REPORT TO THE SCIENTIFIC REVIEW PANEL ON BENZENE*

Prepared by the Staffs of
The Air Resources Board and
The Department of Health Services

November 27, 1984

* Includes changes pursuant to the October 10, 1984 Scientific Review Panel (SRP) public meeting, as made available to the public and submitted to the SRP on November 15, 1984, and considered by the SRP at its public meeting on November 26, 1984. Also includes changes recommended by the SRP at the November 26, 1984 public meeting and revision of the lower bound of the risk estimate from 24 x 10^{-6}/1 ppb to 22 x 10^{-6}/1 ppb throughout the report, for consistency with the SRP's findings.

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OVERVIEW

I. INTRODUCTION

Assembly Bill 1807 (Stats. 1983, Ch. 1047; Health and Safety Code Section 39650 et seq., Food and Agriculture Code Section 14021 et seq.), enacted in September 1983, sets forth a procedure for the identification and control of toxic air contaminants (TAC) in California. Staff is proposing, in accordance with the provisions of AB 1807, that benzene be identified as a toxic air contaminant. This overview reviews briefly the ARB's report on the uses of, and the extent of emissions of and public exposure to benzene in California, (Part A of this report) and the DHS' evaluation of the health effects of benzene (Part B of this report). The findings in these reports comprise the rationale for the selection of benzene as a candidate substance for listing as a toxic air contaminant.

AB 1807 defines a "toxic air contaminant" as an air pollutant which may cause or contribute to an increase in mortality or an increase in serious illness, or which may pose a present or potential hazard to human health" (Section 39655).[1/] Under AB 1807, the Air Resources Board (the Board) is responsible for the identification and control of toxic air contaminants, except in their pesticidal use. The Department of Food and Agriculture is responsible for the regulation of toxic air contaminants in their pesticidal use (Sections 39650(g) and 39655; Food and Agriculture Code Section 14021 et seq.). AB 1807 specifies expressly that substances which have been identified

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1/ All statutory references are to the Health and Safety Code unless otherwise indicated.

by the Environmental Protection Agency as hazardous air pollutants (Section 112 of the Clean Air Act) shall be identified as toxic air contaminants by the Air Resources Board (Section 39655). Benzene has been identified as a hazardous air pollutant by EPA.

Included in AB 1807 are the Legislature's findings with respect to substances which may be toxic air contaminants (Section 39650). The Legislature declares:

> "That public health, safety, and welfare may be endangered by the emission into the ambient air of substances which are determined to be carcinogenic, teratogenic, mutagenic, or otherwise toxic or injurious to humans."

The findings also include directives with respect to the consideration of scientific evidence and the basis for regulatory action. With respect to the control of toxic air contaminants, the Legislature declares:

> "That it is the public policy of this state that emissions of toxic air contaminants should be controlled to levels which prevent harm to the public health."

The Legislature further declares that, "while absolute and undisputed scientific evidence may not be available to determine the exact nature and extent of risk from toxic air contaminants, it is necessary to take action to protect public health."

With respect to the evaluation of substances, the Legislature declares that the best available scientific evidence, gathered from both public agencies and private sources, including industry, should be used. The Legislature also finds that this information should be reviewed by a scientific review panel and by members of the public.

The procedures established in AB 1807 implement the Legislature's findings. Specifically, determination by the Board as to whether a substance is a toxic air contaminant includes several steps. First, the ARB staff requests the DHS to evaluate the health effects of a substance (Section 39660). The evaluation includes a comprehensive review of all available scientific data. Second, upon receipt and in consideration of the DHS evaluation and recommendation, the staff prepares and submits a health effects report to the Scientific Review Panel (SRP) for its review (Section 39661). The report is prepared in a form which may serve as the basis for regulatory action by the Board. The report is also made available to the public, which may comment directly to the SRP. After review by the SRP, the report, with the written findings of the SRP, is considered by the Board in determining whether the substance is a toxic air contaminant. The Board's determination as to whether a substance is a toxic air contaminant must be set forth in a regulation and considered at a noticed public hearing (Section 39662). AB 1807 also includes procedures for the development and adoption of control measures for substances identified as toxic air contaminants (Sections 39665-39667).

II. EVALUATION OF BENZENE

In accordance with the procedures specified in AB 1807, the ARB and the DHS first prioritized substances for evaluation and regulation as "toxic air contaminants" pursuant to Section 39660(f). Briefly, selection of a substance for the Board's consideration is to be based on the risk to the public from exposure to the substance, amount or potential amount of emissions, manner of usage in California, atmospheric persistence, and ambient concentrations. The

ARB staff, after consulting the Department of Health Services (DHS), selected benzene as the first substance for the Board's consideration for listing as a TAC. A central factor in its selection was that, as a "hazardous air pollutant" designated by the U.S. Environmental Protection Agency (EPA) pursuant to Section 112 of the Clean Air Act, benzene must, according to AB 1807, be identified as a TAC by the Board. In addition, the staff selected benzene because it is a known human carcinogen (the primary basis for EPA's "hazardous air pollutant" designation), it is ubiquitously emitted by the marketing and burning of gasoline, it is persistent in the atmosphere, and its presence in the atmosphere is well documented. Pertinent data are shown below.

Emissions (California)	
Stationary sources	
Gasoline-related	480 tons/year
Other	630 "
Vehicular	15,000 "
Atmospheric Half-Life	
(OH· attack, polluted atmosphere)	12 days
Ambient Concentration	
South Coast Air Basin population-weighted year-round average	4.6 parts per billion (ppb)
South Coast Air Basin range (24 hr. average)	1.2-16 ppb

Pursuant to Health and Safety Code Section 39660, the ARB then requested that the Department of Health Services conduct a health effects evaluation of benzene. The DHS evaluation was conducted in accordance with the provisions of that section, which requires that the DHS consider all available scientific data, including, but not limited to, relevant data provided by the State Board, the Department of Industrial Relations, international and federal

health agencies, private industry, academic researchers, and public health and environmental organizations. To facilitate the identification of all available data, the ARB, prior to formally requesting the DHS evaluation, sent a letter to owners of sources of benzene emissions in California and other interested members of the public requesting that they submit any information they considered pertinent to the DHS evaluation. The ARB also received a reference search on benzene health effects using the MEDLARS II and DIALOG Information Services and included a bibliography from that search in its request for information. The data compiled in the search were provided to the DHS. Also, the DHS report was released to the public upon its completion on July 27, 1984, providing additional time during the ARB's preparation of the report to the SRP for the public's preparation of comments. The DHS report was also provided to the SRP on that date.

Section 39660 specifies that the evaluation shall assess the availability and quality of data on health effects, including potency, mode of action, and other relevant biological factors of the substance. Section 39660 also requires that the evaluation contain an estimate of the levels of exposure which may cause or contribute to adverse health effects, and, in the case where there is no threshold of significant adverse health effects, the range of risk resulting from current or anticipated exposure.

In accordance with these requirements, five major issues discussed in the DHS health effects evaluation of benzene are: 1) Is benzene a human and/or animal carcinogen? 2) Does benzene have a threshold below which cancer does not occur? 3) Are health effects other than cancer expected to occur at usual ambient levels? 4) What is the range of added lifetime cancer risk for

populations continuously exposed to California's urban air benzene concentrations? and 5) Is this risk sufficient to recommend listing benzene as a toxic air contaminant? Based on its review of all available scientific data, the DHS evaluation concludes that: 1) benzene is a human and animal carcinogen; 2) benzene should be treated as a substance without a carcinogenic threshold; 3) health effects other than cancer are not expected to occur at usual ambient levels; 4) the added lifetime cancer risk from ambient air benzene exposure ranges from 22 to 170 cases per million per ppb; and 5) benzene should be listed as a toxic air contaminant.

The DHS report finds that epidemiological studies associate exposures to tens to hundreds of parts per million benzene with an increased incidence of leukemia. Also, recent animal cancer bioassays show benzene causes leukemia and a variety of other cancers including lymphoid cancers, cancers of the skin, ovary, oral cavity, lip, tongue, lung, mammary gland, and two uniquely rodent secretory organs, the zymbal and preputial glands. Thus, the DHS concludes that benzene is a human and animal carcinogen.

To determine that a substance has a carcinogenic threshold, the DHS requires strong positive evidence that the substance acts only through mechanisms which ought to have a threshold. No positive evidence exists for this position with respect to benzene. Also, benzene causes many kinds of cancer in animals of which only one - leukemia - is postulated by some experts to act by a mechanism which may have a threshold. Because the statistical and mechanistic arguments for a benzene threshold are not compelling, the DHS concludes that benzene should be treated as a substance without a carcinogenic threshold in humans.

The DHS estimated the low-dose carcinogenic potency of benzene using both animal and epidemiological data. Figure A shows dose-response curves derived from these human and animal studies. Line 1 (Mantel-Bryan) and line 2 (95 percent UCL Multistage) are dose-response curves for the most sensitive site in animals, the preputial gland in mice. Line 1 is based on the Mantel-Bryan model and line 2 is based on the 95 percent upper confidence limit (UCL) for the multistage model. The DHS staff recommends line 2 (95 percent UCL Multistage) for calculating the upper bound of risk.

Line 3 (Mouse Mammary and Ovary) is the dose-response curve for mammary and ovarian cancers in mice based on the multistage model. Lines 4 (Leukemia and Lymphoma in Mice) and 5 (Rinsky) are overlapping. Line 4 is the dose-response curve for leukemia and lymphoma in mice based on the multistage model. Line 5 is the dose-response curve for the Rinsky re-evaluation of human data from the Infante epidemiologic study. Line 6 (CAG #1) is the dose-response curve for human data from the Infante, Aksoy and Ott epidemiologic studies. Lines 5 and 6 are based on the dose-response model from EPA's Carcinogen Assessment Group (CAG). The DHS staff recommends line 6 for calculating the lower bound of risk. Line 7 (Probit) is the dose-response curve for the preputial gland in mice based on the Probit model. This curve lies far below the others.

The DHS staff suggests that the ARB consider that the dose-response curves that lie between line 6 (CAG #1) and line 2 (95 percent UCL Multistage) constitute the most reasonable estimates of risk from ambient benzene exposure. While less conservative curves can also be defended as reasonable, the DHS staff does not feel that any can be clearly preferred, and

the more conservative of equally reasonable elements should constitute the basis for regulation. Using these curves (lines 2 and 6) as grounds for the range of risk, then, the added lifetime cancer risk from exposure to benzene in urban air ranges from 22 to 170 cases per million per ppb.

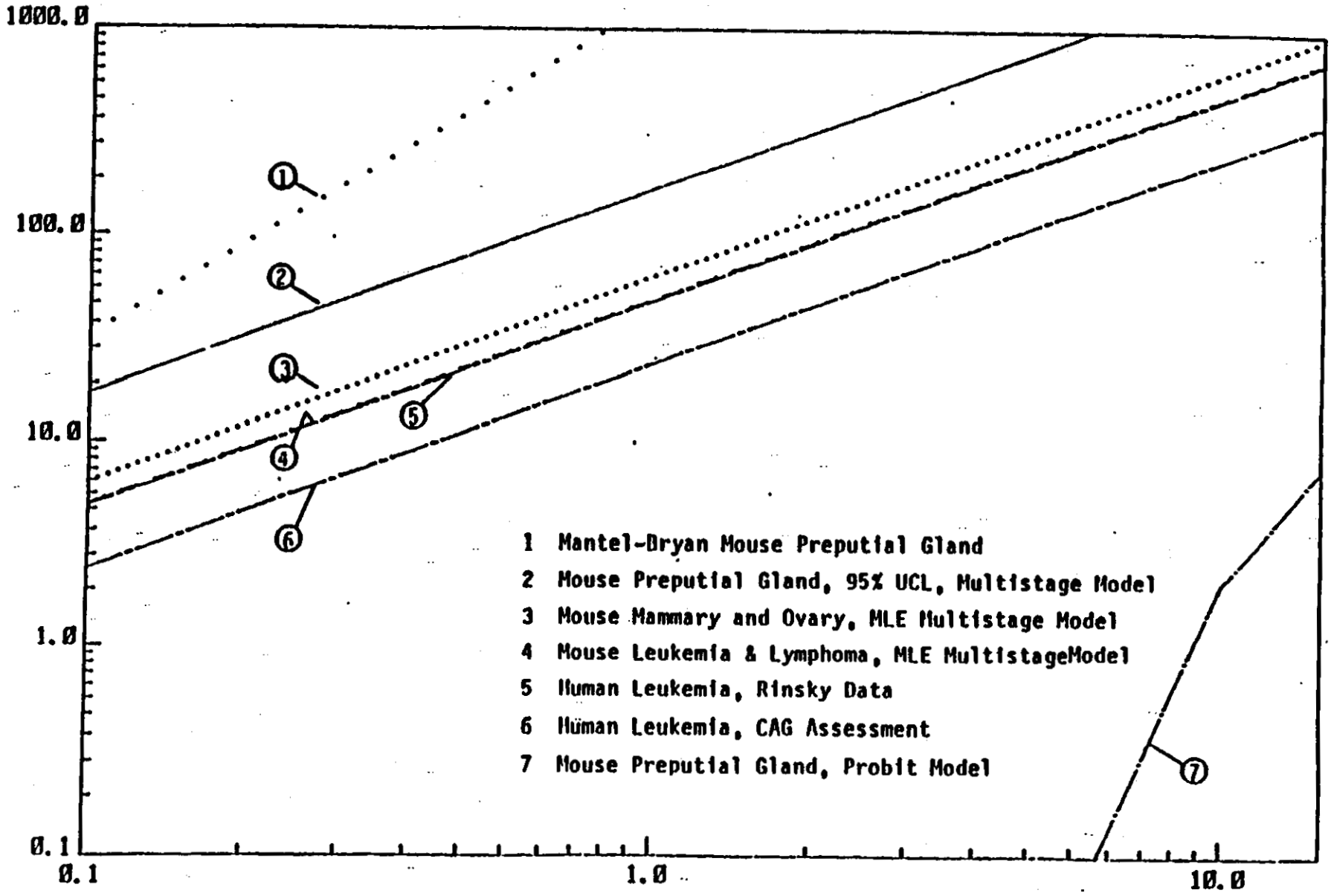
Using the range of dose-response curves suggested by the DHS, the ARB staff estimates that the added lifetime cancer risk to a population exposed to benzene at the population-weighted average concentration of 4.6 ppb estimated for the South Coast Air Basin is in the range of 101 to 780 cases per million persons exposed. To place this in context, the comparable baseline lifetime risk of all cancers combined (SEER program, 1981, Surveillance Epidemiology and End Results Incidence and Mortality Levels, 1973-77, NCI Monograph #57), can be estimated at 23.7 percent or 237,000 cases per million persons exposed.

