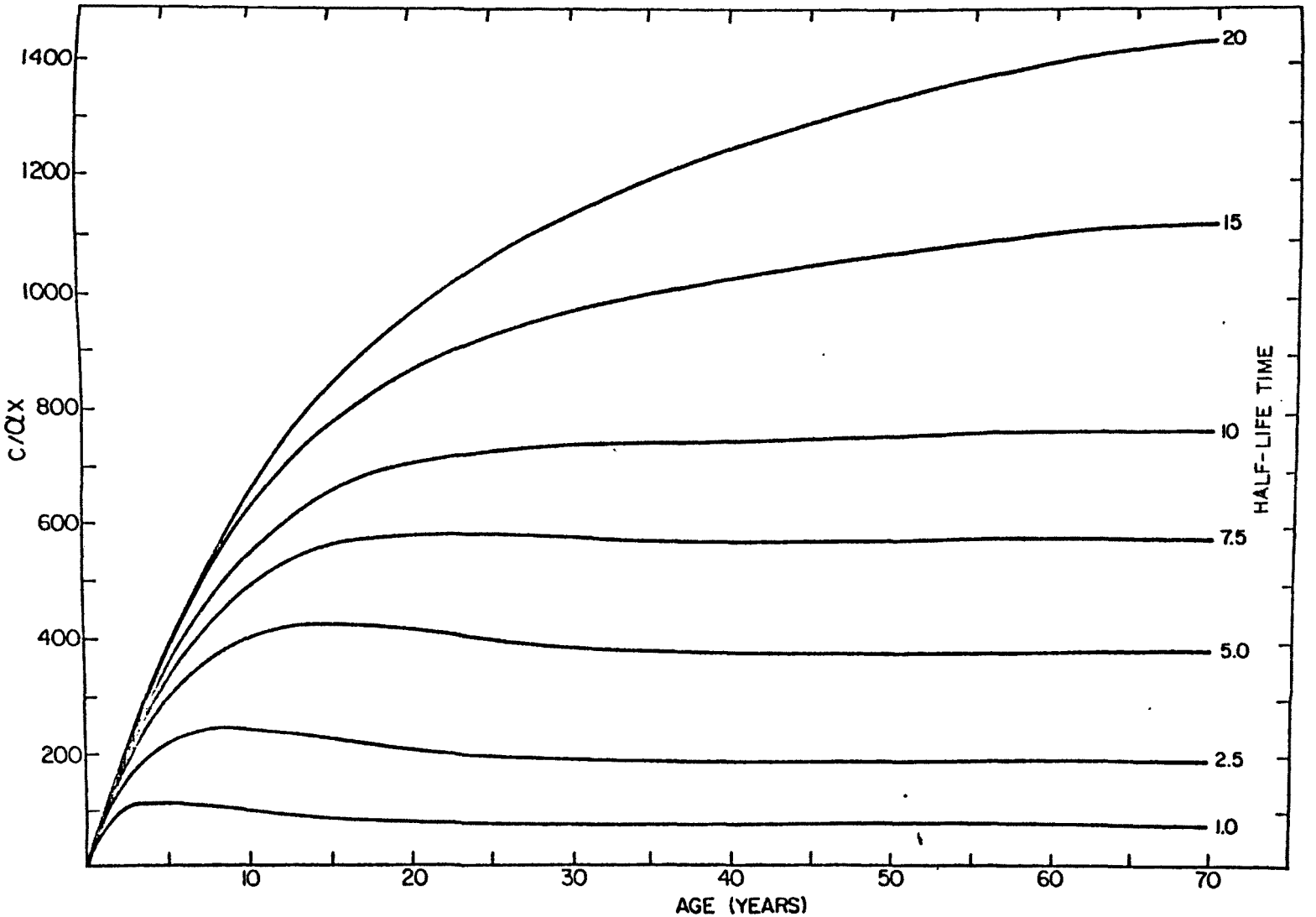


Figure 15. Ratio of body concentration to effective pollutant concentration of air for pollutants with different half-life times in the body. Calculated for age dependent breathing frequencies according to equ. (97). Indicated half-life of the pollutant in years.

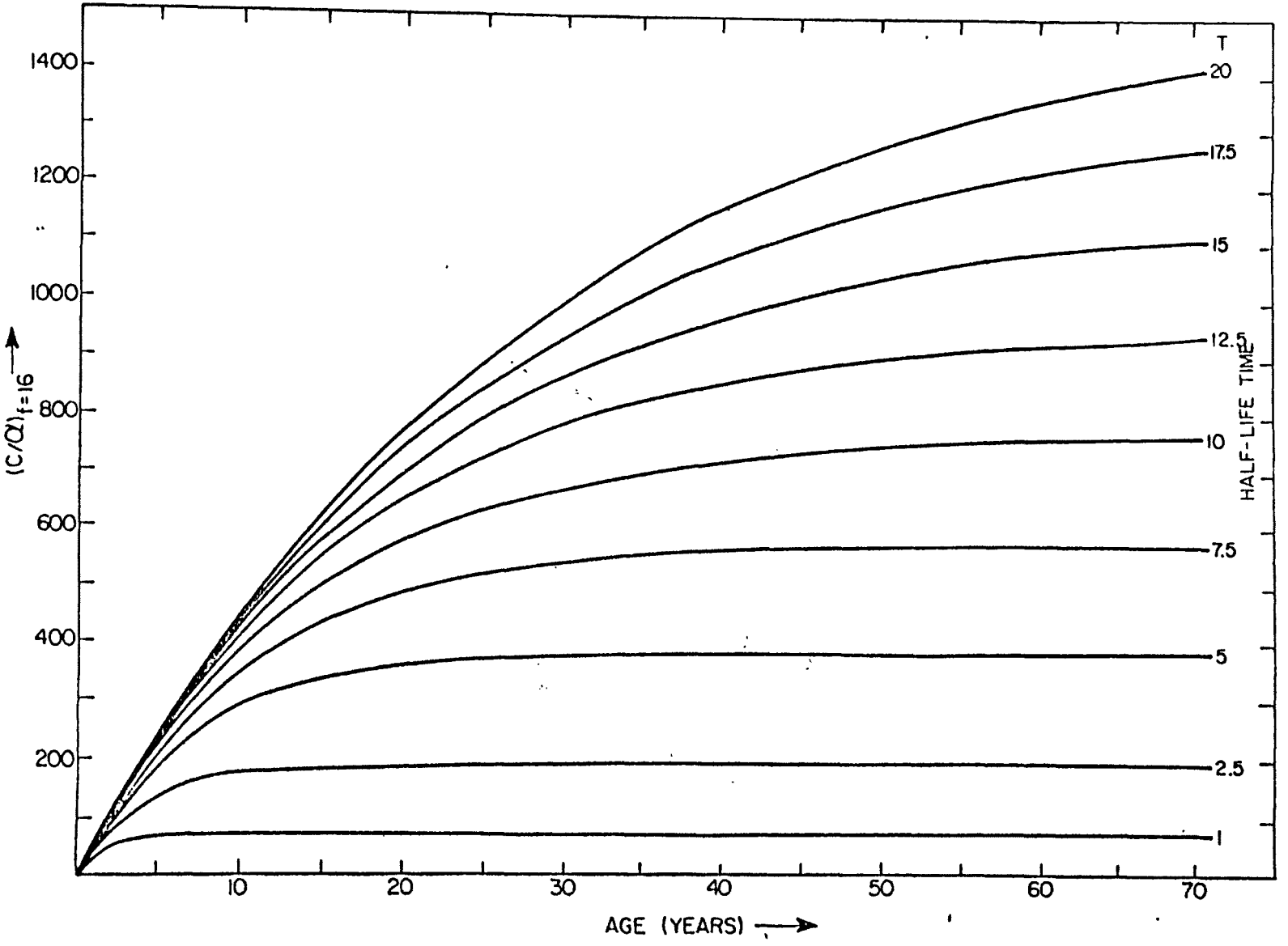


Figure 16. Ratio of body concentration to effective pollutant concentration in air for pollutants with different half-life times in the body. Calculated for the constant breathing frequency of an adult. Indicated half-life of the pollutant in years.

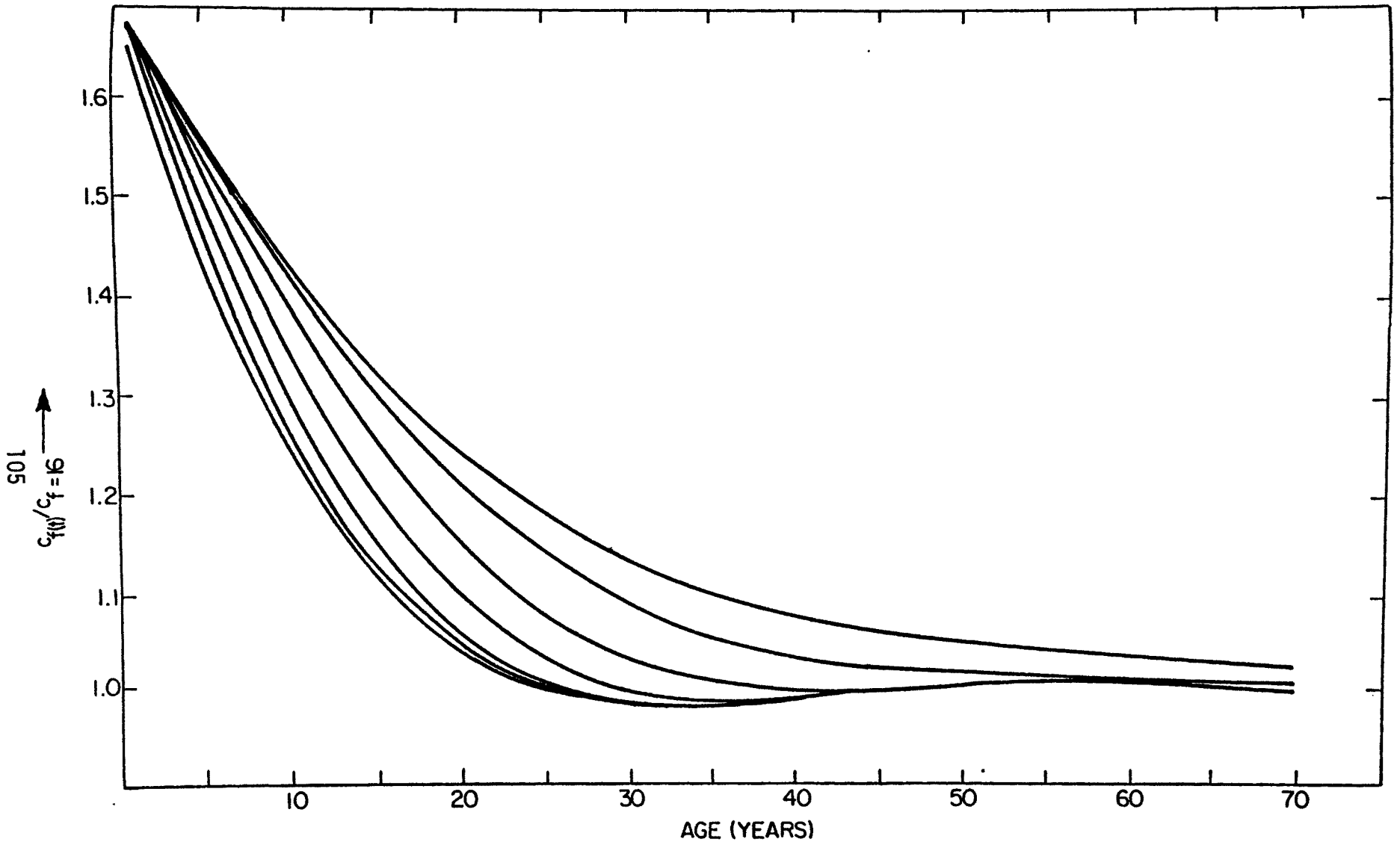


Figure 17. Effect of age dependent breathing frequency on the body concentration of pollutants with different biological half-life times. Half-life times in years from left to right: 0.1, 0.5, 1.0, 2.5, 5, 10 and 20.

$$c_{f(t)}/c_{f=16} = \text{Equ. (97)/Equ. (103)} \tag{104}$$

The lowest curve in Figure 17 corresponds to half-life times of pollutants shorter than 36 days (0.1 years). For these conditions, the ratios of body concentrations are identical with the relative breathing frequencies referred to a constant value of 16 min^{-1} for adults (last column of Table 33). This result is obvious since for such short half-life the body concentration approaches a quasi-stationary state during such a short time interval that the change in breathing frequency during this interval can be neglected. Even for pollutants with half-life times up to one year (second and third curves of Figure 17) pseudo-stationary states can be assumed with good approximations.

The effect of the higher breathing frequencies of infants and children as compared to adults is clearly demonstrated in Figure 18. Ratios of body concentration to effective pollutant concentration are shown for children and adults as a function of exposure time for a pollutant with a half-life time of 36 days. The twofold time scale in Figure 18 assumes that a newly born child and an adult of 25 years of age are both exposed simultaneously to a pollutant concentration of x mg m^{-3}.

The lower curve in Figure 18 corresponds to the adult and shows that in less than one year a constant body concentration is established. This equilibrium value in mg kg^{-1} is 7.6 times the air concentration in mg m^{-3}, provided the absorption factor α is unity. The body concentration of the child is considerably higher and indicates a maximum value at about the age of one when it is about 1.7 times the stationary state concentration of an adult. The body concentration of children slowly declines with increasing age due to the decrease in the average breathing frequency.

Pollutants with longer half-life times (4th to 7th curve in Figure 17 corresponding to half-life times of 2.5, 5, 10, and 20 years, respectively) show pronounced deviations from quasi-stationary states. Because of their low excretion rates and the high rate of uptake in infants, such pollutants are readily accumulated in the body during early life. Nevertheless, data of Figure 17 demonstrate that the body concentration of infants never exceeds the body concentration of adults by more than a factor of 1.7. This factor has to be considered in the modification of decision criteria for ambient pollutants based on biological considerations. The modified

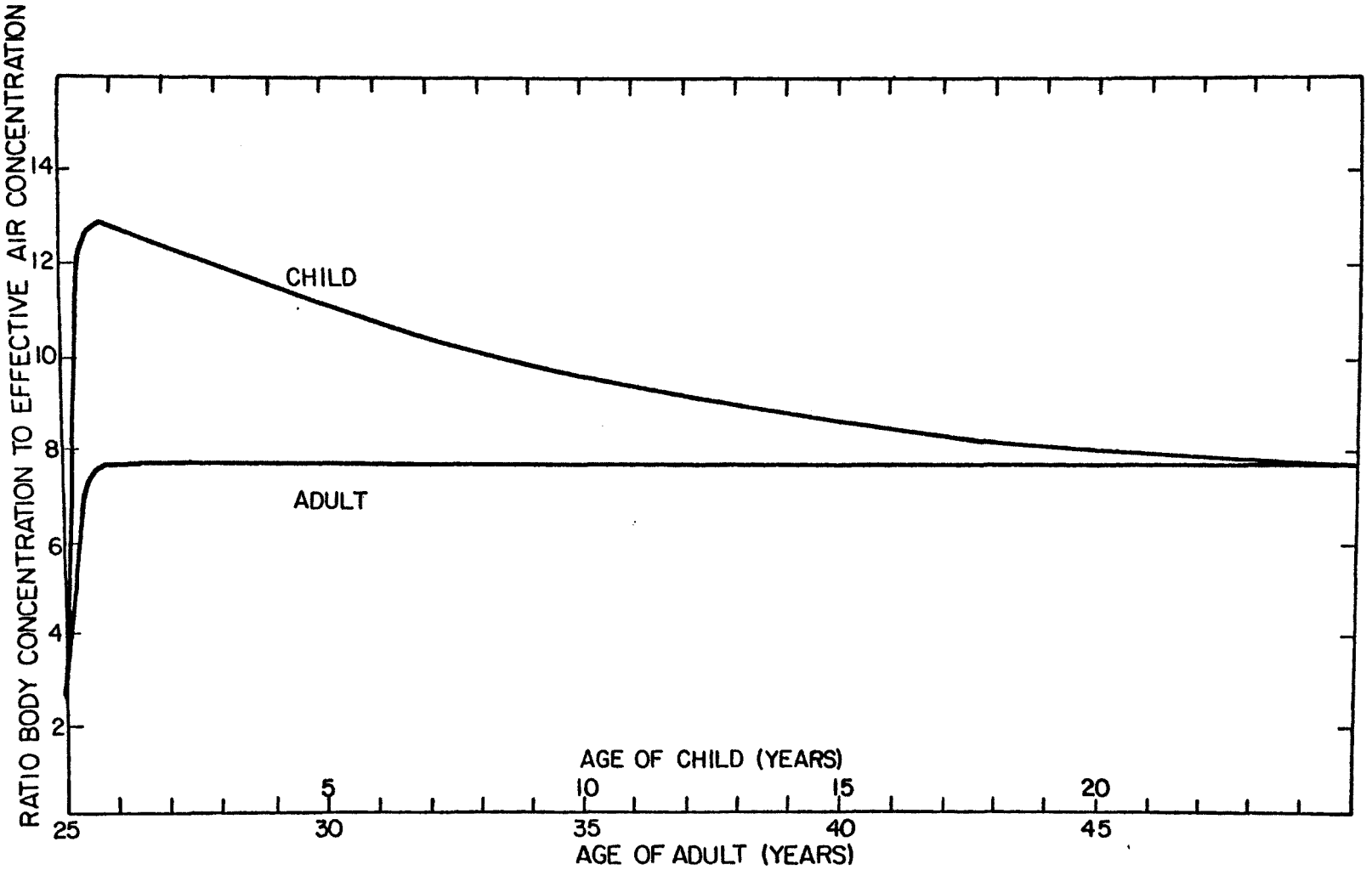


Figure 18. Comparison of the body concentrations of children and adults exposed to the same level of a pollutant with a biological half-life time of 36 days.

decision criteria for possible health hazard are then given by

$$\frac{x_m}{4.77 \times 10^{-5} \, (LD_{50})} \geq 1.0 \qquad (105;\ \text{see } 35)$$

for individual pollutants and for multicomponent systems by

$$\sum_{1}^{n} \frac{(x_m)_i}{4.77 \times 10^{-5} \, (LD_{50})_i} \geq 1.0 \qquad (39)$$

In both cases, if the parameter is equal or greater than unity for any pollutant(s), a hazard is judged to exist.

B. Average Accumulated Body Concentration During Intermittent Exposure

List of Symbols and Definitions

B	rate constants for pollutant uptake by respiration (m^3/kg day)
c	instantaneous pollutant concentration in the body (mg/kg)
C_o	initial pollutant concentration in the body (mg/kg)
C'_n	final body concentration at the end of the n-th uptake interval
C''_n	final body concentration at the end of the n-th recovery interval
$\bar{C}_n$	average body concentration during the n-th period
$\bar{C}_\infty$	average body concentration during the stationary state of intermittent exposure
C_∞	stationary body concentration for continuous exposure
k	first order rate constant of excretion (hr^{-1})
t	time (hours or days as stated)
T'	duration of uptake interval
T''	duration of recovery interval
T	length of one uptake-recovery period
x	pollutant concentration in air (mg/m^3)
τ	biological half-life time of pollutant in the body (hours or days as stated)

Kinetics of Intermittent Exposure

The change in the body concentration of a compound was expressed as a function of constant pollutant uptake and first order excretion.

$$dc/dt = Bx - kc \tag{9}$$

where c = instantaneous body concentration

x = constant air concentration of pollutant

B = rate constant of pollutant uptake (respiratory tidal volume per day per kg body weight)

k = first order rate constant of excretion

t = time

Equation (9) indicates that for continuous exposure the body concentration will approach a steady state value, C_∞, the maximum concentration for which is

$$C_\infty = Bx/k. \tag{106}$$

Integration of Equ. (9) describes the change of concentration with time, which is given by

$$c = C_\infty [1 - \exp(-kt)] + C_0 \exp(-kt), \tag{107}$$

where C_0 is the initial body concentration at time zero and C_∞, the steady state value.

Under working conditions, the exposure to polluted air occurs periodically with a period length of 24 hrs, e.g., an 8 hours working interval followed by a 16 hours recovery interval in unpolluted surroundings. Designating the uptake interval by (') and the recovery interval by (") one obtains the following expressions for the concentration changes during these intervals.

uptake interval: $c'_n = C_\infty [1 - \exp(-kt)] + C''_{n-1} \exp(-kt)$ (108)

recovery interval: $c''_n = C'_n \exp(-kt)$. (109)

In these recursion equations the subscript n designates the number of periods which have occurred since the start of the first exposure. The

concentrations c'_n, c''_n, C'_n, and C''_{n-1} have the following meaning:

- c'_n instantaneous concentration during the n-th uptake interval
- c''_n instantaneous concentration during the n-th recovery interval
- C'_n final concentration at the end of the n-th uptake interval which is identical with the concentration at the start of the n-th recovery interval
- C''_{n-1} final concentration at the end of the (n-1)-th recovery interval which is identical with the concentration at the start of the n-th uptake interval

Both of the latter concentrations are extremes, the highest concentration in one 24 hr period being given by C'_n, the lowest one by C''_n. Fluctuations in body concentrations are most pronounced with compounds possessing short biological half-life, i.e., high excretion rates. If the duration of exposure exceeds about seven-times the half-life, the maximum body concentration, C_∞, will be attained during each exposure interval and complete excretion will take place during the recovery interval.

Under this condition, it follows from Equs. (108) and (109) that the body concentration averaged over a 24 hr period is equal to the maximum concentration for continuous exposure, C_∞, times the fraction of time exposure occurred during the 24 hr period, e.g., for 8 working hours the 24 hrs average is only 1/3 of the maximum value.

Compounds possessing long biological half-lifes will accumulate during subsequent periods since the recovery interval is too short for complete excretion. If one designates the duration of uptake and recovery intervals by T' and T", respectively, and the length of the whole period by T = T' + T", the average concentration during the n-th period is given by

$$\bar{C}_n = (1/T) \int_0^{T'} c'_n dt + (1/T) \int_0^{T''} c''_n dt. \qquad (110)$$

Performing the integration after solving the recursion equations, Equs. (108) and (109), one obtains

$$\bar{C}_n = C_\infty(T'/T) - (C_\infty/kT)\,[1 - \exp(-kT')]\,\exp(-nkT') \qquad (111)$$

With an increasing number of periods, the last term in Equ. (111) becomes smaller and smaller and finally approaches zero when a stationary average body concentration, $\bar{C}_\infty$, is reached,

$$\bar{C}_\infty = C_\infty \, (T'/T). \tag{112}$$

In addition, the stationary average body concentration for intermittent exposure, $\bar{C}_\infty$, is equal to the maximum concentration reached during continuous exposure times the fraction of time in one period during which exposure occurred.

After a stationary state has been achieved, the fluctuation in body concentrations is given by

$$C'_\infty/C''_\infty = \exp\,(kT''). \tag{113}$$

The subsequent figures show changes in body concentration with time for two compounds for which biological half-lifes were known. The instantaneous concentration is divided by the maximum stationary concentration for continuous exposure to make the plots more general, i.e., to make them independent of the actual air concentration. Normal working conditions with 8 hrs exposure followed by 16 hrs of recovery in unpolluted surroundings were assumed in each case. Prolonged recoveries during weekends were not considered in Figures 19 and 20.

The first example (Fig. 19) illustrates p-nitrophenol uptake for which a half-life in man of 0.99 hrs was reported. Because of the short half-life time the maximum concentration ($c/c_\infty = 1$) is obtained during each exposure interval and complete excretion takes place during the recovery interval.