III. ENVIRONMENTAL IMPACTS

The identification of benzene as a toxic air contaminant is not expected to result in any adverse environmental impacts. Rather, in light of the adverse health effects associated with benzene, as described in this report, and, in that, upon the identification of benzene as a toxic air contaminant, the Board will be required to identify and the Board and air pollution control districts will be required to adopt airborne toxic control measures in accordance with the provisions of AB 1807. Therefore, the identification of benzene as a toxic air contaminant is expected to result in environmental benefits. Environmental impacts identified with respect to specific control measures, will be included in the consideration of such control measures pursuant to Sections 39665 and 39666.

Figure A

CANCER RISK FROM BENZENE



IV. RECOMMENDATION

Since the evidence strongly suggests that benzene is a known human carcinogen, since the evidence does not warrant the assumption that carcinogenicity is confined to the dose above any threshold, and since the range of conservative reasonable dose-response curves predicts a range of added lifetime cancer risks which are not negligible, the ARB staff considers available evidence sufficient to recommend listing benzene as a toxic air contaminant. Furthermore, the staff is recommending listing benzene as a toxic air contaminant because AB 1807 requires that all pollutants identified by EPA as hazardous air pollutants be identified as a toxic air contaminant.

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REPORT TO THE SCIENTIFIC REVIEW PANEL ON BENZENE

PART A - A REVIEW OF BENZENE USES, EMISSIONS AND PUBLIC EXPOSURE

Prepared by the Staff of
The Air Resources Board

November 1984

SUMMARY

Part A of the benzene report to the Scientific Review Panel includes information on 1) benzene sources and emissions in California; 2) atmospheric persistence of benzene; 3) benzene concentrations in the community; and 4) population exposures to benzene. About 15,000 tons of benzene per year are emitted from motor vehicle exhaust and evaporative emissions, representing 93 percent of total emissions. Benzene is persistent in the atmosphere, having an estimated half life of about 12 days. Recent ambient monitoring in the South Coast Air Basin identified a daily range between 1.2 and 16 ppb with an average of 5.7 ppb. We estimate the SCAB population weighted exposure to be 4.6 ppb. We have no recent ambient data for other areas of California and therefore are unable to estimate such exposures. Such data will be obtained during the risk management phase as part of the development of control measures.

REPORT TO THE SCIENTIFIC REVIEW PANEL ON BENZENE

Part A - A Review of Benzene Uses, Emissions, and Public Exposure

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I. BENZENE USAGE AND EMISSIONS

A. PRODUCTION AND USAGE

Benzene is a hydrocarbon naturally occurring in crude oil and present in gasoline and diesel fuels. Gasoline contains about one to three weight percent benzene,[1,2] most of which results from the distillation of the crude or chemical reactions during the refining of the distillates.

With the recent shutdown of benzene production at Chevron's El Segundo refinery, benzene is no longer produced in California. Chevron produced about 14,000 tons of benzene in 1983. Most of the benzene Chevron produced was blended into gasoline to increase the octane rating. However, these 14,000 tons represent a minor fraction of the total benzene content of gasoline. The remainder of benzene produced was used to produce detergent alkylates.[3]

Since 1977, benzene use in formulated industrial and consumer products such as adhesives and paint removers has been negligible.[4] Also, other uses of benzene as a solvent and chemical intermediate have decreased and are expected to continue to decrease.

B. CURRENT AND PROJECTED STATIONARY AND MOBILE SOURCE EMISSIONS

Benzene emissions in California were estimated using data from local air pollution control districts, the Environmental Protection Agency (EPA), the Society of Automotive Engineers (SAE) studies, the Air Resources Board (ARB), a KVB, Inc. study, and a Statewide Air Pollution Research Center (SAPRC) study.

Preliminary emission estimates show motor vehicles contribute about 93 percent of the estimable benzene emissions in California. The major stationary emission sources are gasoline marketing, agricultural burning, wildfires, petroleum refineries, asphalt plants, and detergent alkylate production facilities.

Stationary fuel combustion sources emit benzene due to incomplete combustion, but there are insufficient data to estimate benzene emissions from these sources. Thus, no estimate from stationary source fuel combustion is included. Other sources of benzene emissions are geothermal plants and miscellaneous burning. Miscellaneous burning includes residential wood combustion and structural fires. Table I-1 summarizes the ARB staff's estimates of benzene emissions in California.

Stationary Emission Sources

Benzene evaporative emissions from gasoline marketing are considered to be a major stationary source of benzene at an estimated 300 tons per year. (Gasoline marketing includes bulk terminals, bulk plants, service station tanks, and vehicle refueling operations.) This estimate is based on an estimated factor of 1.0 weight percent benzene in total hydrocarbon (THC) emissions from gasoline marketing sources. This emission estimate takes into account the reduction in evaporative emissions due to vapor recovery systems.

A benzene emission estimate of 552 tons per year for agricultural burning/forest management burning, wildfires and miscellaneous burning is based on emission factors developed by the SAPRC,[7] and ARB data on burning practices in California.[22] The SAPRC emission factors are rough approximations because benzene emissions from open burning are difficult to measure and because the SAPRC tests were conducted under controlled conditions that may not accurately duplicate field conditions. The emissions from forest management burning and wildfires can vary significantly from year to year.

Benzene emissions from petroleum refineries and asphalt plants were estimated to be 180 tons per year based on data from a 1980 consulting firm study[5] and a survey of petroleum refiners.[2] Petroleum refining

Table I-1

Estimated Benzene Emissions in California

Source	Source Type	Emissions** (tons/yr)	Inventory Year	Reference
Gasoline Marketing	Area	300	1981	14,15
Agriculture Burning/ Management Burning	Area	410	1981	7,22
Wildfires	Area	130	1981	7,14
Miscellaneous Burning	Area	12	1979	7,14
Petroleum Refineries & Asphalt Plants	Point	180	1982	5,12
Detergent Alkylate Prod.				
Chevron, Richmond	Point	55	1983	3,11
Witco Chemical, Carson	Point	16	1982	3
Geothermal Plants	Point	2	1982	13
Benzene Production*				
Chevron, El Segundo	Point	1	1983	3
STATIONARY SOURCE TOTAL		1,110		
Vehicular Exhaust	Area	13,400	1983	10,16,17, 18,19,20, 21
Vehicular Evaporative Emissions	Area	1,600	1983	10,16
MOBILE SOURCE TOTAL		15,000		
TOTAL		16,100		

* This benzene production facility was closed indefinitely in 1984.
** The estimated emission totals are rounded.

processes that may emit benzene include fluid catalytic cracking, hydrocracking, gasoline treating, and pumps, flanges and other fugitive emission sources, waste-water treatment, heaters, boilers and storage facilities. The emission factor applied to petroleum refineries and asphalt plants provides a rough estimate of benzene emissions from these sources. Additional testing of benzene emissions from petroleum refineries and asphalt plants should be performed prior to considering control measure development for these sources.

Data from the Bay Area Air Quality Management District (BAAQMD)[11] and the SCAQMD[3] were used to estimate benzene emissions at 71 tons per year from California's two detergent alkylate production facilities.

Other stationary sources of benzene are geothermal plants and a benzene production plant, which are estimated to emit 3 tons per year. The benzene production plant was closed indefinitely in 1984.[25]

Recent trends in benzene production and uses in California were evaluated to predict future stationary source benzene emissions. Such emissions are predominantly gasoline-related and should track gasoline consumption. However, the future trend of gasoline consumption is not clear. The California Energy Commission[23] projects a 12 percent decrease in automotive fuel use from 1980 to 1997; but recent data[24] show that after a two-year decrease, the gasoline use rate in late 1983 regained its 1980 level. Future emissions are further clouded by the uncertainty in the benzene content of gasolines as the fraction of gasoline that is unleaded increases.

Mobile Emission Sources

Data from the EPA,[10,17,19] the Society of Automotive Engineers (SAE) studies[18] and the ARB[16] were used to estimate benzene emissions from

motor vehicles in California. Motor vehicles contribute about 93% of the estimable benzene emissions in California, or about 15,000 tons per year.

EPA and SAE studies measured the fraction of benzene (weight %) in the total hydrocarbon (THC) evaporative and exhaust emissions from automobiles. A study published in 1980[10/] found the benzene portion of evaporative emissions to average 1.2 percent of the total evaporative hydrocarbons. To estimate benzene from motor vehicle exhaust, the staff used the following factors based on these studies:

Vehicle Type	Average Weight Percent Benzene of THC Exhaust Emissions
Catalyst	4.1
Non-Catalyst	4.2
Diesel	2.3

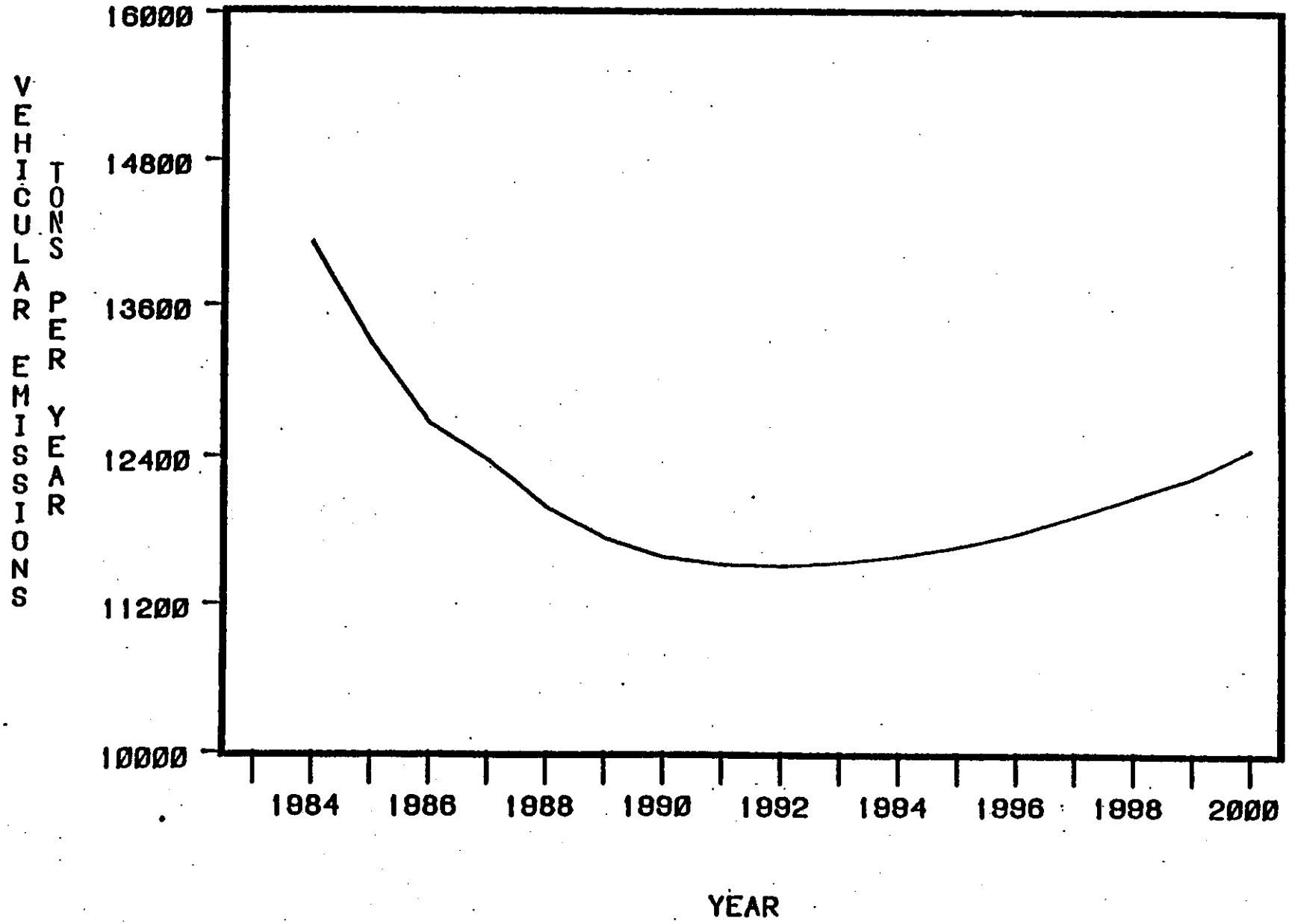
The EPA and SAE studies show the weight percent benzene of THC exhaust emissions increases with increasing aromatic content of the fuel. As the lead content in leaded fuels has decreased, the aromatic content has increased to maintain the octane level.[8/] Therefore, the 4.2 weight percent benzene may underestimate the current benzene emissions from non-catalyst vehicles. Additional motor vehicle testing using California fuels and motor vehicles representing the spectrum of in-use vehicles is needed to refine the benzene emissions estimate for motor vehicles.

Recent trends in THC emissions from motor vehicles and vehicle population were used to predict benzene emissions from motor vehic es beyond 1983. Motor vehicle benzene emissions are expected to decrease through 1992 as more stringent controls decrease THC emissions. After 1992, motor vehicle benzene

emissions are expected to increase as the number of vehicle-miles travelled increases. Figure II-1 is a graph of the benzene emission estimates for motor vehicles from 1984 to 2000. These estimates assume the aromatic content of gasoline remains stable.

In summary, benzene is known to be emitted in substantial amounts, mostly directly related to the use and, to a minor extent, the production of gasoline. Because of the predominance of vehicles in urban areas, benzene is expected to be found in urban atmospheres.

FIGURE I-1. PROJECTED* BENZENE EMISSIONS FROM MOTOR VEHICLES (TOTAL EXHAUST AND EVAPORATIVE)



* based on 1983 inventory

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II. PERSISTENCE IN THE ATMOSPHERE

A. PHYSICAL AND CHEMICAL PROPERTIES

The benzene molecule, C_6H_6, has a planar hexagonal carbon ring. The electronic structure of that geometry makes benzene unusually stable. Although the molecule is non-polar, its physical and electronic structures make benzene polarizable. As a result, benzene is unusually soluble in water compared to other non-polar hydrocarbons. Solvents for benzene include acetone, alcohols, chloroform, ethers, carbon disulfide, carbon tetrachloride, acetic acid, and oils.

The carbon adsorption capacity of benzene from air is shown in Figure II-1.

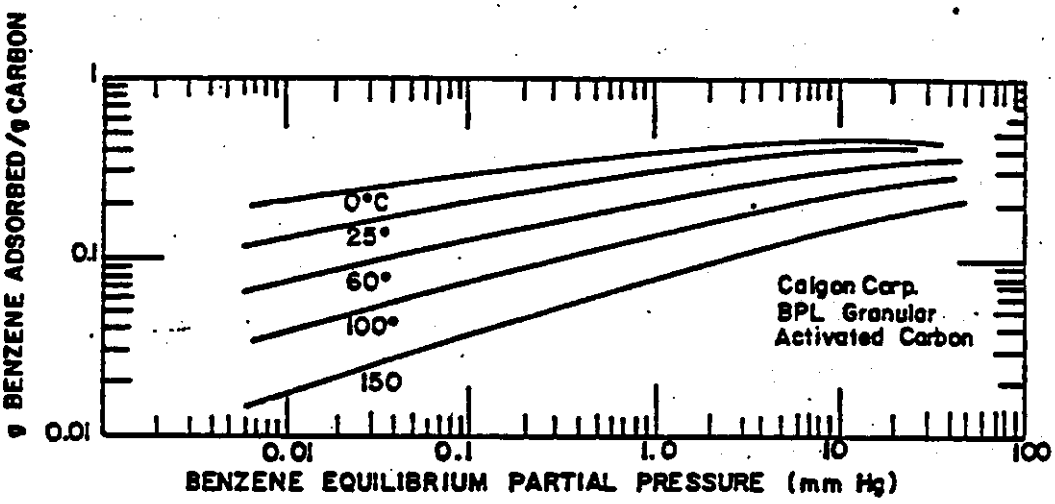

Figure II-1 Benzene Adsorption Isotherm on Calgon/BPL Granular Activated Carbon (from Ref. 7)

Table II-1 shows physical and chemical properties related to the emission, transport, and control of benzene.

Table II-1

Physical Properties of Benzene

Property	Value	Reference
Activity coefficient in water, 25°C	2,400	5
Boiling point, 1 atm	176°F	3
Carbon adsorption capacity		
from water, 1 mg/l, 60°F	1 mg/g	4
from air, 1 mmHg, 25°C	.2 g/g	7
Density, liquid	.88 g/cm^3	3
Diffusivity in air, 25°c	.088 cm^2/sec	5
Flame temperature, max. adiabatic	4150°F	8
Flammability limits in air	1.2 to 9.1 vol. %	3
Heat capacity, 60°F, 1 atm	.42 cal/°C/gm	8
Heat of formation, liquid, 25°C	150 cal/gram	3
Heat of fusion	30.1 cal/gram	3
Heat of vaporization, 25°C	104 cal/gram	3
Heat of combustion, 25°C (HHV)	10 kcal/gm	3
Henry's law constant, water, 25°C	.0055 atm-m^3/mole	5
Ignition temperature, air	1097°F	3
Index of refraction	1.5	6
Molecular weight	78.11	
Octanol: water part tion ($\log_{10}$)	2.14	8
Solubility in water, 20°C	.82 mg/g	8
Vapor pressure, 40 to 176°F	lnP (mmHg) = -4033 x 1/T(°K) + 18.0	3
Ultraviolet absorption band	275 nm	6

B. FORMATION AND FATE IN THE ATMOSPHERE

The only significant chemical loss of benzene in polluted atmospheres containing oxides of nitrogen (NO_x) is through the gas phase reaction with the hydroxyl radical ($OH^{\cdot}$) during daylight hours.[1/] Other reactions are negligible under atmospheric conditions. This reaction with OH radicals proceeds slowly. It produces, among other products, phenol (C_6H_5OH), though the yield is not known. Other reaction pathways are not fully characterized but include ring opening to form dicarbonyl compounds such as glyoxal.

The half-life for benzene in the atmosphere from the reaction with $OH^{\cdot}$ depends on the concentration of hydroxyl radicals in ambient air; it is around 12 days at an $OH^{\cdot}$ concentration of 1×10^6 cm^{-3}, a 24-hour average typical of the northern hemisphere cities. Over this time, benzene will become widely dispersed from its emission source. It is thus a persistent pollutant apt to be present throughout an urban air shed.

Gaseous phenol also reacts with the $OH^{\cdot}$ during daylight hours with a half-life in the range of two hours to about 10 hours, again depending on the ambient $OH^{\cdot}$ concentration. However, a much faster sink for phenol is reaction at night with the gaseous nitrate radical NO_3.[2/] At typical $NO_3^{\cdot}$ concentrations in Southern California airsheds (e.g., 50-100 ppt), the atmospheric lifetime of phenol with respect to this nighttime process is less than seven minutes. Therefore, even in relatively unpolluted atmospheres (low concentrations of $OH^{\cdot}$), phenol is quantitatively removed within 24 hours.

The ultimate products of the atmospheric reactions of phenol with OH and NO_3 radicals are not fully characterized, but probably include quinones and gaseous and particulate nitrophenols. Both phenol and quinones are considered hazardous by EPA, but each is of much less concern than benzene as an air contaminant. The possible hazards of atmospheric nitrophenols are not as yet established.

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3. Chemical Engineer's Handbook, Perry and Chilton (ed.), 5th Edition, 1973.

4. Dobbs, R. A. and Cohen, J. M., Carbon Adsorption Isotherms for Toxic Organics, EPA 600/8-80-023, 1980.

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6. Mara, S. J. and Lee, S. S.; Assessment of Human Exposures to Atmospheric Benzene, Stanford Research Institute, for EPA, May 1978.

7. Kiang, Y.-H.; "Controlling Benzene Emissions," in Benzene, Cheremisinoff and Morresi (ed.), Marcel Dekker, Inc. 1979.

8. Cheremisinoff, P. N. and Morresi, A. C; Benzene, Marcel Dekker, Inc. 1979.

III. BENZENE CONCENTRATIONS IN THE COMMUNITY

A. AMBIENT AIR DATA

The California Air Resources Board Haagen-Smit Laboratory has been monitoring ambient benzene at four locations in the South Coast Air Basin (SCAB) since September 12, 1983. All analyses are of samples collected over a 24-hour period, from 9 a.m. to 9 a.m. the following day. The samples are collected in Tedlar bags at a constant flow rate yielding integrated bag samples containing benzene and other organic constituents.

Samples are collected five days per week at the El Monte site and about once every six days at the Downtown Los Angeles (DOLA), Dominguez, and Riverside sites. The data reported for each site are shown in Appendix E. The estimated accuracy of the reported values is within 10 percent of the actual values.

From mid-September 1983 to March 1984, 209 samples were collected and analyzed. The benzene values range from 1.2 ppb at three sites on three different occasions to 16.0 ppb at the El Monte sampling site on December 8, 1983. The average for all individual samples was 5.7 ppb. The average value for El Monte (123 samples) was 6.1 ppb, for DOLA (30 samples) the value was 6.4 ppb, for Dominguez (23 samples) the value was 5.5 ppb, and for Riverside (33 samples) the value was 4.9 ppb.

To check the accuracy of using Tedlar bags for monitoring ambient benzene concentrations, Haagen-Smit Laboratory performed a bag material stability test and validation tests on Tedlar bags. The results of these tests are included in Appendix D. The bag material stability test shows benzene is not generated

or lost within the bag material. The validation tests show there are no appreciable changes in benzene concentrations in the bag from the time that sampling starts until the sample is placed in the gas chromatograph.

The Haagen-Smit monitoring program provides the only long-term, multi-site ambient benzene data for any place in California. Data from several limited studies at various locations are available from an EPA data base.[4/] These data, synopsized in Appendix E, are too few and variegated in age and experimental design to characterize current ambient concentrations for other locations as is done in the next section for the South Coast Air Basin (SCAB). However, they do confirm concentrations in the urban air outside the four-station monitoring area similar to those reported by Haagen-Smit Laboratory.

B. ESTIMATE OF AMBIENT BENZENE EXPOSURE

Long-Term General Exposure

The annual average* benzene concentration in the SCAB was estimated based on data taken by Haagen-Smit Laboratory at the four monitoring sites from September 12 to December 29, 1983. Linear regression of those data against measurements of ambient CO yields a significant correlation ($r = .82$ at the .01 percent significance level**). This linear relationship was used to calculate annual average benzene concentrations for two years at all CO monitoring stations in the basin (31 stations). These calculated values were then interpolated to grid cell centers. (See Figures 2 and 3 in Appendix E

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* "Annual average" denotes the mean of all 24-hour data available from one year.

** There is one chance in 10,000 that the populations do not correlate but still yield a calculated correlation coefficient of .82.

the 1983 benzene measurements (fourth quarter, four stations, 5.7 ppb) was multiplied by the ratio of basinwide annual average CO to basinwide fourth quarter average CO. This was done using CO data from both 1981 and 1982. The resulting estimates of the 1983 annual average benzene concentration among the four monitors are 4.0 and 3.9 ppb, respectively, using the 1981 and 1982 CO data.

The conclusions from these estimates are that the population-weighted benzene concentration is about 20 percent higher than the geographic average and that the four stations taken together represent well the geographic average for the entire basin.

The details of the modeling performed and the monitoring data are presented in Appendix E.

Short-Term or Local Exposures

In addition to the widespread, long-term average concentrations estimated in the previous section, some people are locally exposed to airborne benzene from specific sources. Such exposure may be more or less continuous and long-term -- for example, through residence near and prevailingly downwind of a freeway. The exposure may be short but repetitive -- for example, while driving on a busy road or filling one's automobile gas tank.

There are very few data regarding near-source exposure to benzene. A summary of extant data on concentrations follows in Table III-2. (See Appendix E for details.) This data should be augmented by field work when control strategies for benzene emissions are considered. However, the ARB staff believes that the general ambient concentrations discussed previously and their attendant health risks provide sufficient information for considering benzene as a TAC.

for graphical presentations of the results.) The annual benzene concentrations at grid centers were then used to calculate the geographic average and the population-weighted average for the SCAB. (The latter statistic is more useful for risk assessment.) Table III-1 shows the results. The 1982 population-weighted average of 4.6 ppb was used by DHS to estimate the range of risk from ambient benzene exposure.

Table III-1

Estimates of Annual Benzene Concentrations
in the South Coast Air Basin
(ppb)

	1981	1982
Geographic average (standard deviation)[a/]	4.0 (1.6)	3.7 (1.6)
Population-weighted average	4.8	4.6

a/ "Geographic average" is the average of all interpolation grid cells. "Standard deviation" applies to the calculated annual averages at the 31 CO monitors.

By overlaying the population and benzene data by grid cell, the distribution of exposure (annual average concentration) versus number of people exposed was estimated. According to the resultant plots, shown in Appendix E, 80-90 percent of the population of the SCAB is exposed to 4 ppb or more of benzene as a year-round average.

The foregoing method could not be used for 1983 because 1983 data for CO were not yet complete. To use the benzene monitoring data directly in an estimate for 1983, a second estimation method was used. The average of all

Table III-2
Benzene Concentrations Near Sources [a]

Sources	Type of Data	Distance from Source (feet)	Sampling Time (hours)	Benzene (ppb)	Comments
filling stations	ambient monitoring	100 to 1300	8 to 19	0.3 to 1.9 (range)	six or seven sites at four locations; no vapor recovery; ref.5
filling station	personal air monitoring	(employee workplaces)	0.5	4 to 65[c] (range)	British study; results were adjusted to reflect the benzene content of gasoline and the use of vapor recovery in Calif.[c]; ref.6
filling station	personal air monitoring	(air space of person filling tank)	(during fill)	60[d]	US study; results were adjusted to reflect the use of vapor recovery in Calif.[d]; ref.11
freeway	modeling results	0 160 490	1 1 1	50[b] 19 7	results apply to rush hour on a large freeway under worst-case meteorology;[b] above background concentrations; ref.7
busy intersection	modeling results	80 (4 sites)	1 (worst hour)	9.7 to 17[e] (range)	results apply to typical weekday traffic at the intersection of Wilshire Blvd. and Veterans Avenue (in South Coast Air Basin); above background concentrations; based on ref.7
busy street	ambient montioring	6 to 10	25	3.0 to 7.1	the higher numbers were measured upwind; poor correlation with traffic density; ref.5

a Except as noted, the data are absolute (total ambient) concentrations.

b Annual average concentrations would probably be less than 10% of these values.

c For stations without vapor recovery (dispensing 12% of the gasoline), analogous estimates are 80 to 1350 ppb.

d Actual average results from stations without vapor recovery was 1,210 ppb (average).

e The maximum annual average benzene concentrations varied from 0.5 to 1.4 ppb above background concentrations.