The second example (Fig. 20) shows dinitro-o-cresol with a biological half-life in man of 139 hrs. The graph shows the change in concentration for the first 40 days of exposure. There is a slow increase in body concentration which after about 35 days remains fluctuating around a value corresponding to 33% of the maximum concentration resulting during continuous exposure.

In both examples recovery during weekends was not considered. If a periodically occurring 64 hr recovery interval is considered, the body concentration averaged over a week is again given by Equ. (112), but this

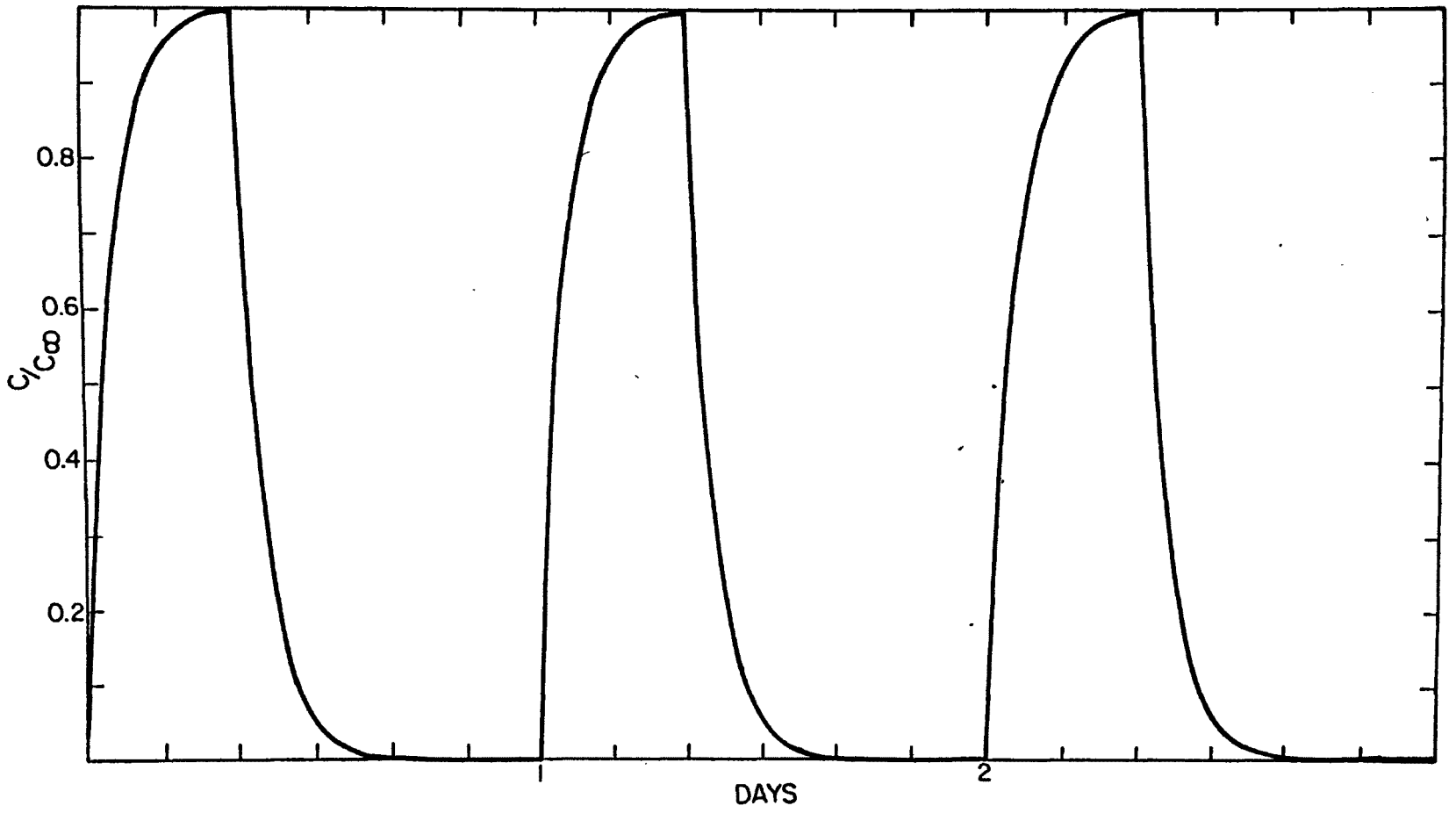


Figure 19. Body concentration versus time during intermittent exposure to p-nitrophenol with a known biological half-life time in man of 0.99 hrs. Weekends not considered.

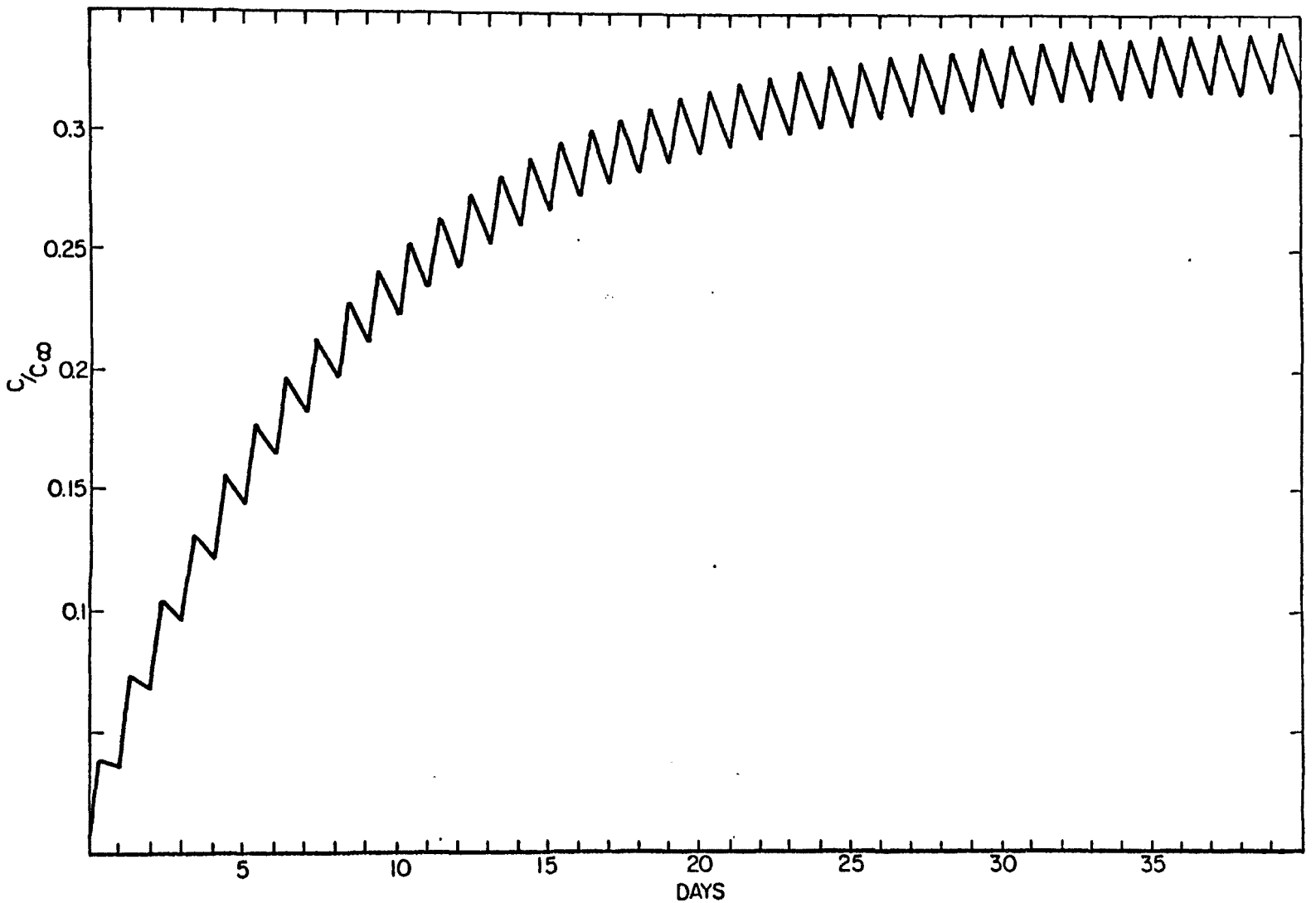


Figure 20. Body concentration versus time during intermittent exposure to dinitro-o-cresol with a known biological half-life time in man of 139 hrs. Weekends not considered.

time T' = 5 x 8, the total exposure time during the week, and T = 7 x 24, the total length of the period. Consequently, the body concentration averaged over a week will be only 23.8% of the stationary concentration obtained during continuous exposure.

In Figure 21 fluctuations in body concentration are shown for p-nitrophenol (τ = 0.99 hrs) with and without taking into account recovery during weekends. Because of its short half-life, the maximum body concentration is reached at the end of each working interval and complete recovery occurs during the subsequent 16 hrs. The average concentration during one working day equals 1/3 of the stationary concentration resulting from continuous exposure, thus being given by 8/24. It is immediately obvious, in order to average over a full week, the five daily averages have to be averaged over seven days. This gives a value of 5 x (8/24)/7 = 0.238. Whether such a weekly average is biologically meaningful seems to be questionable but the situation changes considerably if the compound possesses a longer biological half-life. In Figure 22 changes in body concentration are shown for a compound with τ = 72 hrs. In this case, weekends are very effective in reducing the maximum body burden and a weekly average concentration does become meaningful.

In Figure 23 the situation for dinitro-o-cresol (τ = 139 hrs) is shown graphically. Because of its long half-life, the stationary state condition is not obtained inside the time interval of the graph.

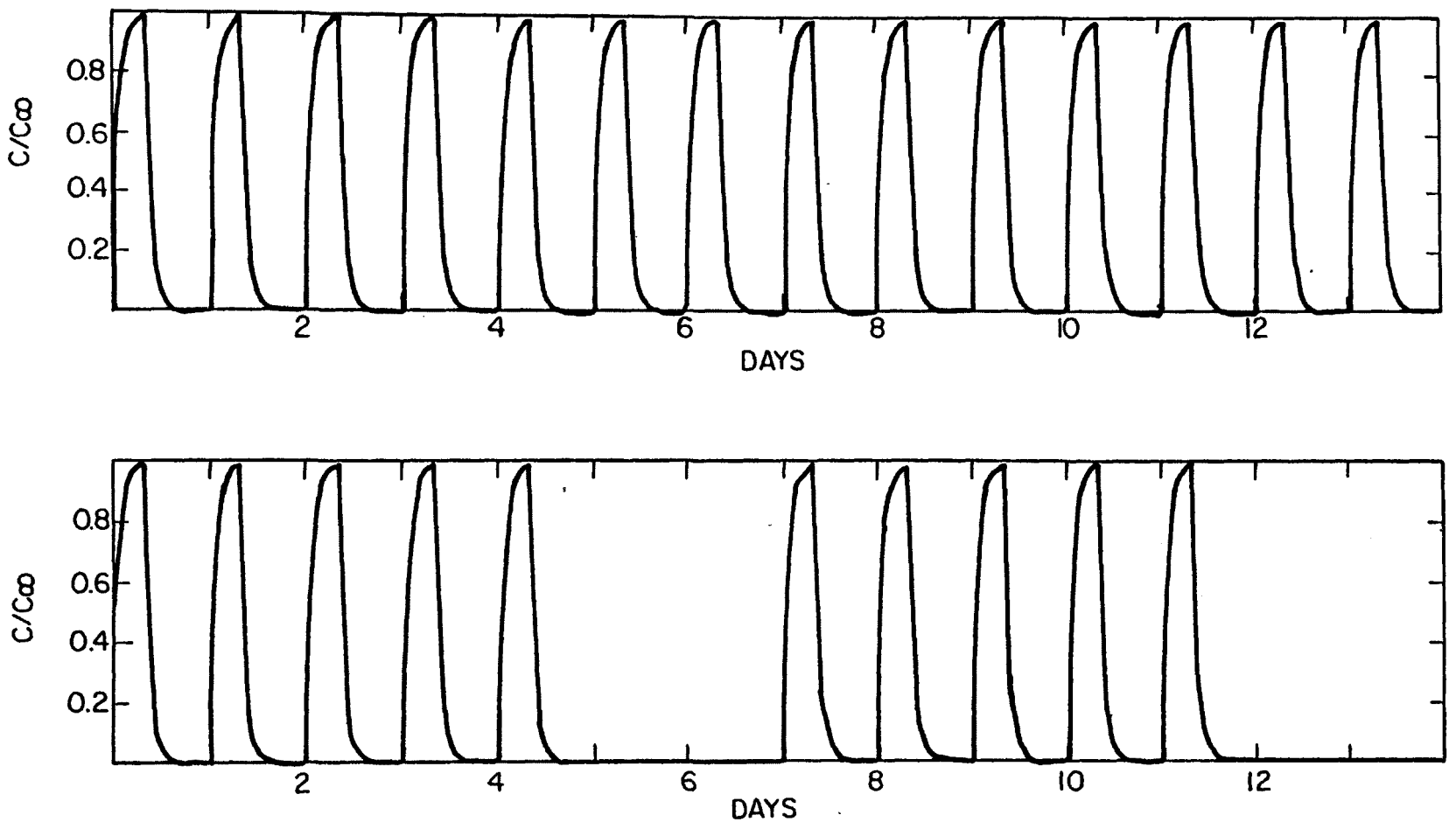


Figure 21. Effect of weekends on the body concentration during intermittent exposure to p-nitrophenol with a biological half-life time in man of 0.99 hrs. Upper plot: 8 hr uptake period followed by 16 hr recovery period; weekends not considered. Lower plot: 8 hr uptake period followed by 16 hr recovery period for 5 day workweek.

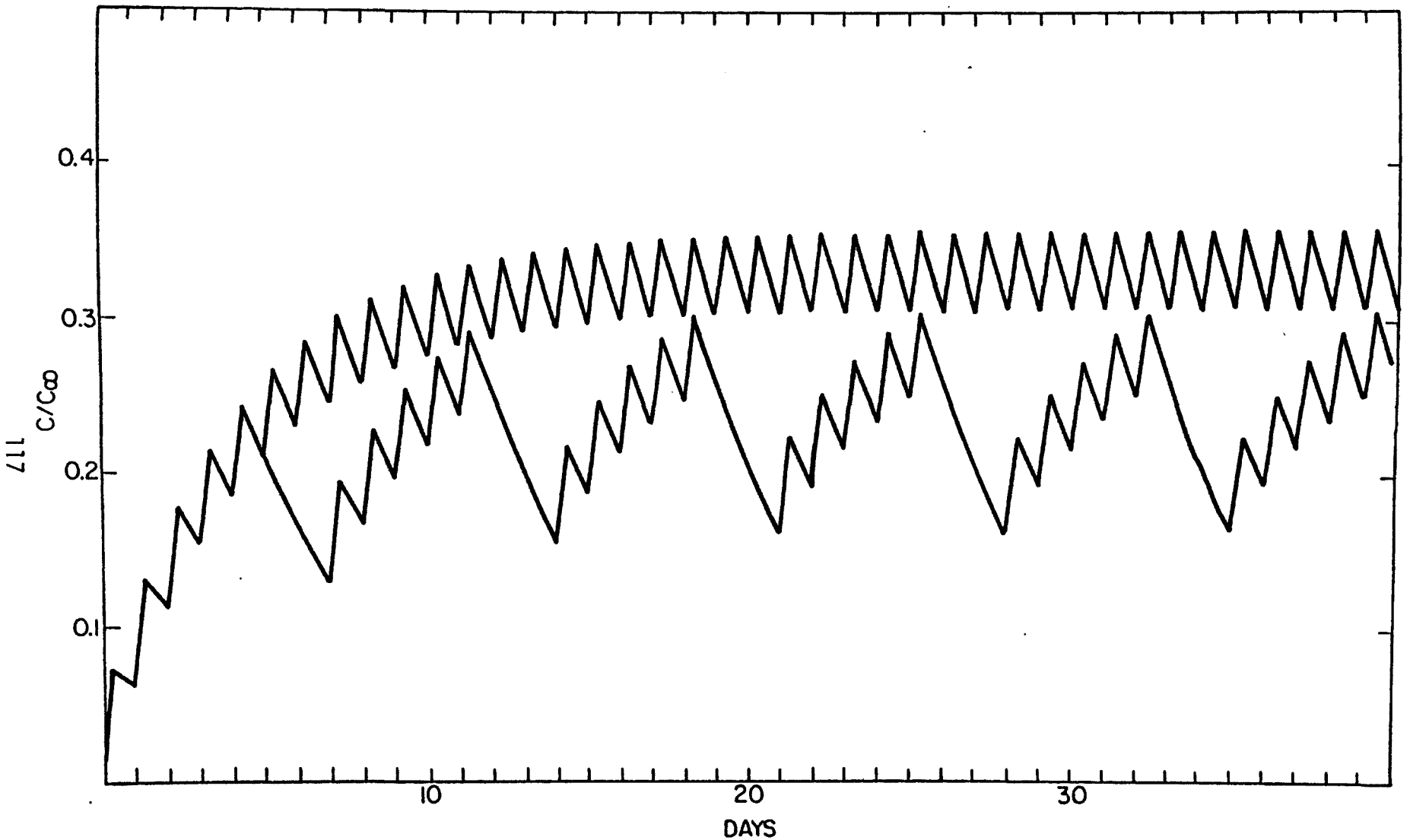


Figure 22. Effect of weekends on the body concentration during intermittent exposure to a pollutant with an assumed biological half-life of 72 hours. Upper curve: 8 hrs uptake period followed by 16 hrs recovery period; weekends not considered. Lower curve: 8 hrs uptake period followed by 16 hrs recovery period for 5 day workweek.

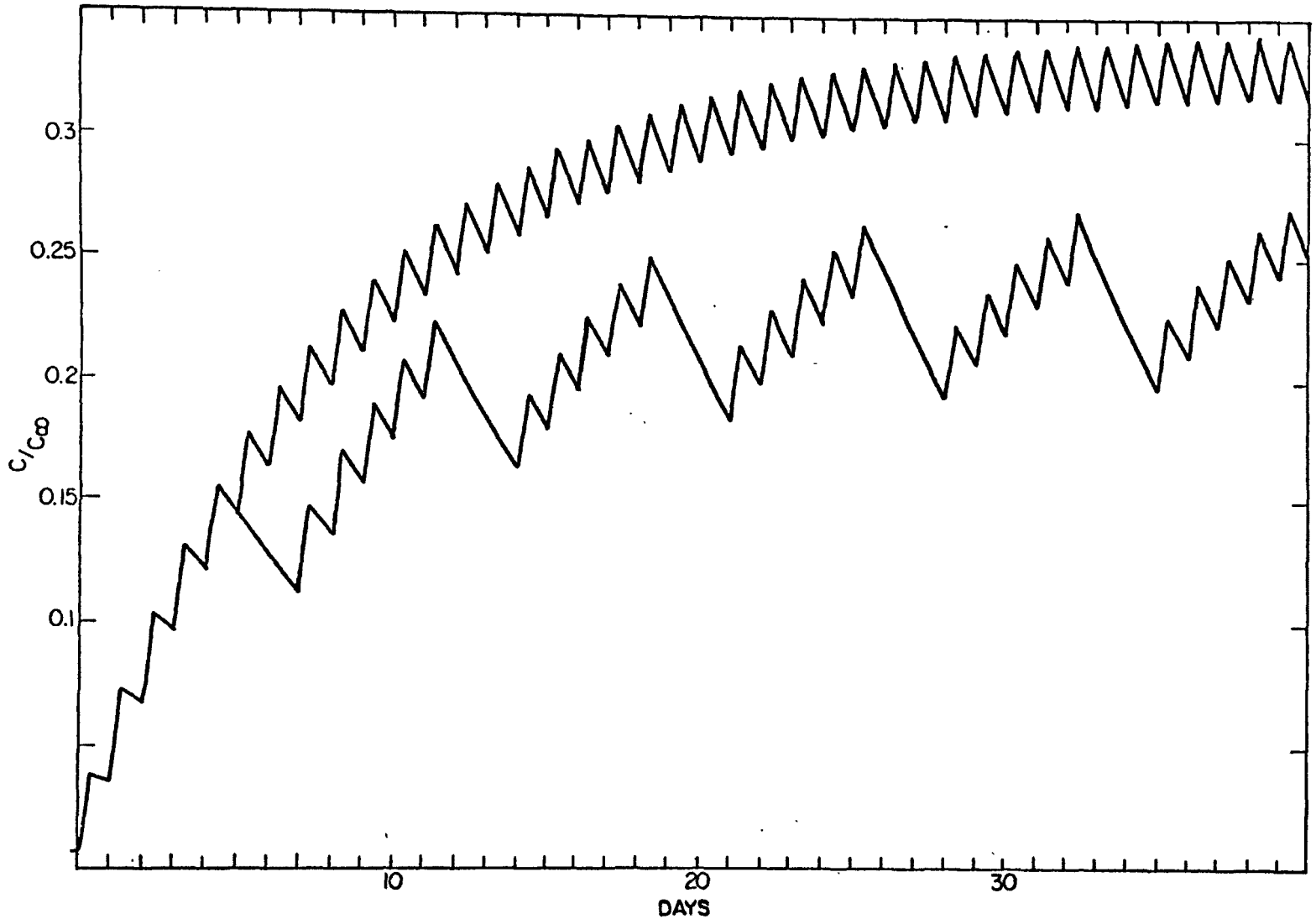


Figure 23. Effect of weekends on the body concentration during intermittent exposure to dinitro-o-cresol with a known biological half-life time in man of 139 hrs. Upper curve: 8 hrs uptake period followed by 16 hrs recovery period; weekends not considered. Lower curve: 8 hrs uptake period followed by 16 hrs recovery period for 5 day workweek.

C. Nomographic Correlation of Stack Emission Rates and Maximum Ground Level Concentrations

List of Symbols and Definitions

a,b	empirical constants describing the dependence of σ_y on the downwind distance from the source [Equ. (119)]
A thru F	stability categories [Fig. 31]
D	inside stack diameter
f(H)	function of H yielding the maximum ground level concentration [Equ. (122)]
H	effective height of stack emission [Equ. (115)]
h	stack height [Equ. (115)]
ΔH	plume rise above stack [Equ. (116)]
L	downwind distance from source
L_{max}	downwind distance from source at which the ground level concentration attains its maximum value [Equ. (121)]
m,n	empirical constants describing the dependence of σ_z on the downwind distance from the source [Equ. (120)]
p	atmospheric pressure
Q	uniform emission rate of pollutant
T_a	air temperature
T_s	stack gas temperature
u	wind speed
V_s	stack gas exit velocity
x_m	maximum ground level concentration
x_p	maximum permissible ground level concentration
x(x,0,0;H)	ground level concentration along center line of plume [Equ. (114)]
σ_y	standard deviation of plume concentration distribution in horizontal direction [Fig. 26]
σ_z	standard deviation of plume concentration distribution in vertical direction [Fig. 27]

Introduction

Assessments of health hazards associated with air pollutants from process industries require the knowledge of the maximum ground level concentration, x_m, of a pollutant during a 24 hr period. According to the first decision criteria for possible health hazards proposed by the Chemical Process Section of EPA, the value of x_m must not exceed the permissible ground level concentration, x_p. For a multicomponent system this decision criteria can be formulated by

$$\sum_{1}^{n} [(x_m)_i/(x_p)_i] \geq 1.0 \tag{36}$$

where $(x_m)_i$ and $(x_p)_i$ are the observed maximum ground level concentration and the permissible ground level concentration of the i-th pollutant, respectively. If the ratio is equal to or greater than unity a hazard is judged to exist.

In order to decide whether a source satisfies the above criteria and can be considered safe under given operation conditions, estimates of the generated maximum ground level concentration as a function of weather conditions are required.