It is difficult to translate data like those in Table III-2 into population exposure information except in qualitative terms. Although people visiting filling stations can experience concentrations well above the general ambient concentrations (i.e., 4.6 ppb), such exposure is short.* For example, a person driving 15,000 miles per year in a vehicle achieving 20 miles per gallon of gasoline would augment his annual average benzene exposure by 0.2 ppb if he always fills his own tank at stations without vapor recovery and experiences 1,210** ppb of benzene while pumping. The data suggest that people spending considerable time in the neighborhood of (not in) a filling station may not experience concentrations noticeably above the general ambient air concentrations. The same may be true of people living or working near busy roadways except during worst-case conditions of traffic and meteorology. Usually, long-term average concentrations are predicted to be much smaller than worst-case short-term concentrations like those presented for a freeway in the table.

We emphasize that the database portrayed in Table III-2 is extremely small; it is insufficient to characterize short-term or near-source exposures.

Semi-quantitative information on benzene concentrations experienced by people in vehicles can be deduced from measurements of carbon monoxide (CO) in vehicles. During "rush hour" on typical commuter routes in Los Angeles researchers found values two to three times the annual average CO measurements at monitors in LA County.[8,9] Hence, we conclude that drivers likely experience benzene concentrations two to three times higher than the

---

* This is not true for station employees.
** Previously erroneously cited in draft report as 60 ppb which applies to stations with vapor recovery.

4.6 ppb (annual basin average) corresponding to general ambient CO concentrations. Because many SCAB residents spend considerable time driving on busy roads, such exposure may be a significant part of total population-wide exposure to benzene. However, neither the in-vehicle benzene concentrations nor the person-hours of exposure are known.

C. INDOOR AIR DATA

An estimate of the total population exposure to benzene through inhalation would require information on indoor benzene concentrations. Indoor concentrations may or may not equal ambient concentrations, depending on factors such as number and type of indoor benzene sources and air exchange rates. Indoor benzene sources include tobacco smokers, heating and cooking systems, drift from automobiles parked in a garage or nearby, cleaning solvents, and evaporation from various products used in a home or work area. Unfortunately, very few data on indoor benzene concentrations are available and no data are available for California.

In an attempt to evaluate benzene exposure from indoor air, studies by the Environmental Protection Agency (EPA)[1/] and the Oak Ridge National Laboratory (ORNL)[2/] were reviewed. In the 1981 Total Exposure Assessment Methodology (TEAM) study sponsored by the EPA, overnight (6 p.m. to 6 a.m.) air samples were collected on personal Tenax monitors by 97 residents of Elizabeth and Bayonne, New Jersey. Since most of these residents did not leave their homes during sampling, the measurements are assumed to be representative of the overnight indoor environment of their homes. The personal air benzene concentrations ranged from .01 ppb to 37.7 ppb with an average concentration of 6.3 ppb. Simultaneous outdoor air samples were

collected in the backyards of the 97 residents. The outdoor air benzene concentrations ranged from .02 to 28.6 ppb with an average concentration of 3.1 ppb. Thus, the average indoor air benzene concentration was about two times the average outdoor benzene concentration. The EPA study indicates that benzene is more prevalent in smokers' homes than in nonsmokers' homes. However, the study does not specify the benzene concentrations found in smokers' vs. nonsmokers' homes. The percentage of smokers in the sample population was 12 percent greater than the national average of 33 percent. Thus, personal air measurements in smokers' homes may explain the high benzene levels found in the EPA study.

A status report on indoor air quality monitoring conducted by the ORNL for the U.S. Consumer Product Safety Commission indicates ORNL monitored for volatile organic compounds in forty homes in the Oak Ridge, Tennessee area. However, the status report discusses only limited data from one home. This status report indicates that indoor pollutant concentrations decrease when the air exchange rate increases.

These data on indoor concentration are very limited. The sources of indoor benzene concentrations were not identified in either report. Thus, there is no reconciliation between indoor data available and benzene concentrations expected in California homes or offices. The EPA is completing an indoor air study for California homes. The results of this study are expected to be available by December 1984. These indoor exposure data will be included for the Board's consideration during the risk management phase.

Daily benzene exposure from food and water intake was compared to daily benzene exposure from ambient air in the South Coast Air Basin (SCAB). A 1980 study by the National Research Council[10/] estimates the average U.S. urban dweller is exposed to as much as 250 ug. benzene daily from food intake and about 2 ug. benzene daily from water intake. Assuming an ambient benzene concentration of 4.6 ppb (SCAB average), an urban dweller is exposed to nearly 300 ug. benzene daily from ambient air (assuming daily air intake is 20 m^3). These limited data show ambient and indoor benzene exposures are greater than exposure from food and water.

Summary

In the South Coast Air Basin, where roughly half the state's population lives, most people are exposed to at least 4 ppb ambient benzene on the year-round average. Air sampling data confirm that benzene is widespread in the urban atmosphere. Exposure to benzene in vehicles may be significant. Data are too few to characterize near-source ambient exposures or indoor exposures. Such information will be neccessary during risk management to determine and rank total and relative exposures.

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4. Brodzinski, R. and Singh, H. B., Volatile Organic Chemicals in the Atmosphere - An Assessment of Available Data, SRI International, EPA 600/3-83-027a, April 1983.

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APPENDIX A

INFORMATION REQUEST LETTER AND RESPONSES

STATE OF CALIFORNIA
AIR RESOURCES BOARD
Q STREET
)OX 2815
SACRAMENTO, CA 95812

GEORGE DEUKMEJIAN, Governor

February 10, 1984

Dear Sir or Madam:

Subject: Request for Information Regarding Benzene

I am writing to request information on the health effects of benzene as part of our toxic air contaminant program. This program is based on legislation enacted in September 1983, Assembly Bill 1807 (Tanner). AB 1807 (Health and Safety Code Sections 39650, et seq.) requires the ARB to identify compounds as toxic air contaminants and once identified to develop and adopt control measures for such compounds. After consultation with the staff of the Department of Health Services (DOHS), we have selected benzene as a candidate toxic air contaminant to be evaluated in accordance with the provisions of AB 1807.

Before the ARB can formally identify a compound as a toxic air contaminant, several steps must be taken. First, the ARB must request the Department of Health Services to evaluate the health effects of candidate compounds. Second, the ARB staff must prepare a report which includes the health effects evaluation and then submit the report to a Scientific Review Panel for its review. The report submitted to the Panel will be made available to the public. Any person may also submit information to the Panel for its consideration. The Panel reviews the sufficiency of the information, methods, and data used by the DOHS in its evaluation. Lastly, after review by the Scientific Review Panel, the report with the written findings of the Panel will be considered by the Air Resources Board and will be the basis for any regulatory action by the Board to officially identify a compound as a toxic air contaminant.

Prior to formally requesting the DOHS to prepare a health effects evaluation of benzene, we are providing, pursuant to the provisions of Section 39660(e) of the Health and Safety Code, an opportunity to interested parties to submit information on the health effects of benzene which he or she believes would be important in DOHS's evaluation of benzene as a candidate toxic air contaminant.

In December 1983, ARB staff received a reference search on benzene health effects using the MEDLARs II and DIALOG Information Services. These

information services include material available to the public on or before July 1983. The attached bibliography lists the references from this information search. We are requesting pertinent information on benzene health effects, including any material that may not be available to the public, that is not included in the attached bibliography.

I would appreciate receiving any relevant information you wish to submit by March 12, 1984. To expedite the review process, we ask that any information which you believe should be regarded as "trade secret" be clearly marked and separated from other information. Your help in expediting our review will be greatly appreciated.

Health and Safety Code Section 39660(e) provides that you may identify portions of the information you submit as "trade secret." The ARB may later request that you provide documentation to support any claim of trade secret. In addition, information other than trade secrets may be identified as confidential in accordance with the provisions of Section 91011, Title 17, California Administrative Code. The information which you provide pursuant to this request may be released "(1) to the public upon request, except trade secrets, which is exempt from disclosure or the disclosure of which is prohibited by law, and (2) to the federal Environmental Protection Agency, which protects trade secrets as provided in Section 114(c) of the Clean Air Act and amendments thereto (42 USC 7401 et seq.) and in federal regulations." (Section 91010, Title 17, California Administrative Code.) The information, including trade secret and other confidential information, may also be released to other public agencies, which are also required to preserve the protections accorded to trade secret and confidential information.

Please send the information to the attention of:

William V. Loscutoff, Chief
Toxic Pollutants Branch
Re: Benzene
California Air Resources Board
P. O. Box 2815
Sacramento, CA 95812

If you have any further questions regarding health effects information, please contact Mr. John Batchelder at (916) 323-1505. For any other questions, please contact Mr. Robert Barham at (916) 322-4586.

If you are not the person to whom this request should be addressed, please forward it to the appropriate person in your organization. Also please let us

know whether you would like to continue to receive information inquiries for other candidate compounds, and if not, if there is anyone in your organization to whom such requests should be sent.

Sincerely,

William V. Loscutoff for

Peter D. Venturini, Chief
Stationary Source Division

cc: Alex Kelter, DHS
Lori Johnston, DFA
Wayne Morgan, President CAPCOA
Jan Bush, Executive Secretary CAPCOA
David Howekamp, EPA Region IX
Sal Barajas, Assemblywoman Tanner's Office
APCO's

Attachment

adcoat, inc.
172 East La Jolla Road, Placentia, California 92670 - (714) 630-7311

February 14, 1984

Mr. Peter D. Venturini, Chief
Stationary Source Division
Air Resources Board
1102 Q Street
P.O. Box 2815
Sacramento
CA 95812

Dear Mr. Venturini:

We do not use benzene in any of our products, so we can not provide you with toxicity information not available to the public.

We are very interested in remaining on your mailing list, however, since we may be able to contribute needed information regarding the use of other solvents, such as perchloroethylene, at a later date.

Very truly yours,
ADCOAT, INC.

Hugh Muller

HUGH H. MULLER
PRESIDENT

HHM/mw

The Adhesive & Sealant Council

Suite 910 – 1600 North Wilson Boulevard – Arlington, Virginia 22209
Phone: (703) 841-1112

April 2, 1984

Mr. Peter D. Venturini
Chief
Stationary Source Division
Air Resources Board
1102 Q Street
P.O. Box 2815
Sacramento, CA 95812

Dear Mr. Venturini:

I received a belated copy of your request for information regarding benzene. I would appreciate being placed on your mailing list to receive information inquiries for other candidate compounds, so that I may inform the membership of the Adhesive and Sealant Council of such inquiries.

Thank you for your assistance.

Sincerely,

Kris A Monteith

Kris Anne Monteith
Coordinator
Government Relations

KAM/nat

1670 Beverly Blvd., Los Angeles, CA 90026 (213) 484-9300

AMERICAN LUNG ASSOCIATION
of CALIFORNIA

March 7, 1984

Mr. William V. Loscutoff, Chief
Toxic Pollutants Branch
Re: Benzene
California Air Resources Board
Box 2815
Sacramento, California 95812

Dear Mr. Loscutoff:

We are pleased to respond to your February 10, 1984 memo requesting information regarding benzene.

The literature review attached to your memo is extensive and we have only one additional reference to suggest. It is a subsequent article to reference #97 in the bibliography.

White, M.C., Infante, P.F. and Chu, K.C.; A Quantitative Estimate of Leukemia Mortality Associated with Occupational Exposure to Benzene. Risk Analysis, 1982, Vol. II, pages 195-204.

Please continue to send information or requests for response on the toxic air contaminant program to our staff person in the Southern California office, Gladys Meade. She is coordinating the joint response of the American Lung Association of California and the California Thoracic Society.

Yours truly,

Ralph C. Jung, M.D.
President

RCJ;M;g

CC: Dean Sheppard, M.D.
California Thoracic Society

Mailing Address: Box 2679 - T. A.
Los Angeles, California 90051
Telephone 213 486 8724

Paul M. Koplow
Manager
Environmental and Regulatory Affairs
Health, Safety and Environmental Protection

March 9, 1984

Mr. William V. Loscutoff
Chief Toxic Pollutants Branch
California Air Resources Board
P.O. Box 2815
Sacramento, California 95812

Re: Request for Information Regarding Benzene

Dear Mr. Loscutoff:

This letter is in response to Mr. Peter Venturini's February 10, 1984 request for information regarding the health effects of benzene. The Atlantic Richfield Company appreciates the advance notice provided by ARB staff to members of the public advising us of your intention to shortly submit a request to the Department of Health Services (DHS) for a health hazard and risk assessment for benzene. Taking advantage of opportunities such as this for cooperation between ARB staff and the public can greatly enhance the regulatory implementation of AB 1807.

During the past few years A.R.Co. and its operating companies have been actively participating in several state and federal regulatory proceedings involving benzene. We also participate in research efforts of various trade organizations who have addressed the health effects of benzene. Representatives of our Corporate Toxicology group have reviewed the bibliography of studies attached to the February 10 letter and have compared it to recent studies and reviews in our files.