The objective of the presented nomographs is to provide a simple means for correlating stack emission rates and maximum ground level concentrations with both weather and source conditions.

The nomographs are based on data reported in "Workbook of Atmospheric Dispersion Estimates" by D. Bruce Turner, EPA, Office of Air Programs Publication No. AP-26, 7th Printing, January 1974.[1] Pertinent graphs from Ref. 1 used for the construction of the nomographs are included.

Caveats

The nomographs are intended as an aid for obtaining first estimates of the effects of changes in both, the emitting source and the weather conditions, on the maximum ground level concentration of the emitted pollutant. Because of the wide ranges of the input variables covered by the nomographs the results can be considered only as first estimates. All of the numerous complications that arise in the determination of atmospheric dispersions could not be resolved. In this respect, the caveats expressed in the preface of Ref. 1 apply even more stringently.

Maximum Ground Level Concentrations

The maximum ground level concentration, x_m, occurs along the center line of the plume. The dispersion of the pollutant along the center line of the plume is given by Equ. (3.3) of Ref. 1.

$$x(x,0,0;H) = (Q/\pi u \sigma_y \sigma_z) \exp[-0.5 (H/\sigma_z)^2] \quad (114)$$

where $x(x,0,0;H)$ = ground level concentration along center line of plume ($g\ m^{-3}$)

Q = uniform emission rate of pollutant ($g\ sec^{-1}$)

u = wind speed ($m\ sec^{-1}$)

σ_y = standard deviation of plume concentration distribution in horizontal direction (m)

σ_z = standard deviation of plume concentration distribution in vertical direction (m)

H = effective emission height (m)

The effective emission height, H, is equal to the sum of stack height, h, and the plume rise above stack, ΔH

$$H = h + \Delta H \quad (115)$$

The plume rise above stack, ΔH, can be calculated by Holland's equation, Equ. (4.1) of Ref. 1 and is given by

$$\Delta H = (V_s D/u) [1.5 + 0.00268\ p\ D\ (1 - T_a/T_s)] \quad (116)$$

where ΔH = plume rise above stack (m)

V_s = stack gas exit velocity ($m\ sec^{-1}$)

u = wind speed ($m\ sec^{-1}$)

D = inside stack diameter (m)

p = atmospheric pressure (millibar)

T_a = air temperature (°K)

T_s = stack gas temperature (°K)

The estimation of maximum ground level concentrations from source emission rates requires two equations to be evaluated: Equ. (116) for obtaining plume rise above stack and Equ. (114) for correlating emission

rate and maximum ground level concentration. Both evaluations are presented in nomographic forms.

Nomograph for the Evaluation of Holland's Equation (Plume Rise Above Stack)

For the determination of plume rise above the stack, Holland's equation[2] was applied as suggested in Refs. 1 and 3. This equation is one of the most successful to date as shown by a critical evaluation[4] of different formulas proposed, although the final height of the plume is somewhat underestimated.[3]

Holland's equation, Equ. (116), contains seven variables which makes the construction of a nomograph rather complex. The equation was therefore simplified by neglecting changes in barometric pressure, which generally varies only a few percent. Consequently, a pressure of 970 millibars was assumed, yielding an equation of the form

$$\Delta H = (V_s D/u)\ [1.5 + 2.6\ D\ (1 - T_a/T_s)]. \qquad (117)$$

Equation (117) is presented in nomographic form by breaking it up into two factors: one given by the term in parenthesis and the other, given by the term in brackets.

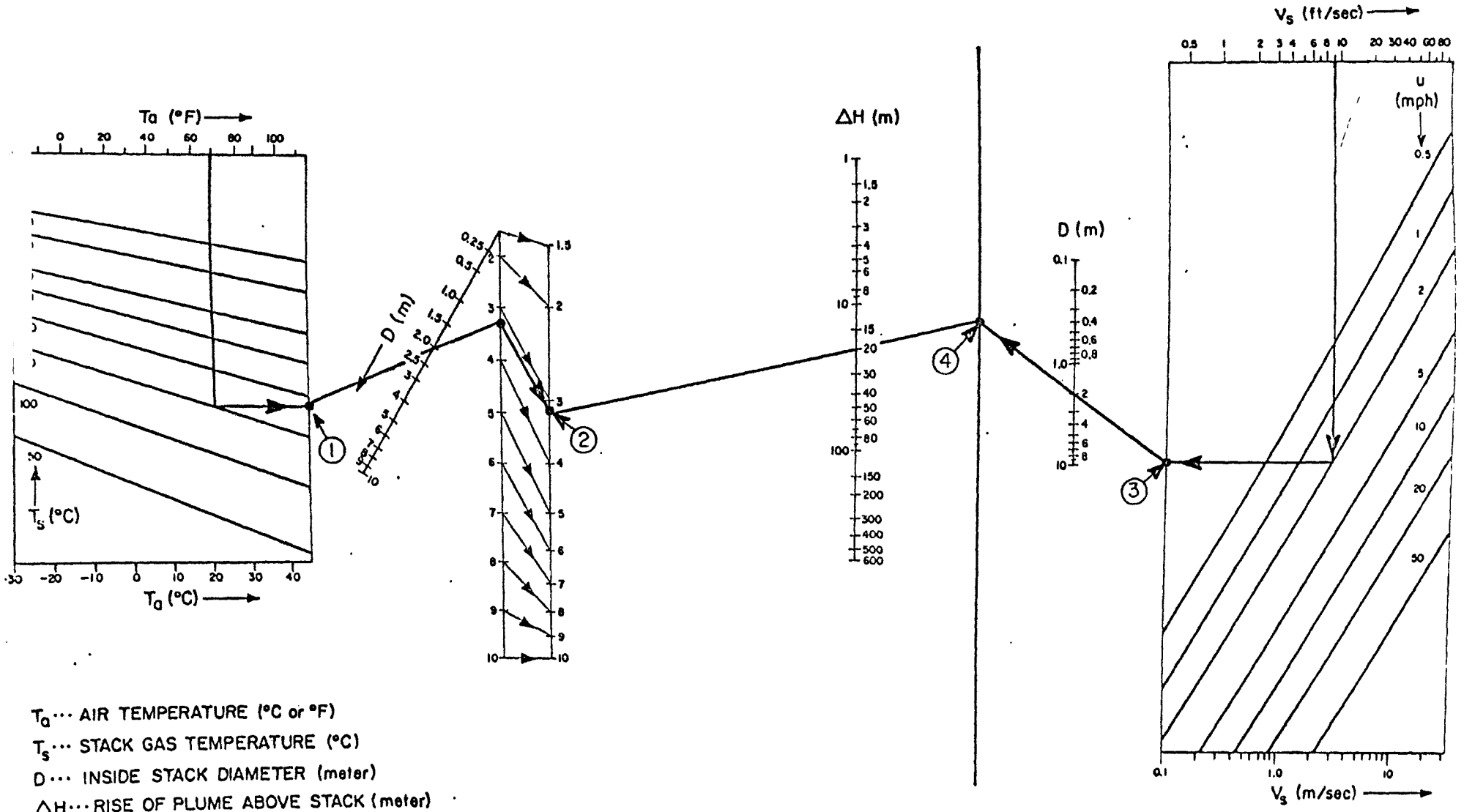
The nomograph for Holland's equation is presented in Figure 24, the evaluation being discussed in the subsequent section. An additional nomograph is given in Figure 30.

The left hand diagram of the nomograph shows the dependence of $(1 - T_a/T_s)$ on both the air temperature, T_a, and the stack gas temperature, T_s. The right hand diagram of the nomograph presents values of (V_s/u) as a function of both the stack gas exit velocity, V_s, and the wind speed, u. Wherever possible, scales for input data were provided in metric and engineering dimensions.

The value of $[1.5 + 2.6\ D\ (1 - T_a/T_s)]$ is obtained on the auxiliary scale I and is then transformed logarithmically by following the guiding arrows from scale I to scale II. The value of log $(V_s D/u)$ is obtained on the auxiliary scale III. Multiplying the latter value with the value on scale II yields the desired value of plume rise above stack on scale ΔH.

Example for the Determination of Plume Rise Above Stack

An example for the use of the nomograph is presented in Figure 24. The following source and weather conditions were assumed to apply:



T_a ··· AIR TEMPERATURE (°C or °F)

T_s ··· STACK GAS TEMPERATURE (°C)

D ··· INSIDE STACK DIAMETER (meter)

ΔH ··· RISE OF PLUME ABOVE STACK (meter)

V_s ··· STACK GAS EXIT VELOCITY (m/sec or ft/sec.)

u ··· WIND SPEED (miles/hr)

Figure 24. Nomographic example for the determination of plume rise above stack by Holland's equation.

Air temperature T_a = 70°F

Stack Gas Temperature T_s = 150°C

Inside Diameter of Stack D = 2 meter

Stack Gas Exit Velocity V_s = 9 ft/sec

Wind Speed = 2 miles/hr

Stack Height h = 80 meter

Evaluation Procedure:

Step 1. On left hand diagram select air temperature (°C on lower scale or °F on upper scale) and go vertically until the line representing the stack gas temperature (°C) is met (interpolate if necessary). From this point go horizontally to the right border line of the diagram obtaining point 1.

Step 2. Select stack diameter on slanted D-scale and connect with point 1. Extension of the line cuts the auxiliary line I at some value (2.1 in this example). By use of the guiding arrows the same value is located on the auxiliary line II corresponding to point 2.

Step 3. On the right hand diagram select stack gas exit velocity (meter/sec on lower scale or ft/sec on upper scale) and go vertically until the line representing the wind speed (miles/hr) is met (interpolate if necessary). From this point go horizontally to the left border line of the diagram obtaining point 3.

Step 4. Select stack diameter on the adjacent D-scale and connect with point 3. Extension of the line yields point 4 on the auxiliary line III.

Step 5. Connect point 4 with the previously obtained point 2. The tie-line intercepts the ΔH-scale yielding the plume rise above stack in meter. In this example, the value of ΔH is found to be 20 m and consequently the effective height of emission is 80 + 20 = 100 m.

Nomograph for the Correlation of Emission Rate and Maximum Ground Level Concentration

The nomograph correlating emission rates with maximum ground level concentration as a function of effective heights of emission is based on data from Figure 25 (Fig. 3-9 of Ref. 1).