Appendix A to this letter lists selected studies and articles not cited in the ARB Bibliography which we recommend for inclusion in the package of materials to be submitted to DHS for their evaluation. Copies of certain of the studies (i.e. those marked with an "*") have been provided for your convenience. If you do not already have, or have difficulty obtaining copies of any of the other cited materials, please contact Dr. Charles Lapin of our Corporate Toxicology Group at (213)486-3825. The transmittal of these materials and the identification of health effects studies in Appendix A should not be construed as reflecting any statement regarding the technical accuracy or the contents or conclusions of the studies. It also does not necessarily indicate A.R.Co. support or agreement with the various author's views on the health effects or risk of benzene exposure.

Please feel free to call us if we can provide additional assistance in the ARB's ongoing regulatory activities to implement AB 1807.

Sincerely,

Paul M. Kaplow

PMK/ML:jap

Attachments

pc: Mr. John Batchelder

BARNES-HIND HYDROCURVE INC.
A Revlon Vision Care Company

[illegible]
Sunnyvale, California 94086
[illegible]

February 29, 1984

William V. Loscutoff, Chief
Toxic Pollutants Branch
California Air Resources Board
P.O. Box 2815
Sacramento, CA 95812

Dear Mr. Loscutoff:

Reference: Benzene

Regarding February 10, 1984 ARB request for information on the health effects of benzene. We have no data to submit at this time. Presently, we only purchase and use 10 to 15 gallons of benzene per year for QC and R & D lab testing purposes.

We would like to continue to receive information inquiries, etc. for other potential toxic air contaminants.

Sincerely,

Dale B. Hanson

Dale B. Hanson
Director, Engineering

DBH/dpc

cc: P. Charley
G. Sweeney

California State University, Fullerton
Fullerton, California 92634

Dean's Office
School of Mathematics, Science and Engineering
(714) 773-2638

March 5, 1984

Peter D. Venturini, Chief
Stationary Source Division
Air Resources Board
P.O. Box 2815
Sacramento, California 95812

Dear Venturini:

Concerning your February 10 letter regarding benzene, there is no one at our institution wishing to submit information. I do not desire to continue receiving information inquiries for other candidate components, but I recommend that requests be sent to the Chairman, Chemistry Department, CSUF, Fullerton, CA 92634.

Sincerely yours,

A. James Diefenderfer
Dean, School of Mathematics,
Science and Engineering

JO:jk

CALIFORNIA STATE UNIVERSITY
LONG BEACH

ice of Associate Vice President for
Academic Affairs--Academic Personnel
(213) 498-5157

March 8, 1984

Mr. William V. Loscutoff, Chief
Toxic Pollutants Branch
RE: Benzene
California Air Resources Board
P.O. Box 2815
Sacramento, CA

Dear Mr. Loscutoff:

California State University, Long Beach is not conducting any scientific evaluations involving the health effects of benzene and its impact on the environment. Therefore, I am unable to provide you with any information that could be submitted to the Scientific Review Panel for its consideration.

I have reviewed your bibliography on benzene and cannot add to it. I appreciate you providing the opportunity to review and comment on the study being conducted on benzene.

Sincerely,

June M. Cooper
Associate Vice President
for Employee Relations

JMC:pj
cc: President Horn
Dick Hunt

LONG BEACH CALIFORNIA 90840
THE CALIFORNIA STATE UNIVERSITY AND COLLEGES

DEPARTMENT OF THE ARMY
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010

REPLY TO ATTENTION OF

MAR 15 1984

Occupational and Environmental
Medicine Division

Mr. William V. Loscutoff
Chief, Toxic Pollutants Branch
California Air Resources Board
P. O. Box 2815
Sacramento, California 95812

Dear Mr. Loscutoff:

Although this Agency has an interest in benzene health effects, a review of our files has not revealed any information that we feel would be of use in your evaluation, or which would not already be available to you in the general scientific literature.

Recommend that future requests of this nature be addressed to:

Preventive Medicine Consultants Division
Professional Services Directorate
Office of The Surgeon General
Washington, D. C. 20310

Further questions or comments concerning this response should be directed to Major R. Petzold, this Agency, at (301) 671-3534.

Sincerely,

Joel C. Gaydos

Joel C. Gaydos, M.D.
Colonel, Medical Corps
Director, Occupational and
Environmental Health

Memorandum

To : Peter D. Venturini, Chief
Stationary Source Division
Air Resources Board
1102 Q Street
Sacramento, CA 95814

Date : March 7, 1984

Place : Sacramento

From : **Department of Food and Agriculture**

Subject: Request for Information Regarding Benzene

Thank you for your letter regarding your information search for Benzene. I think it expressed the new mandate of Assembly Bill 1807 succinctly and clearly indicated why the requested information is needed in order to evaluate materials as toxic air contaminants.

Benzene is not registered as a pesticide and, to my knowledge, is no longer used in current agricultural practices. It is not an inert ingredient in current pesticide formulations and has not been identified as a breakdown product from other pesticides. The CDFA registration library no longer keeps health effects data on Benzene since its registration was dropped over three years ago.

In summary, Benzene is no longer used in current agricultural practices and is not registered as a pesticide by the Department of Food and Agriculture.

Lori Johnston

Lori Johnston, Assistant Director
Pest Management, Environmental
Protection & Worker Safety
(916) 322-6315

URNAME						
SO-10C						

DOW CHEMICAL U.S.A.

WILLARD H. DOW CENTER
MIDLAND, MICHIGAN 48640

February 15, 1984

Mr. Peter D. Venturini, Chief
Stationary Source Division
Air Resources Board
1102 Q Street
Sacramento, CA 95812

Dear Mr. Venturini:

Thank you for your letter of February 10, 1984, in which you reviewed AB1807 and the process under which toxic air contaminant "candidates" will be handled. I have forwarded a copy to other parts of our company that may have some information on benzene to submit.

Please continue to keep me informed of these proceedings, and copy me on all future requests for such information.

Sincerely,

Hugh A. Farber, Ph.D.
Manager, Environmental Affairs
Inorganic Chemicals Department
Phone: (517) 636-5658

pjr

Getty Synthetic Fuels, Inc. | 2750 Signal Parkway, Signal Hill, California 90806 • Telephone (213) 595-4964

William R. Taylor, Manager, Public Affairs

February 29, 1984

Peter D. Venpurini
California Air Resources Board
P. O. Box 2815
Sacramento, CA 95812

Dear Mr. Venpurini:

I am writing to respond to your letter of February 10, subject: Request for Information Regarding Benzene.

We do not have any pertinent information on benzene health effects not included in your attached bibliography.

We would like to continue to receive information inquiries for other candidate compounds.

Sincerest regards,

William R Taylor

William R. Taylor

WRT/wpr

HALOGENATED SOLVENT INDUSTRY ALLIANCE (202) 659-0060
1612 K Street, N.W., Washington, D.C. 20006

February 22, 1984

Mr. Peter D. Venturini
Chief
Stationary Source Division
California Air Resources Board
1102 Q Street
P.O. Box 2815
Sacramento, CA 95812

Dear Mr. Venturini:

My office recently received your open request for information on the health effects of benzene. Thank you for keeping us informed. Unfortunately, we do not have any information at this time that would be of benefit to you.

We are very much interested in remaining on your request list for all candidate compounds. Please change the appropriate addressee in your files from Mike Italiano (who is no longer with us) to my name.

I will forward your letter to other parties who may have information on benzene.

Sincerely,

Paul A. Cammer
Executive Director

PC/srp

IT CORPORATION

February 21, 1984

Mr. William V. Loscutoff, Chief
Toxic Pollutants Branch
California Air Resources Board
P. O. Box 2815
Sacramento, CA 95812

Dear Bill:

Re: Benzene

A. First, on your bibliography:

1. References number 76 and 77 seem to be a duplicate.

2. References 93 and 94 appear to deal with a substance other than benzene (styrene, or "vinyl benzene").

3. Additional Reference, published since July 1983, include:

   a. M. A. Mehlman, J. Air Pollut. Control Assoc. 33:834-6 (1983)
   b. R. E. Albert, J. Air Pollut. Control Assoc. 33:836-7 (1983)

B. I don't have any additional data to submit.

C. Please continue to send information queries to me.

Note that my mailing address, effective February 27, 1983, will be:

IT Corporation
P. O. Box 2995
Torrance, CA 90509

With best regards,

Nick

R. Nichols Hazelwood
Project Manager
Environmental Affairs

RNH:vh

Corporate Office
IT Corporation • 336 West Anaheim Street • Wilmington, California 90744 • 213-830-1781

MOTOR VEHICLE MANUFACTURERS ASSOCIATION
of the United States, Inc.

300 NEW CENTER BUILDING • DETROIT, MICHIGAN 48202 • AREA 313-872-4311

PHILIP CALDWELL, *Chairman*
V. J. ADDUCI, *President and Chief Executive Officer*
THOMAS H. HANNA, *Senior Vice President*

March 30, 1984

Mr. William F. Loscutoff, Chief
Toxic Pollutants Branch
California Air Resources Board
P. O. Box 2815
Sacramento, California 95812

Dear Mr. Loscutoff:

Re: Benzene

The Motor Vehicle Manufacturers Association of the United States, Inc. (MVMA)* is a trade association whose members represent the major domestic motor vehicle manufacturers. We are responding to your request for information regarding benzene.

The bibliography generated by CARB appears very thorough. However, we suggest that you access the docket file on benzene at the U.S. Occupational Safety and Health Administration and fully utilize this important information source for additional technical information.

Also, the U.S. Supreme Court decision (Industrial Union Department AFL-CIO v. American Petroleum Institute, No. 78-911, U.S. Supreme Court, July 2, 1980) on the U.S. OSHA benzene proposed standard may provide insight on a legal precedent for the health risks associated with benzene.

We trust this information is useful to you.

Sincerely,

Lawrence E. Stimak for

Fred W. Bowditch
Vice President
Technical Affairs

*MVMA members are American Motors Corporation, Ford Motor Company, Chrysler Corporation, General Motors Corporation, International Harvester Company, M.A.N. Truck & Bus Corporation, PACCAR Inc, Volkswagen of America, Inc., and Volvo North America Corporation.

25 KEARNY STREET
SAN FRANCISCO, CALIFORNIA 94108
415 421-6561

Washington Office
[illegible] I STREET, N.W.
SUITE 600
WASHINGTON, D.C. 20006
202 223-8210

New York Office
122 EAST 42ND STREET
NEW YORK, N.Y. 10168
212 949-0049

March 16, 1984

William V. Loscutoff, Chief
Toxic Pollutants Branch
California Air Resources Board
P.O. Box 2815
Sacramento CA 95812

RE: Benzene

Dear Mr. Loscutoff:

I am writing in response to your February 10, 1984 letter requesting information on benzene. I have no additional suggestions for your extensive list. I would appreciate it very much if future information inquiries for other candidate compounds, along with all other mailings pertaining to toxic air contaminants, be sent here to my attention.

Thank you.

Sincerely,

Laura B. King

Laura B. King

New England Office: 16 PRESCOTT STREET • WELLESLEY HILLS, MA. 02181 • 617 237-0172
Public Lands Institute: 1720 RACE STREET • DENVER, CO. 80206 • 303 377-9740

OCAW
Oil, Chemical & Atomic Workers
International Union, AFL-CIO

1126 Sixteenth St. NW, Suite
Washington, D.C. 20036 202/223 5770

Dan Edwards, Director Health and Safety Department
OSHA "New Directions" Training Grant
255 Union Blvd., Lakewood, CO 80228
P.O. Box 2812, Denver, CO 80201 303/987-2229

March 13, 1984

To Whom It May Concern:

I am writing to you on behalf of the Oil, Chemical and Atomic Workers International Union and, in particular, our members in the State of California. As you know, we represent thousands of petrochemical workers in California. Many of these people are exposed, on a daily basis, to benzene in production, transfer and chemical intermediate operations. For this reason, we have been extensively involved in regulatory activities with regard to benzene for many years.

Recently, one of our representatives in California forwarded your request for information regarding benzene to me. I applaud the Air Resources Board's decision to consider regulating ambient exposures to benzene and I would like to call to your attention two significant pieces of information on the health effects of benzene.

Specifically, after reviewing the attached bibliography, I noticed that the following documents were not mentioned:

1) Environmental Protection Agency Carcinogen Assessment Group - Quantitative Risk Assessment of Benzene, March 10, 1983.

   In my view, this report demonstrates that there is a significant risk for leukemia at an exposure level of 1 part per million (ppm) for a working lifetime exposure.

   This report follows the 1979 Carcinogen Assessment Group's Report on Population Risk to Ambient Benzene Exposure which estimated the cancer risk of lifetime exposure at 1 ppm to be 2 per 100 persons exposed.

2) National Toxicology Program Technical Report [Draft 10/19/83]: The Toxicology and Carcinogenesis Studies of Benzene in F344N rats and B6C3F mice (Gavage Studies). James Huff, PhD. NIH Publication #84-2545.

   This study demonstrates malignant response at levels lower than previously demonstrated. I have enclosed the abstract for your information.

m hopeful that this information will be of use to the California Air Resources Board in your determination of a policy with respect to ambient exposures to benzene.

Please feel free to contact me at your convenience if you have any further questions.

Sincerely,

Kenneth B. Miller, M.D.
Occupational Health Physician

Enc.
cc: Robert Boudreau, International Representative
OCAW District #1
Dan Edwards, Director
OCAW Health & Safety Department

PACIFIC GAS AND ELECTRIC COMPANY

77 BEALE STREET • SAN FRANCISCO, CALIFORNIA 94106 • (415) 781-4211 • TWX 910-372-6587

April 6, 1984

Mr. William V. Loscutoff, Chief
Toxic Pollutants Branch
California Air Resources Board
P. O. Box 2815
Sacramento, CA 95812

Dear Mr. Loscutoff:

Information Inquiries Mailing List
Requests for Public Health Information

Pacific Gas and Electric Company received your February 10, 1984 request for additional public health information regarding benzene. We reviewed your bibliography and concluded that we were not aware of any additional information which should be submitted to you.

Please send all furture information inquiries to me at the above address.

Thank you.

Sincerely,

J. F. McKENZIE

TEXAS AIR CONTROL BOARD

6330 HWY. 290 EAST
AUSTIN, TEXAS 78723
512/451-5711

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R. HAL MOORMAN

Mr. William V. Loscutoff, Chief
Re: Information Regarding Benzene
Toxic Pollutants Branch
California Air Resources Board
P. O. Box 2815
Sacramento, CA 95812

Dear Mr. Loscutoff: Bill

I recently received a letter from Mr. Peter D. Venturini of your office requesting information about benzene. He asked that I direct my response to you.

We do not have any information regarding benzene that is not already listed in the bibliography attached to Mr. Venturini's letter, but I would appreciate remaining on your mailing list and receiving further reports of your work.

Enclosed is a copy of the mailing label used to send the "Request for Information Regarding Benzene" to me.

Sincerely,

James H. Price, Jr.
Acting Director
Research Division

Enclosures

UNIVERSITY OF CALIFORNIA, DAVIS

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SANTA BARBARA • SANTA CRUZ

OFFICE OF THE DEAN
COLLEGE OF LETTERS AND SCIENCE

DAVIS, CALIFORNIA 95616

February 14 1984

William V. Loscutoff, Chair
Toxic Pollutants Branch
Re: Benzene
California Air Resources Board
P.O. Box 2815
Sacramento, Ca. 95812

Dear Mr. Loscutoff:

I have forwarded your request for information on benzene to Mr. Richard Holdstock, Environmental Health and Safety, on the Davis campus. All requests of this nature are addressed by his office.

Yours sincerely,

L. J. Andrews
Dean

LJA:meh

UNIVERSITY OF CALIFORNIA, DAVIS

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DAVID PIERPONT GARDNER
President of the University

EMIL M. MRAK
Chancellor Emeritus

UNIVERSITY HOUSE
DAVIS, CALIFORNIA 95616

February 16, 1984

Peter D. Venturini, Chief
Stationary Source Division
Air Resources Board
1102 Q Street
P. O. Box 2815
Sacramento, CA 95812

Dear Mr. Venturini:

I have just read your request for information regarding benzene. I find this most interesting, and I would certainly like to remain on the list to receive inquiries for other candidate compounds.

I would also suggest that Dr. Dale Lindsay receive these inquiries. His address is: 562 Reed Drive, Davis, CA 95616.

I presume that you have seen the THIRD ANNUAL REPORT ON CARCINOGENS--SUMMARY 1983 of the U.S. Department of Public Health Services. There is a little write-up starting on page 28 on benzene.

Kindest personal regards,

Emil Mrak

RECEIVED

FEB 21 1984

Stationary Source
Division
Air Resources Board

Lloyd M. Kozloff
Dean, Graduate Division, S-140
San Francisco, CA 94143
(415) 666-2310

University of California, San Francisco . . . A Health Sciences Campus

February 21, 1984

Peter D. Venturini, Chief
Stationary Source Division
Air Resource Board
1102 "Q" Street
P.O. Box 2815
Sacramento, CA 95812

RE: REQUEST FOR INFORMATION REGARDING BENZENE

Dear Mr. Venturini:

I have forwarded your letter to Prof. Neal Castagnoli of our School of Pharmacy. Professor Castagnoli is quite knowledgeable about this area.

I would be willing to consider from time-to-time inquiries about various compounds.

Sincerely yours,

LLOYD M. KOZLOFF
Dean, Graduate Division

LMK:ch

UNIVERSITY OF CALIFORNIA, SANTA CRUZ

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ENVIRONMENTAL HEALTH & SAFETY SANTA CRUZ, CALIFORNIA 95064

March 6, 1984

William V. Loscutoff, Chief
Toxic Pollutants Branch
Re: Benzene
California Air Resources Bd
PO Box 2815
Sacramento, CA 95812

Dear Sir:

Your letter of February 10, 1984, requesting information regarding Benzene has been reviewed. Benzene sees very limited use on this Campus since it was identified as a suspect human carcinogen some years ago. Primary Benzene use has been in mass spectrometry for dissolving samples at about one milliliter per sample delivered by pipette. We have not acquired regular grade Benzene for some time though we have a small quantity on hand. Acetone has been substituted as a solvent for some cleaning purposes and chloroform has been substituted in many other analytical protocols.

As information is developed on Benzene toxicology and related safety, we would be pleased to be informed. We did not receive the bibliography referred to in your letter. This would be useful information. For this campus, you may maintain liaison with the undersigned.

Cordially,

James C. Lang
Environmental Health and Safety Officer

Western Oil and Gas Association
727 West Seventh Street, Los Angeles, California 90017
(213) 627-4866

March 13, 1984

Federal Express

William V. Loscutoff
Chief
Toxic Pollutants Branch
California Air Resources Board
1102 "Q" Street
Sacramento, California 95814

Re: Request for Information Concerning Benzene

Dear Bill:

By this letter, the Western Oil and Gas Association ("WOGA") responds to your request for information concerning the health effects of benzene to be used in the consideration of whether benzene should be listed as a toxic air contaminant pursuant to California Health and Safety Code §§ 39650 et seq. WOGA is pleased to submit the attached bibliography which we believe contains the most important research done to date concerning the health effects of benzene. Since benzene has been and continues to be the topic of a significant amount of research, we will continue to search for other studies which we will send to you as we become aware of them. We thank you for the opportunity to submit this information and stand ready to answer any questions you may have.

We understand that benzene is the first substance to undergo review as a potential toxic air contaminant. California Health and Safety Code § 39660(f) states that:

> "The state board shall give priority to the evaluation and regulation of substances based on factors related to the risk of harm to public health, amount or potential amount of emissions, manner of usage of the substance in California, persistence in the atmosphere, and ambient concentrations in the community."

We would like an explanation as to why benzene was chosen as the first substance for evaluation based on these criteria. We are also interested in learning the other substances you intend to evaluate in the next year.

Thank you for the opportunity to submit this health data. If you have any questions, please contact Dr. Michael Cardin at (213) 977-6734.

Very truly yours,

Robert Harrison

Robert N. Harrison
Assistant General Manager

RNH:vb

Enclosure

ZERO WASTE SYSTEMS, INC.
2928 POPLAR STREET · OAKLAND, CA 94608 · 415/893-8261

February 15, 1984

William V. Loscutoff, Chief
Toxic Pollutants Branch
California Air Resources Board
P.O. Box 2815
Sacramento, California 95812

Dear Sir:

We have no special information on benzene to submit for your evaluation.

ZERO WASTE SYSTEMS

P.S. We do not wish to receive further requests for information.

APPENDIX B

PUBLIC INPUT REQUESTS, COMMENTS AND PART A RESPONSES

STATE OF CALIFORNIA
GEORGE DEUKMEJIAN, Governor

AIR RESOURCES BOARD
1102 Q STREET
P.O. BOX 2815
CRAMENTO, CA 95812

June 20, 1984

Dear Sir or Madam:

Subject: ARB Draft Report on Benzene

In my February 10, 1984, letter requesting health effects information on benzene, I indicated that we would prepare a report on benzene for review by the Scientific Review Panel (SRP). Also in that letter, I stated that the report submitted to the Panel will be made available to the public upon its submittal to the Panel.

This letter is to inform you of an opportunity we are providing to review and comment on a part of the draft benzene report prior to its submittal to the SRP. The report will consist of two parts; Part A - "A Review of Benzene Uses, Emissions, and Public Exposure" and Part B - "A Review of Benzene Health Hazards." Part B, which is being prepared by the Department of Health Services, will be available for review when the report is submitted to the SRP. However, a preliminary draft of Part A is expected to be available by June 29, 1984.

In order to obtain a copy of the preliminary draft to Part A of the report, please send your request to the attention of:

Public Information Office
Re: Draft Benzene Report - Part A
California Air Resources Board
P.O. Box 2815
Sacramento, CA 95812

or call the office at (916) 322-2990. A copy of the preliminary draft will be sent to you as soon as it is available. Since we plan to submit the final benzene report to the SRP in early August 1984, we need your comments on the Part A draft by July 20, 1984.

Sincerely,

Peter D. Venturini, Chief
Stationary Source Division

cc: Alex Kelter, DHS
Lori Johnston, DFA
Wayne Morgan, President CAPCOA
David Howekamp, EPA Region IX
Assemblywoman Tanner
APCOs

STATE OF CALIFORNIA GEORGE DEUKMEJIAN, Governor

AIR RESOURCES BOARD
1102 Q STREET
P.O. BOX 2815
SACRAMENTO, CA 95812

July 19, 1984

Dear Sir or Madam:

Subject: Draft Report on Benzene to the Scientific Review Panel

Enclosed is the draft of Part A of the subject report: "A Review of Benzene Uses, Emissions, and Public Exposure" per your request.

We invite your comments on Part A by August 15. If your written comments will not reach us by that date, please precede them with a telephone call to Barbara Fry at (916) 322-8276. Written comments should be addressed to:

William V. Loscutoff, Chief
Toxic Pollutants Branch
Air Resources Board
P.O. Box 2815
Sacramento, CA 95812

I regret the delay in producing the draft report.

Sincerely,

Peter D. Venturini, Chief
Stationary Source Division

Enclosure

cc: Assemblywoman Tanner

515 South Flower Street
Los Angeles, California 90071
Telephone 213 486 8750

David A. Smith
Consultant
Environmental Regulatory Compliance

August 30, 1984

William V. Loscutoff, Chief
Toxic Pollutants Branch
Air Resources Board
Post Office Box 2815
Sacramento, California

Dear Mr. Loscutoff:

Attached are brief ARCO Petroleum Products Company (APPCo) comments on the California Air Resources Board preliminary draft report entitled, "Part A - A Review of Benzene Uses, Emissions and Public Exposure." APPCo personnel also contributed to and fully support the comments submitted to you by the Western Oil and Gas Association (WOGA) on Part A and the associated Department of Health Services Part B report entitled, "Health Effects of Benzene."

In particular, we wish to emphasize WOGA's point that the DOHS did not present the "range of risks to humans resulting from current or anticipated exposure" of benzene required by the Health and Safety Code Section 39660(c). A range of risk determination requires the use of various assumptions and methods to evaluate risks at certain dose levels. DOHS failed to do this. This omission is exemplified in the Department's dismissal of data from human studies which have been used by all other governmental agencies in assessing human benzene exposure risks. It is these types of problems that make us believe the Part B report is seriously deficient.

If you wish to discuss any of the attached comments on Part A, please call me at the above phone number. Please call Dr. Charles Lapin at 213/486-3825 if you have questions with regard to Part B which you wish to discuss with us.

Sincerely,

D. A. Smith
Consultant, Environmental/Health Planning

DAS/bf
Attachment

cc: Dr. C. A. Lapin

ARCO Petroleum Products Co.
Comments on
Part A: A Review of Benzene Uses, Emissions and Public Exposure

Stationary Source Emissions

The report identifies the largest stationary benzene source as gasoline marketing. Gasoline marketing should be further defined in the report to more clearly identify the particular source for which the emission estimate is made. EPA within an August 8, 1984 Federal Register notice that discusses regulatory strategies for the gasoline marketing industry identifies bulk terminals. bulk plants, service station tanks and vehicle refueling operations as potential gasoline marketing emission sources. The staff report should identify which of these sources are included in this source category.

Additionally, the CARB assumption of 2.4 wt% benzene in the total hydrocarbon emissions from gasoline marketing sources over simplifies the real situation. The attached European CONCAWE Report discusses benzene evaporative emission concentrations and their dependence on fuel temperature, Reid Vapor Pressure and benzene content of the intank and dispensed fuel. The benzene concentrations in the attached CONCAWE Report averages approximately 1.5 wt% rather then the 2.4 wt% in the CARB report. This combined with our earlier comment casts serious doubt ont he usefulness of the published emission rate.

Vehicular Exhaust Emissions

The draft report does not present an adequate discussion on the relationship between vehicular exhaust benzene emissions to benzene and aromatic fuel content. The attached CONCAWE Report concludes that a significant portion of the fuel benzene passes out through the exhaust system. The remainder of the exhaust benzene is formed somewhere within the combustion/exhaust system. This type of information which has significant importance in selecting control options has led the Coordinating Research Council to proceed with a recently approved testing program of several cars and fuels to investigate these and other issues. The test results are to be available early next year. This uncertainty on how benzene exhaust emission are actually formed and thereby controlled should be reflected in the report.

Appendix E: Ambient Monitoring Data Limitations to Analysis

Limitation number four states that, "this study does not include benzene exposures in the workplace." This is certainly not for a lack of available data. Federal OSHA and impacted industries have been working together to review the current federal permissable exposure limit of 10ppm for some time. Considerable exposure limit of information is currently available on employee benzene exposures. A report presented at the Collegium Ramazzini on Nov. 4, 1983 entitled, "Benzene Exposure in the United States 1978-1983—An Overview" by H.E. Kunion and L.M. Scott presents benzene exposures for a number of industries. Such exposure levels can be useful in comparing calculated workplace risk estimates with real life experience.