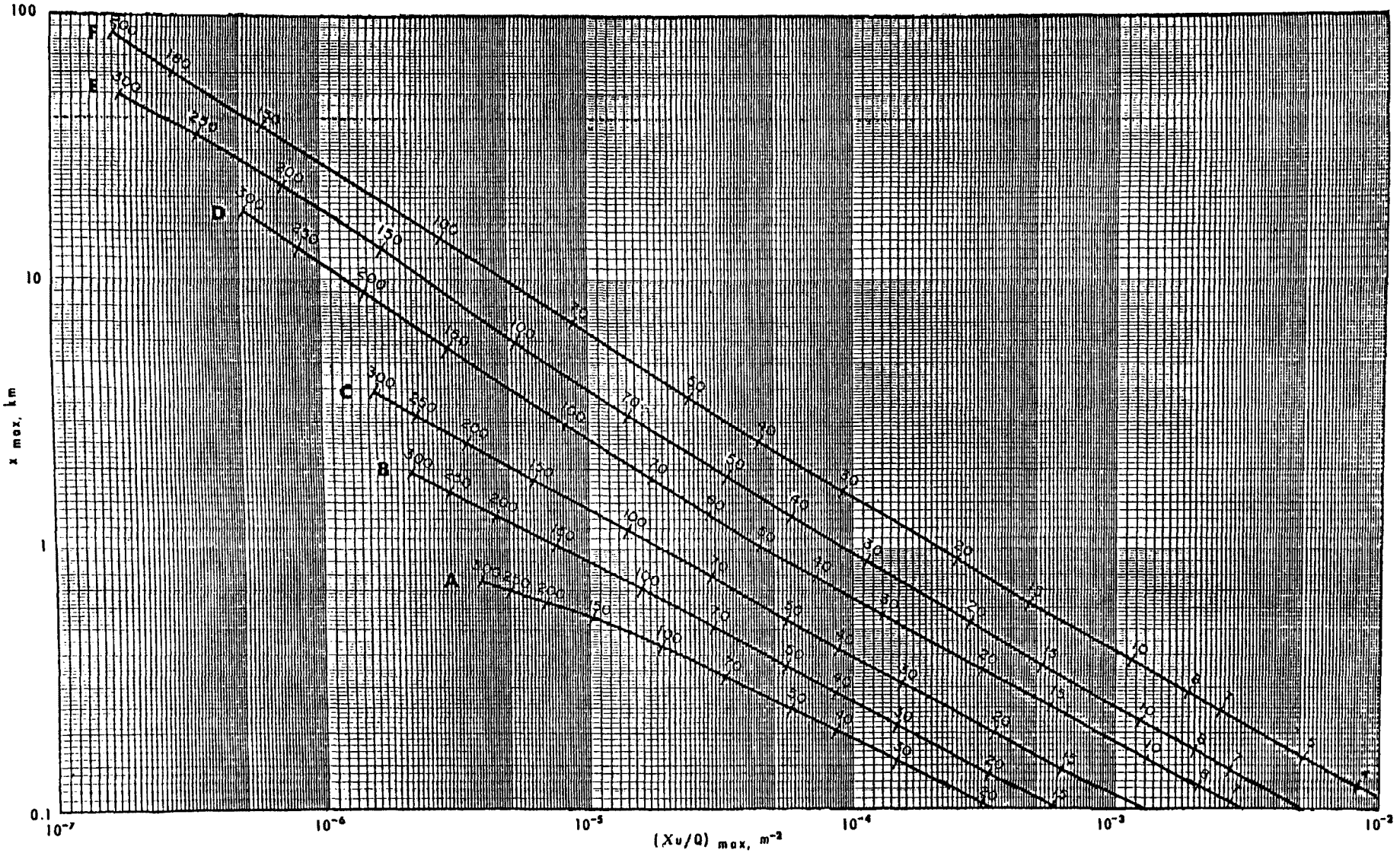


Figure 25. Distance of maximum concentration and maximum (xu/Q) value as a function of weather condition and effective height of emission (Fig. 3-9 of reference 1).

$$(x_m u/Q) = f(H) \text{ for stability categories A thru F} \tag{118}$$

where x_m = maximum ground level concentration
u = wind speed
Q = emission rate
$f(H)$ = function of effective height of emission for which the ground level concentrations attains a maximum value

The data of Figure 3-9 of Ref. 1 are limited to an effective height of emission below 300 m. This range was extended for some of the stability categories although one has to be cautious in the interpretation of the results obtained for the extended range because of the unknown weather conditions at these heights.

The values of horizontal, σ_y, and vertical, σ_z, dispersion coefficient as functions of downwind distance from the source are presented in Figures 26 and 27, respectively, corresponding to Figures 3-2 and 3-3 of Ref. 1. The graph for σ_y indicates that σ_y can be expressed by

$$\sigma_y = a\ L^b \tag{119}$$

where L is the distance downwind from source and a, b are empirical constants. The dependence of σ_z on the downwind distance from the source can be expressed in an analogous way

$$\sigma_z = m\ L^n \tag{120}$$

provided the downwind distance from the source exceeds a limiting value depending on the stability category.

Insertion of Equs. (119) and (120) into Equ. (114) and equating to zero after differentiating with respect to L, yields the downwind distance from the source at which the ground level concentration attains a maximum value, L_{max}.

$$L_{max} = [nH^2/m^2(b + n)]^{1/2n}. \tag{121}$$

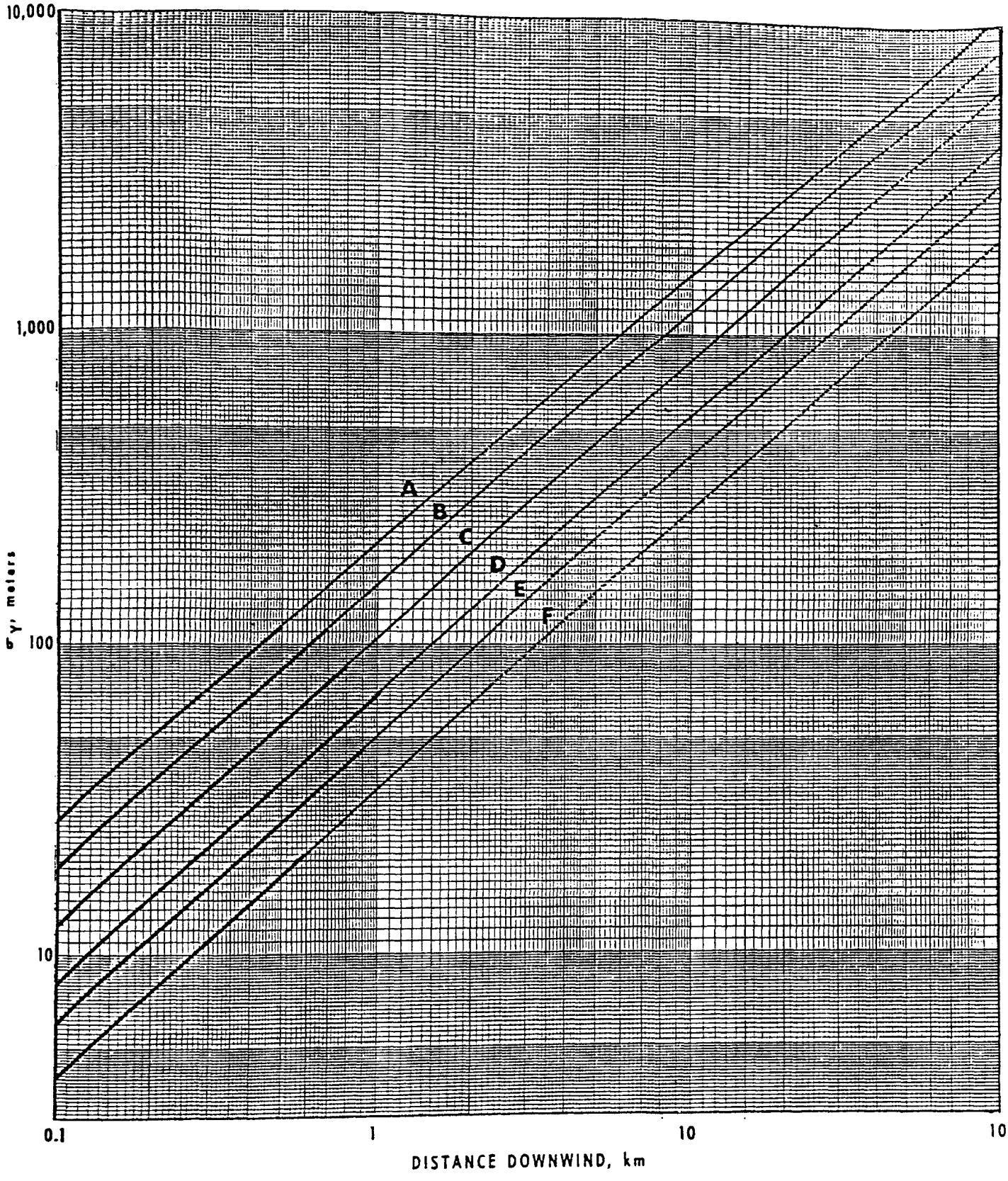


Figure 26. Horizontal dispersion coefficient as a function of downwind distance from the source (Fig. 3-2 of reference 1).

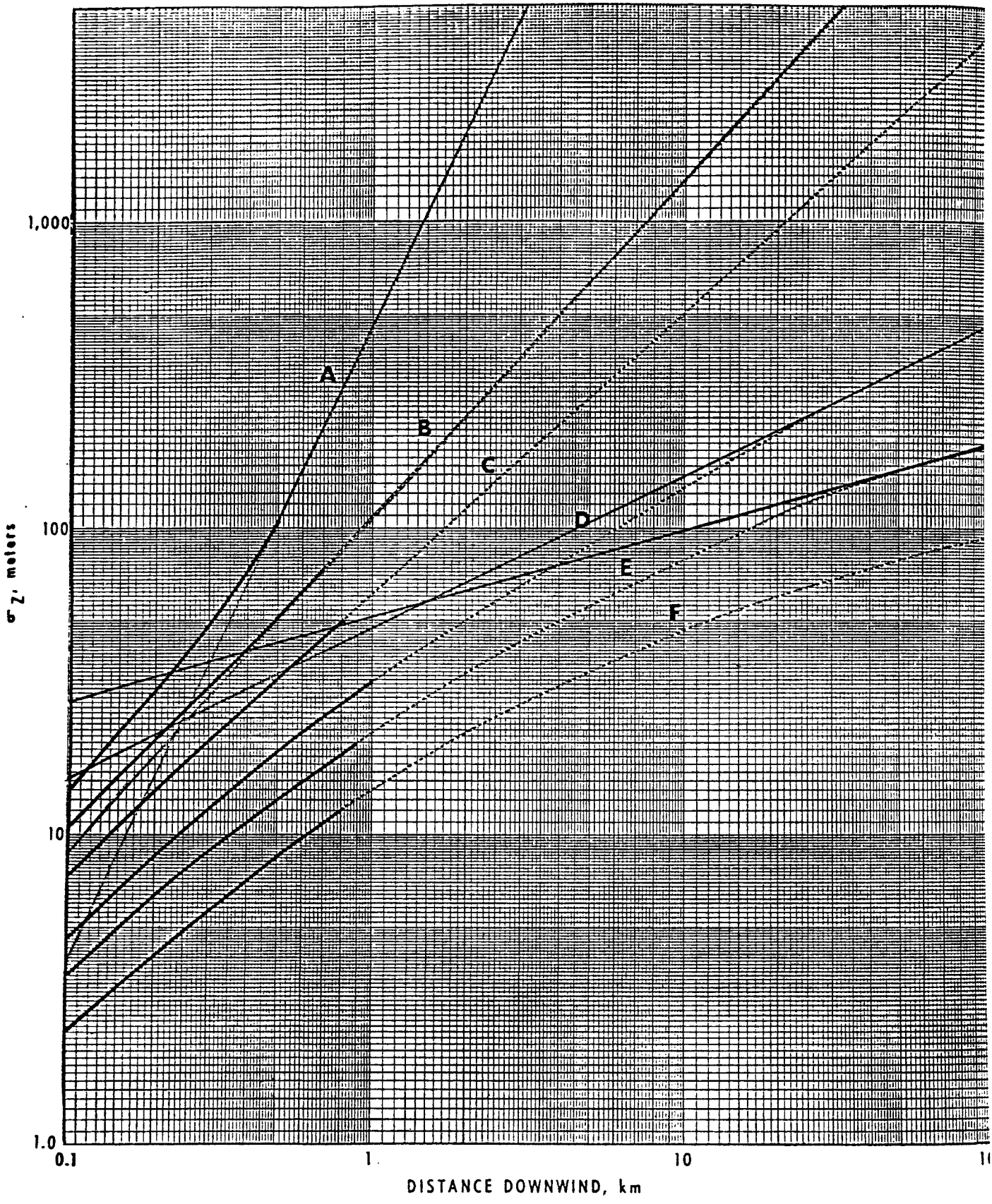


Figure 27. Vertical dispersion coefficient as a function of downwind distance from the source (Fig. 3-3 of reference 1).

Replacing σ_y and σ_z in Equ. (114) with Equs. (119) and (120), respectively, and L with Equ. (121), one obtains the maximum ground level concentration as a function of H only.

$$f(H) = (x_m u/Q)$$

$$= (am\pi)^{-1} \, [nm^{-2}(b+n)^{-1}]^{-(b+n)/2n} \, H^{(b+n)/n} \exp[-(b+n)/2n] \qquad (122)$$

By means of Equ. (122) the range of effective emission heights was extended.