CONCAWE

the oil companies' european organisation for environmental and health protection (established in 1963)

concawe

synopsis

BENZENE EMISSIONS FROM PASSENGER CARS

CONCAWE Report No. 12/83

8/21/84 FYI

TO: BENZENE COORDINATING TASK FORCE

FROM: TOM CORNWELL

Among the sources of benzene in air, gasoline-powered motor vehicles are known to contribute about 80-85% of the total man-made benzene emissions in industrialised countries.

Hydrocarbons, including benzene, are emitted into the air from motor vehicles in three main ways:

- by displacement from vehicle fuel tanks during refuelling;
- by evaporation from fuel tank, carburettor and associated fuel system by temperature effects;
- as unburnt hydrocarbons in exhaust gases.

The first section of this report describes the studies carried out to determine the magnitude of benzene emissions from these sources and to identify the relationship with fuel composition.

In the second section, the relative contributions of re-fuelling, evaporation and exhaust to the total emissions are quantified. Benzene losses during re-fuelling are related not only to the volume and benzene content of the gasoline being dispensed but also to the benzene content of the gasoline already in the fuel tank. During typical use, re-fuelling losses amount to 3-4 milligrams per kilometre. Benzene evaporation from the vehicle carburettor and fuel tank, due respectively to engine heat soak-back and daily temperature variation, is directly related to the benzene content of the gasoline being used. For typical daily service in the average European summer diurnal temperature variation of 7°C, losses amount to ~0-50 milligrams per kilometre. Of the benzene emitted in exhaust gas, only 35-45% is benzene originally present in the gasoline and surviving combustion. The remainder is formed during combustion. Exhaust benzene forms the largest source of vehicular benzene loss, some 81-89% compared with 10-18% evaporative losses and 1-2% re-fuelling losses.

ABSTRACT

This report characterises the losses of benzene into the atmosphere from three typical European passenger cars during average daily use. Three sources of loss are identified: losses during refuelling, evaporation from fuel systems and emissions in exhaust gases. The relative contributions of these sources are discussed and the report evaluates the effectiveness of various alternative means of control, including regulating the composition of motor gasoline by controlling the benzene content, and fitting control devices to passenger cars.

Dit rapport beschrijft de benzeenverliezen in de dampkring van drie representatieve Europese personenauto's bij gemiddeld dagelijks gebruik. Er wordt onderscheid gemaakt tussen drie oorzaken van verlies: verlies tijdens het tanken, het verdampen van benzeen uit de brandstofsystemen en emissie in uitlaatgassen. De relatieve bijdrage van elk van deze oorzaken wordt besproken, en het rapport beoordeelt de doeltreffendheid van een aantal verschillende bestrijdingsmiddelen. Hiertoe behoren het reguleren van de samenstelling van autobenzine door toezicht op het benzeengehalte en het aanbrengen van contrôle-instrumenten in personenauto's.

In diesem Bericht wird die Benzolemission in die Atmospäre bei drei europäischen Pkw im normalen Betrieb dargestellt. Es werden dreierlei Formen der Benzolemission unterschieden: Verluste beim Tanken, Verdunstung aus Kraftstoffleitungen und Emissionen in Auspuffgasen. Nach der relativen Gewichtung dieser drei Ursachen wird die Wirksamkeit verschiedener Methoden zur Begrenzung der Benzolemission durch Beeinflussung der Kraftstoffzusammensetzung durch Kontrolle des Benzolgehalts und der Ausrüstung von Pkw mit Kontrollgeräten erörtert.

Le présent rapport définit les émanations de benzène dans l'atmosphère à partir de trois voitures de tourisme européennes typiques pendant leur utilisation quotidienne. Trois sources d'émanations sont identifiées: émanations pendant le remplissage du réservoir, évaporations provenant des systèmes de carburation et émissions dans les gaz d'échappement. Les contributions respectives de ces sources sont examinées et le rapport évalue l'efficacité des diverses possibilités de contrôle, y compris la règlementation de la composition de l'essence pour les automobiles par le contrôle de la teneur en benzène et le montage de dispositifs anti-pollution sur les véhicules de tourisme.

Este informe caracteriza las pérdidas de benceno a la atmósfera en tres automóviles europeos típicos con un uso diario promedio. Se identifican tres fuentes de pérdidas: las que se producen al repostar, la evaporación en los sistemas de combustible y las emisiones en los gases de escape. El informe trata de las contribuciones relativas de estas fuentes y evalúa la eficacia de los diversos medios de control, que incluyen la regulación de la composición de la gasolina, controlando el contenido de benceno, y la instalación de dispositivos de control en los automóviles.

In questo rapporto si identificano le perdite di benzene nell'atmosfera da parte di tre tipiche autovetture europee in uso giornaliero medio, in base a tre fonti di perdite: durante le operazioni di riempimento, evaporazione dal sistema di alimentazione ed emissioni dallo scarico. I relativi apporti di queste fonti sono oggetto di trattazione ed il rapporto valuta anche l'efficacia di diversi mezzi di controllo, fra cui la regolamentazione della composizione della benzina controllandone il tenore in benzene e l'adozione di dispositivi di controllo sulle autovetture.

CONTENTS: LIST OF FIGURES AND TABLES

Note : Figure 5 and Tables 4-8 will be found in the appendix to this report, commencing on p. 21.

1. INTRODUCTION

There is substantial evidence that high concentrations of benzene encountered in the workplace can cause diseases of the blood and bone-marrow, and many countries have legislation to control occupational exposures. Data regarding chronic effects of low-level exposures or short-term peak exposures of the type experienced by the general public are inconclusive and need further elucidation.

A number of studies have been published on the sources of benzene in air. These make it clear that benzene is ubiquitous in its distribution, being formed during processes of incomplete combustion including natural events such as forest fires. Measurements of ambient benzene in rural areas seldom exceed 5 $\mu g/m^3$ (1). However, in urban areas concentrations fall typically in the range 35-100 $\mu g/m^3$ (1), depending on site-specific factors such as traffic density and local industries.

Data on man-made sources of benzene emissions into the atmosphere are currently available in open literature. Making assumptions about emission factors from systems handling products containing benzene, and from combustion sources producing benzene, the relative contributions to the atmospheric benzene burden have been derived for Canada, Germany and the USA and are given in Table 1.

Table 1 Relative contributions to the atmospheric benzene burden

Source, %	Canada	Germany	USA
Gasoline-powered vehicles	85	81	80
Chemical industry	7	4	11
Gasoline distribution	3	4	6
Solvent operations	4	2	1
Coke ovens	0.5	3	1
Petroleum refineries	0.5	0.5	1
Domestic heating	?	5	?

2. AUTOMOTIVE SOURCES OF BENZENE

Hydrocarbons, including benzene, are emitted into the air from motor vehicles in three main ways:

a) During vehicle re-fuelling liquid gasoline being loaded into a part-empty tank displaces gasoline vapour, which escapes to atmosphere. The composition of the escaping vapour is related to the composition of the fuel already in the tank as well as to that being added.

b) Evaporation of hydrocarbons, including benzene, takes place from the vehicle's fuel tank as a result of expansion and contraction of the tank and its contents caused by temperature changes throughout the 24 hour daily cycle. Evaporation from the carburettor and associated fuel system also occurs as a result of heat soak-back when the engine is switched off.

c) Benzene is present amongst the unburnt hydrocarbons in exhaust gas.

This section describes studies carried out to determine the magnitude of benzene emissions from these sources and to identify the relationship with fuel composition. Typical European cars were used for the test work. Their relevant characteristics are given in Table 4 (Appendix). Similarly, the test gasolines spanned the normal commercial range in terms of benzene content and other characteristics.

The relative contributions of these sources of benzene to the overall benzene emission of the vehicle per kilometre travelled are estimated in Section 3.

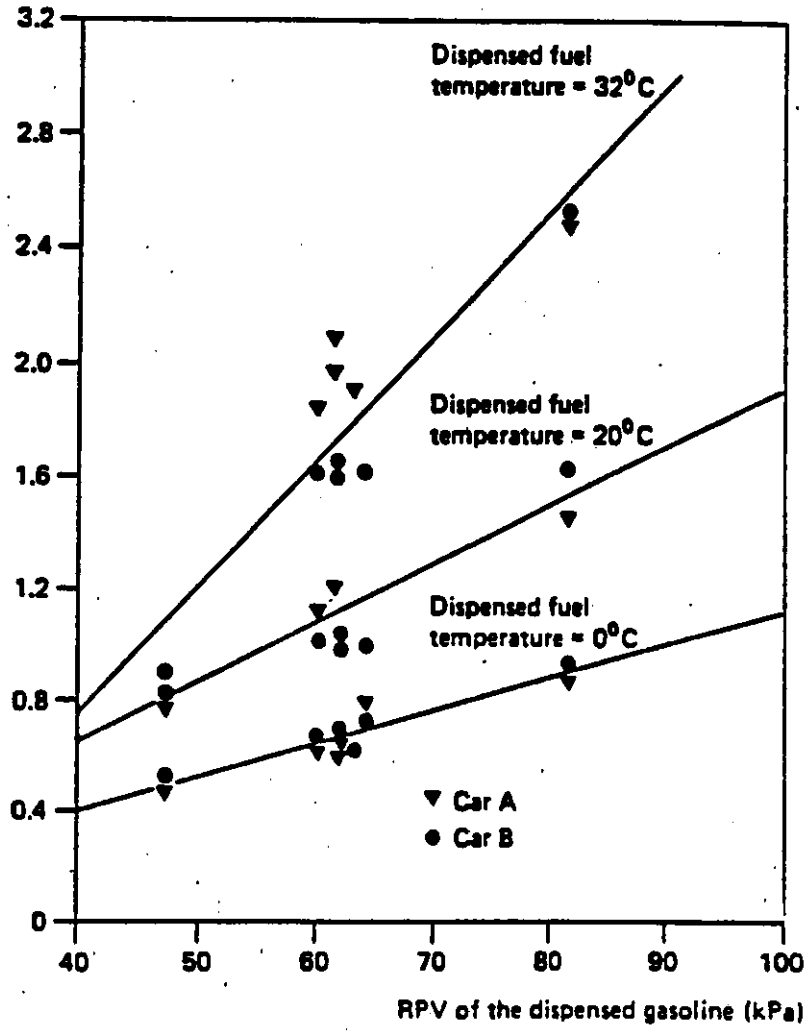
2.1 REFUELLING LOSSES

Studies were carried out to determine how much total hydrocarbon and how much benzene was lost to atmosphere during re-fuelling of two typical European vehicles. Testing was carried out in a Sealed Housing for Evaporative Determinations (SHED), modified so that gasoline could be dispensed into a vehicle located inside the closed SHED by an operator standing outside it. The vehicle tank was emptied of all gasoline vapour from previous tests by leaving off the cap and opening all vents for at least 24 hours. The initial charge of gasoline, at a temperature of 20°C, was dispensed into the tank at least 30 minutes before the beginning of the test, this being the time necessary to saturate the vapour space. The vehicle was then pushed into the SHED, which was then sealed, and the initial temperature, barometric pressure and the hydrocarbon

Re-fuelling hydrocarbon losses from both test vehicles were dependent not only on the Reid Vapour Pressure (RVP) of the gasolines but also on the temperature difference between the dispensed and in-tank gasolines. This is because the volume of vapour displaced from a fuel tank may not be equal to the volume of fuel dispensed.

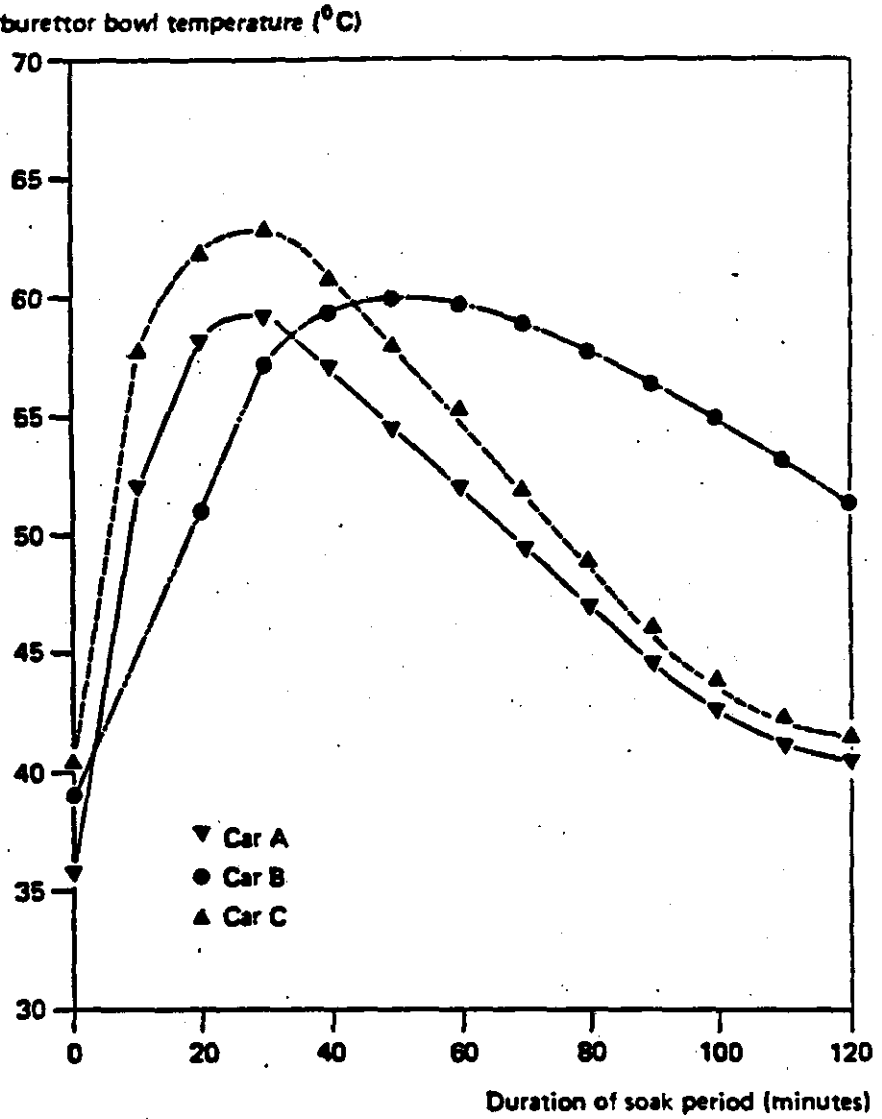
If the temperature of the dispensed fuel is higher than that of the fuel in the tank, then the volume of vapour generated is greater than the volume of fuel dispensed, and vice versa. Fig. 2 (below) and Table 5 (Appendix) show the effects of Reid Vapour Pressure and temperature of dispensed fuel on re-fuelling hydrocarbon losses. Per litre of gasoline dispensed these losses may vary between 0.5 and 2.5 grams.