The nomograph for correlating emission rates and maximum ground level concentrations is presented in Figures 28 and 29. Evaluation examples are discussed in the subsequent section. An additional nomograph is given in Figure 31.

The left hand side of the nomograph contains six scales for the effective emission heights corresponding to the six stability categories. The applicable stability category can be selected from the insert below the auxiliary center line. The scales are graded according to the values of $(x_m u/Q)$ corresponding to the values of H for the stability category under consideration.

With both H and u being given, the nomograph allows either (1) the determination of the maximum emission rate for which the ground level concentration will not exceed a given maximum permissible value, or (2) the determination of the maximum ground level concentration resulting from a given emission rate.

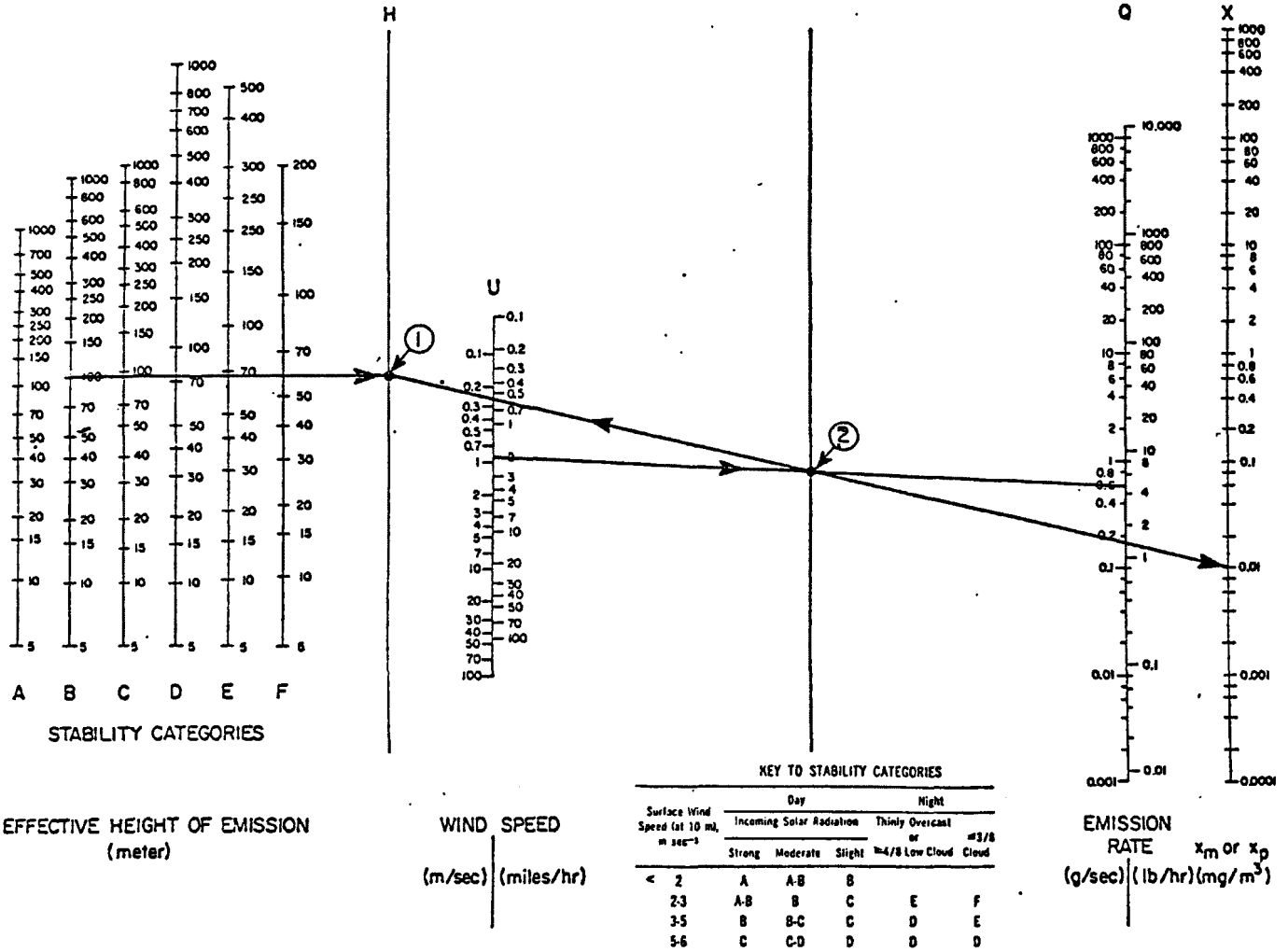
Examples for the Use of Nomograph

Example I. Calculate the maximum emission rate for given source and weather conditions which will not cause the ground level concentration to exceed a given maximum permissible value, x_p.

Given Values: Moderately cloudy day with wind speed of 2 miles/hr corresponding to stability category B. Effective height of emission from previous example H = 100 m. Maximum permissible ground level concentration x_p = 10 μg/m^3.

Procedure: Outlined in Figure 28.

Step 1. Select scale for effective height of emission according to applicable stability category (B in this example).



KEY TO STABILITY CATEGORIES

Surface Wind Speed (at 10 m), m sec⁻¹	Day: Incoming Solar Radiation: Strong	Day: Incoming Solar Radiation: Moderate	Day: Incoming Solar Radiation: Slight	Night: Thinly Overcast or ≥4/8 Low Cloud	Night: ≤3/8 Cloud
< 2	A	A-B	B		
2-3	A-B	B	C	E	F
3-5	B	B-C	C	D	E
5-6	C	C-D	D	D	D
> 6	C	D	D	D	D

The neutral class, D, should be assumed for overcast conditions during day or night.

Figure 28. Nomographic example for the calculation of stack emission rate for which the maximum ground level concentration does not exceed a permissible value.

Step 2. Select value of effective height of emission and project horizontally on line H thereby obtaining point 1.

Step 3. Select x_p value on x-scale (0.01 in this example) and connect with point 1. Intercept on the auxiliary center line corresponds to point 2.

Step 4. Select wind speed (m/sec or miles/hr) on u-scale and connect with point 2 on center line. Extension of this line to Q-scale yields the emission rate either in g/sec or lb/hr (4.5 lb/hr in this example).

Example II. Calculate the maximum ground level concentration, x_m, resulting from a given emission rate, Q, for given weather and source conditions.

Given Values: Cloudy day with wind speed of 2 miles/hr corresponding to stability category C. Effective heigh of emission from previous example H = 100 m. Emission rate Q = 10 lb/hr.

Procedure: Outlined in Figure 29.

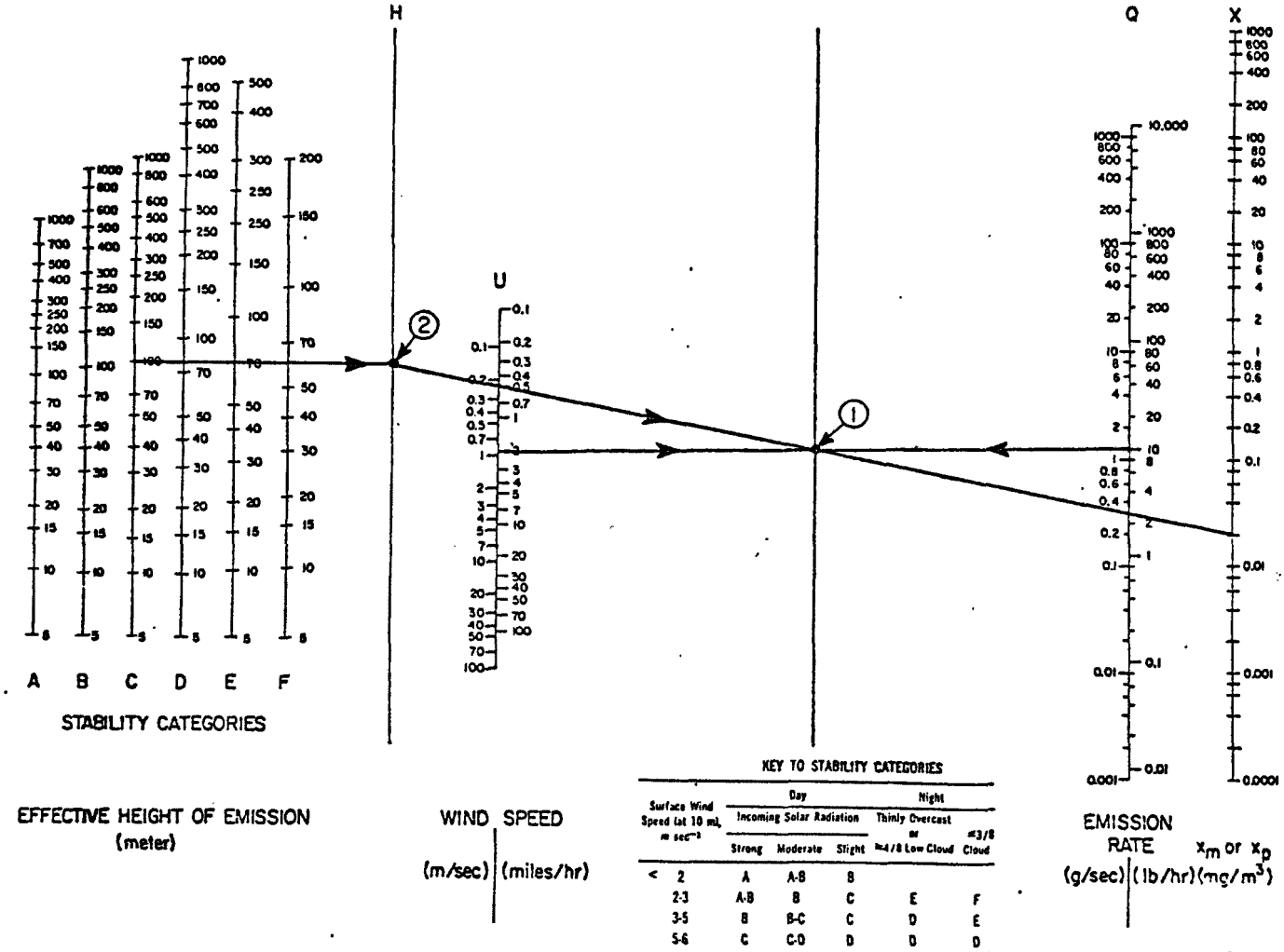
Step 1. Select emission rate on Q-scale and wind speed on u-scale. The connecting line intercepts the auxiliary center line yielding point 1.

Step 2. Select effective height of emission on proper scale corresponding to applicable stability category (C in this example) and project horizontally on line H thereby obtaining point 2.

Step 3. Connect point 1 with point 2 and extend line to x-scale. The intercept on x-scale yields the maximum ground level concentration in mg/m^3 (20 $\mu g/m^3$ in this example).

References

1. D. Bruce Turner, "Workbook of Atmospheric Dispersion Estimates," EPA Office of Air Programs Publication No. AP-26, 7th Printing, January, 1974.
2. J. Z. Holland, "A Meterological Survey of the Oak Ridge Area," U.S. Atomic Energy Commission Report ORO-99, 554-559 (1953).
3. A. Beals, "Guide to Local Diffusion of Air Pollutants," Technical Report 214, Air Weather Service, USAF, Scott AFB, Ill., May, 1971.



KEY TO STABILITY CATEGORIES

Surface Wind Speed (at 10 m), m sec⁻¹	Day: Incoming Solar Radiation: Strong	Day: Incoming Solar Radiation: Moderate	Day: Incoming Solar Radiation: Slight	Night: Thinly Overcast or ≥4/8 Low Cloud	Night: ≤3/8 Cloud
< 2	A	A-B	B		
2-3	A-B	B	C	E	F
3-5	B	B-C	C	D	E
5-6	C	C-D	D	D	D
> 6	C	D	D	D	D[1]

[1] The neutral class, D, should be assumed for overcast conditions during day or night.

Figure 29. Nomographic example for the calculation of maximum ground level concentration resulting from given stack emission rate.

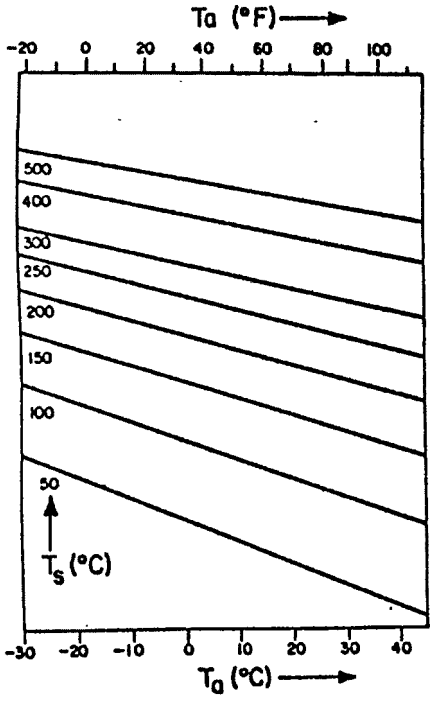
4. H. Moses and G. H. Strom, "A Comparison of Observed Plume Rises with Values Obtained from Well-Known Formulas," J. Air Pollution Control Association, 11, 455 (1961).

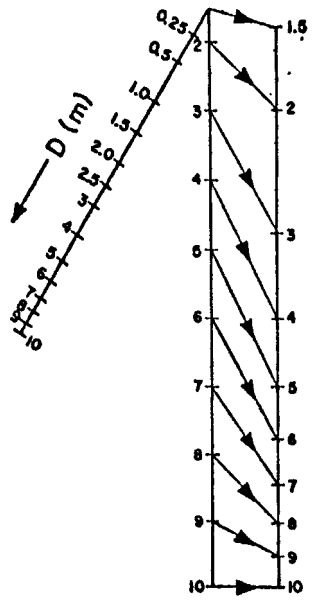
Figure 30. Nomograph for the estimation of plume rise above stack by Holland's equation.

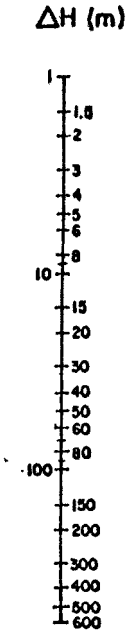
Figure 31. Nomograph for the correlation of stack emission rates and maximum ground level concentrations.

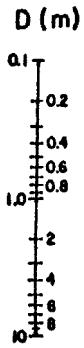
ESTIMATION OF PLUME RISE ABOVE STACK BY HOLLAND'S EQUATION

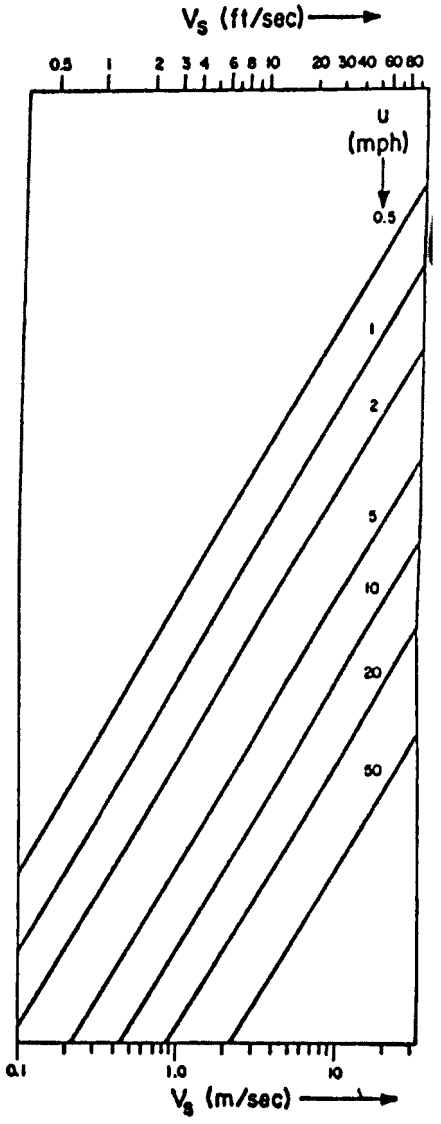
$$H = (V_s\ D/u)\ [1.5 + 2.6D(1 - T_a/T_s)]$$











T_a ··· AIR TEMPERATURE (°C or °F)

T_s ··· STACK GAS TEMPERATURE (°C)

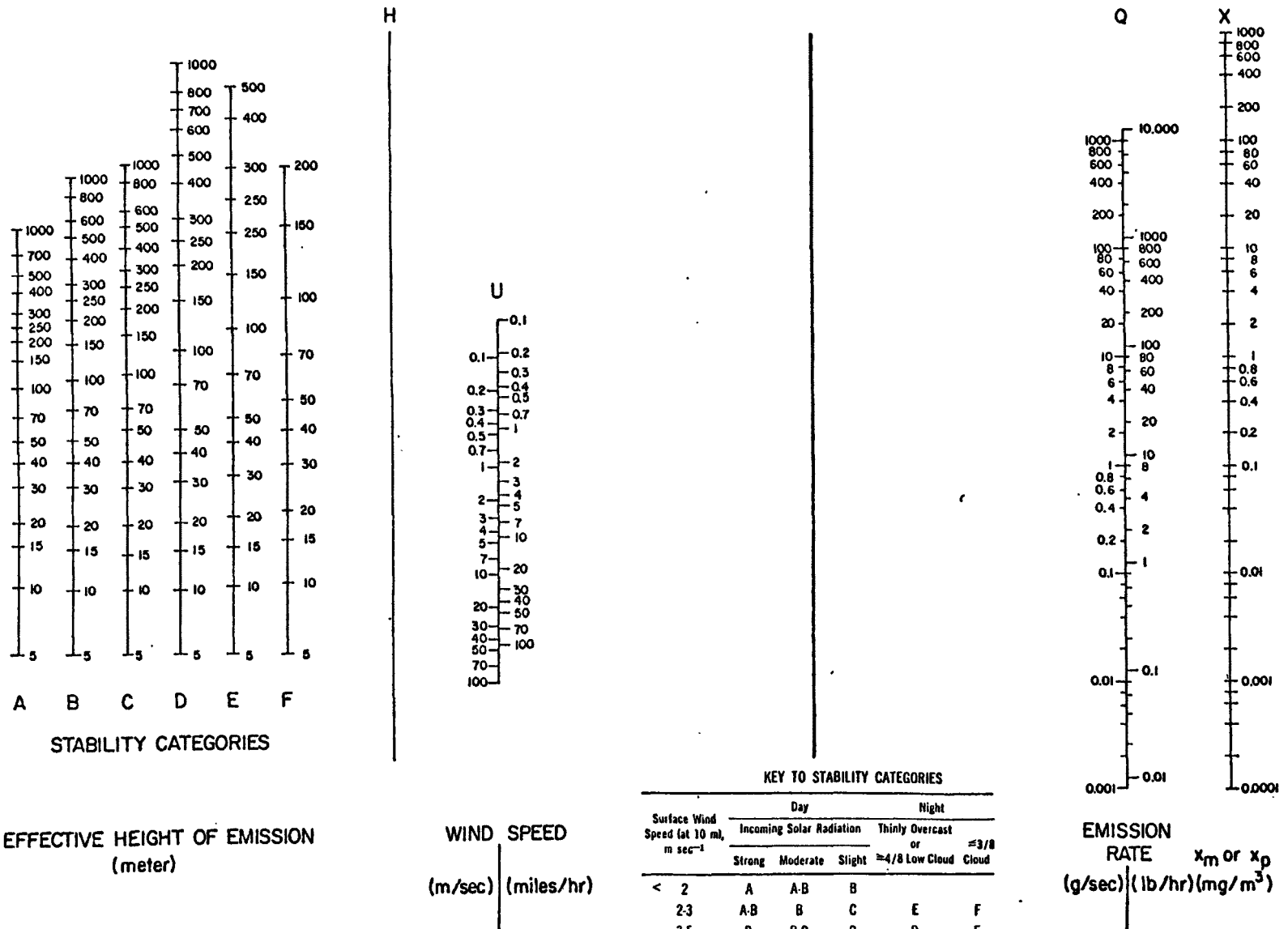
D ··· INSIDE STACK DIAMETER (meter)

ΔH ··· RISE OF PLUME ABOVE STACK (meter)

V_s ··· STACK GAS EXIT VELOCITY (m/sec or ft/sec.)

u ··· WIND SPEED (miles/hr)

CORRELATION OF EMISSION RATES AND MAXIMUM GROUND LEVEL CONCENTRATIONS



KEY TO STABILITY CATEGORIES

Surface Wind Speed (at 10 m), m sec⁻¹	Day: Incoming Solar Radiation: Strong	Day: Incoming Solar Radiation: Moderate	Day: Incoming Solar Radiation: Slight	Night: Thinly Overcast or ≥4/8 Low Cloud	Night: ≤3/8 Cloud
< 2	A	A-B	B		
2-3	A-B	B	C	E	F
3-5	B	B-C	C	D	E
5-6	C	C-D	D	D	D
> 6	C	D	D	D	D

The neutral class, D, should be assumed for overcast conditions during day or night.

TECHNICAL REPORT DATA
(Please read Instructions on the reverse before completing)

1. REPORT NO. EPA-600/2-76-155	2.	3. RECIPIENT'S ACCESSION NO.
4. TITLE AND SUBTITLE Estimation of Permissible Concentrations of Pollutants for Continuous Exposure		5. REPORT DATE June 1976
		6. PERFORMING ORGANIZATION CODE
7. AUTHOR(S) Robert Handy and Anton Schindler		8. PERFORMING ORGANIZATION REPORT NO.
9. PERFORMING ORGANIZATION NAME AND ADDRESS Research Triangle Institute P.O. Box 12194 Research Triangle Park, North Carolina 27709		10. PROGRAM ELEMENT NO. EHE624
		11. CONTRACT/GRANT NO. 68-02-1325, Tasks 34 and 46
12. SPONSORING AGENCY NAME AND ADDRESS EPA, Office of Research and Development Industrial Environmental Research Laboratory Research Triangle Park, NC 27711		13. TYPE OF REPORT AND PERIOD COVERED Final; 6/75-4/76
		14. SPONSORING AGENCY CODE EPA-ORD

15. SUPPLEMENTARY NOTES IERL-RTP task officer for this report is Max Samfield, Mail Drop 62, Ext 2547.

16. ABSTRACT The report gives results of a study aimed at: estimating the maximum permissible continuous exposure to which individuals may be subjected; and computing permissible exposure to a multipollutant system so that the degree of control necessary for a waste stream can be computed. (These capabilities are desirable in the absence of a Federal Standard for a pollutant.) The report deals with three aspects of the problem: permissible continuous exposure for air pollutants; permissible continuous exposure for water pollutants; and permissible continuous exposure to carcinogens in ambient air. For carcinogens, the problem is approached on a probable risk/concentration basis. Calculated permissible levels for 24 hours exposure were compared with 23 substances for which standards have been set or proposed. In general, agreement was within an order of magnitude. An appendix to the report contains a nomograph for easy estimation of maximum ground level concentrations of pollutants issuing from point sources.

17. KEY WORDS AND DOCUMENT ANALYSIS

a. DESCRIPTORS		b. IDENTIFIERS/OPEN ENDED TERMS	c. COSATI Field/Group	
Air Pollution	Carcinogens	Pollution Control	13B	06E
Water Pollution		Stationary Sources		
Estimating		Continuous Exposure	14A	
Concentrations (Composition)		Point Sources	07D	
Exposure			06S	

18. DISTRIBUTION STATEMENT Unlimited	19. SECURITY CLASS (This Report) Unclassified	21. NO. OF PAGES 147
	20. SECURITY CLASS (This page) Unclassified	22. PRICE