Fig. 2 The effect of variations in the dispensed gasoline RVP on the magnitude of the refuelling losses at different dispensed fuel temperatures



US Federal Certification test. The main differences were that eight consecutive ECE 15* cycles were used to condition the vehicle prior to the hot soak phase of 2 hours (cf. one hour in the US Federal Test Procedure). SHED atmospheres were analysed for individual hydrocarbons by gas chromatography.

Fig. 3 *Carburettor bowl temperature during the hot soak period*



Fuel tank losses occur because of increases in temperature during the day, which cause increases in fuel vapour pressure and thermal expansion of vapour in the tank (5)(6). These losses occur whether or not the vehicle is used, and since they occur on a daily cycle they are known as diurnal losses. In the test procedure carried out in the SHED they are simulated by heating the tank through a specified temperature cycle.

* ECE 15 is the abbreviation commonly used to designate the United Nations Economic Commission for Europe Regulation 15

Equations have been developed by regression to relate the benzene emitted to the benzene concentration in the fuel. They are:

Diurnal Loss:

wt% Bz in SHED hydrocarbons = 0.45 x wt% Bz in fuel

(Correlation: $R^2 = 0.73$)

Hot Soak Loss:

wt% Bz in SHED hydrocarbons = 0.89 x wt% Bz in fuel

(Correlation: $R^2 = 0.79$)

It should be emphasised that these relationships are valid only for the temperature regime used in the tests and adjustments could need to be made for other temperature conditions.

2.3 BENZENE IN EXHAUST

Exhaust emissions tests on a range of European cars were carried out, using fuels containing a range of benzene concentrations, according to the ECE 15 cycle using Constant Volume Sampling. Analysis for total and individual hydrocarbons was carried out by conventional gas chromatography. Instead of the cold starts required by Regulation 15, tests were performed starting with a fully warmed engine in order to remove the influence of the choke and give repeatable results.

The concentrations of benzene in both the exhaust emissions and test fuels are given in Table 6. A regression equation linking benzene concentrations in exhaust gas with liquid fuel composition was derived as follows:

- wt% benzene in exhaust emissions = 0.50 + 0.44 Bz + 0.04 Ar

where:

Bz = wt% of benzene in liquid fuel

(Correlation: $R^2 = 0.84$)

Ar = wt% of other aromatics in liquid fuel

The intercept of the equation is significantly different from zero, indicating the formation of benzene from other fuel components.

3. RELATIVE CONTRIBUTIONS OF BENZENE LOSSES

It is of interest to quantify the relative contributions of re-fuelling, evaporation and exhaust to the total. To achieve this, test results have been converted to a gram per kilometre basis as follows.

3.1 REFUELLING LOSSES

It has been shown (Section 2.1) that total benzene loss during a single re-fuelling is proportional to the total volume of gasoline dispensed. A value for benzene lost per litre dispensed can therefore be derived. Official figures for fuel consumption covering the ECE cycle (7) can then be used to correct this to a benzene loss per kilometre. For the two European cars tested in the programme, benzene losses during re-fuelling with a typical European gasoline (2.6 vol% = 3.1 wt% benzene) were 3-4 milligrams per kilometre (mg/km). These figures are comparable with the average value of 6 mg/km for US cars reported in a separate study (8).

3.2 EVAPORATIVE LOSSES

Data obtained from the UK National Travel Survey shows that the average private car completes 3.4 trips per day with an average daily mileage of 39 kilometres. Benzene loss per kilometre can therefore be calculated from SHED hot soak losses by multiplying by the factor 3.4/39. To this must be added the evaporative loss due to diurnal temperature variation. The average summer diurnal variation for Europe is 6.9°C, which is considerably lower than the range of 13.3°C used in the Federal Test procedure. A factor of 0.52 has therefore been applied to SHED test results to convert to benzene loss over the average day. This value has in turn been divided by the average daily mileage to produce a benzene loss per kilometre.

For the two cars tested the sum of diurnal and heat soak losses on a typical European gasoline containing 3.1 wt% benzene was 43-51 mg/km.

3.3 EXHAUST EMISSIONS

A single ECE 15 Type I test corresponds to a distance travelled of 4.052 kilometres. Benzene loss per kilometre can therefore be simply derived from benzene emissions in an ECE test. Results for the two cars used in all tests on typical European gasoline containing 2.6 vol% (= 3.1 wt%) benzene were 225-373 mg/km. These values are consistent with those published by Hasanen, Karlson et al (9).

4. CONTROL OF BENZENE EMISSIONS

4.1 REGULATION OF GASOLINE COMPOSITION

A few countries already limit the maximum concentration of benzene in motor gasolines to 5 vol%. A survey of European motor gasolines carried out in 1976-8 (1) showed a weighted average benzene content of 2.6 vol% (3.1 wt%), with 90% of the 250 samples taken having benzene contents below 3.9 vol% (4.6 wt%)(12). Controlling the benzene content of motor gasoline is, however, a costly and not very effective way of limiting benzene emissions from vehicles.

As little as 15% of the benzene reaching the atmosphere from vehicular emissions is accounted for by losses from re-fuelling and evaporation. A further 37% originates from benzene surviving combustion. This benzene is emitted via the exhaust gases, which are the dominant source of benzene emissions. Reduction of benzene in motor gasoline can therefore reduce benzene emissions from vehicles by about 52% at most (Table 3).

4.2 ON-BOARD VEHICLE CONTROLS

Technology for controlling hydrocarbon emissions from all vehicular sources through on-board hardware is well established. In the USA, where strict hydrocarbon control is necessary to deal with special local problems, devices are in use which can reduce evaporative losses by 70-90% and re-fuelling losses by more than 95%. The absolute amount of emitted hydrocarbons which can be retained by these devices is, however, small (see Table 3).

In the USA, catalytic exhaust converters are fitted to most passenger cars in order to meet the stringent CO, hydrocarbon and NO_x exhaust emission regulations. These devices are up to 90% efficient in removing hydrocarbons, including benzene, from exhaust gas (10, 11).

In Europe, discussions are taking place at Government level which could lead to the introduction of more severe exhaust emissions legislation such that catalytic converters have to be used. If it were to become necessary for motor manufacturers to fit catalytic reactors to vehicles to comply with gaseous exhaust emission regulations, then control of benzene in exhaust gas (its most important vehicular source) would be achieved at no additional cost. A reduction of the total benzene emission of 77% can be achieved (see Table 3). It should, of course, be remembered that, at the present state of the art, fitting of catalytic exhaust converters would require unleaded gasoline, with all its associated costs.

5. CONCLUSIONS

Benzene emissions from three typical European cars have been studied using gasolines spanning the normal commercial range in terms of benzene content and other characteristics. From these studies the following conclusions can be drawn:

1) Benzene losses during re-fuelling are related to the benzene content and temperature of the gasoline already in the tank, and to the benzene content, volume and temperature of the gasoline dispensed. During average usage these losses amount to only 3-4 milligrams per kilometre.

2) Benzene evaporation from the vehicle fuel system due to engine heat and daily temperature variations is directly related to the benzene content of the gasoline. In average European summer conditions losses from this source amount to some 40-50 milligrams per kilometre.

3) Of the benzene emitted in exhaust gas, about 44% is benzene surviving combustion, and the remainder is formed during combustion.

4) The relative contributions of the different vehicular sources of benzene to the total loss are: re-fuelling 1%, evaporation 10-18%, exhaust 81-89%.

5) Even total debenzenisation of gasoline would only reduce benzene emission by about 50%. However, if on-board vehicle control devices such as catalytic converters and evaporative controls are adopted in Europe, total benzene losses from vehicles could be reduced by nearly 90%.

SUPPORTING FIGURES AND TABLES

LIST OF FIGURES AND TABLES

Table 4 Characteristics of vehicles used

Vehicle	A	B	C
Model year	1977	1977	1977
Odometer (miles)	20800	18200	18900
Engine type and capacity (l)	In line 4 1.6	V6 2.7	In line 4 1.1
Fuel tank capacity (l)	50	70	34
Fuel tank venting	2 x 3 mm i.d. tube vents on top of tank	Filler cap + 5 mm i.d. tube vent on top of tank	4 mm i.d. tube vent on top of tank
Carburettor/s	Solex 32/32 DIDTA	Solex 34 TBIA+ Solex 35 CEEI	Motorcraft KEA 77BF9510
Volume of fuel in carburettor float chamber/s (ml)	48	1st = 70 2nd = 25	58
Float chamber venting system	Internal and external vent	Internal vent	External vent

Table 6 Fuel inspection data

Fuel No.	1	2	3	4	5	6	7	8	9
Reid Vapour Pressure, (kPa) (1)(2)	40.0	50.3	40.7	62.1	62.1	67.6	88.9	93.8	83.4
Distillation temp. (3) for % evaporated (°C)									
I.B.P.	36	38	40	28	34	34	35	35	34
10	53	52	60	55	50	48	46	46	44
20	75	59	65	69	60	55	57	54	51
30	87	66	71	81	70	62	69	65	59
40	99	73	78	90	81	72	82	77	67
50	110	82	89	98	94	81	96	90	76
60	119	92	109	106	107	92	111	104	87
70	134	104	132	115	122	106	129	116	99
80	149	121	143	135	139	124	146	134	111
90	165	158	156	168	156	148	163	157	134
F.B.P.	195	202	192	207	190	184	202	187	184
% Evaporated at 70°C	15.5	36.0	28.5	20.5	30.0	38.0	30.5	34.0	43.0
% Evaporated at 100°C	40.5	66.5	56.0	52.0	54.5	65.5	52.5	57.0	71.0
% Evaporated at 150°C	80.5	98.0	86.0	88.0	86.0	90.5	82.0	87.0	93.5
Composition (4)									
Aromatics (5)	40.7	9.3	45.3	10.1	30.1	20.4	23.5	24.7	15.0
Olefins	12.5	10.4	1.1	12.7	14.5	24.1	23.6	17.3	18.5
Saturates	46.8	80.3	53.6	77.2	55.4	55.5	52.9	58.0	66.5

(1) ASTM D 323
(2) Typical commercial gasoline has RVP in the range 50 to 80 kPa.
(3) ASTM D 86
(4) Gas chromatography analysis
(5) Benzene contents in Table 7

Table 8 Concentration of benzene in test fuel and exhaust

Fuel No.	Benzene concentration in Fuel (wt%)	Benzene concentration in exhaust vapour emissions (wt%)	
		CAR A	CAR B
1	3.85	3.01	3.07
2	1.44	1.09	1.09
3	5.46	3.77	4.25
4	0.98	0.82	1.99
5	4.43	2.97	3.56
6	2.26	0.89	1.91
7	1.75	1.77	1.71
8	1.03	1.54	1.90
9	1.75	1.22	2.16

AIR RESOURCES BOARD
1102 Q STREET
P.O. BOX 2815
SACRAMENTO, CA 95812

September 12, 1984

Mr. D. A. Smith, Consultant
Environmental/Health Planning
ARCO Petroleum Products Company
515 South Flower Street
Los Angeles, CA 90071

Dear Mr. Smith:

Subject: Comments on Part A of the Draft Benzene Report

Thank you for your comments on the draft Part A of the benzene report. Your letter and this response will become part of Appendix B of the final report. We will send you a copy of the final report. I am responding to your comments under the titles you have in your letter.

Stationary Source Emissions

Bulk terminals, bulk plants, service station tanks and vehicle refueling operations are included in our estimate of benzene emissions from gasoline marketing. We are revising the report to clarify this point. Also, we have reevaluated the 2.4 wt. percent benzene factor based on an average 1.5 wt. percent benzene in fuel and the relative vapor pressures of benzene and gasoline at 77°F. The gasoline marketing emission estimate is being revised downward with a factor of 1 wt. percent benzene in the total hydrocarbon emissions. The revised emission estimate for gasoline marketing is 300 tons per year.

Vehicular Exhaust Emissions

We did not include a detailed discussion on the relationship between vehicular exhaust benzene emissions and benzene and aromatic fuel content because detailed data for California vehicles burning representative fuels are not yet available. When testing programs such as the Coordinating Research Council study are completed, the information will be useful in evaluating control options.

Appendix E: Ambient Monitoring Data

We believe that indoor air exposures to toxic air contaminants may be an important factor to consider in the risk management phase during which our Board will consider adoption of toxic control measures. However, during the risk assessment (substance identification) phase, AB 1807 requires the Department of Health Services to consider ambient concentrations and risk of harm to public health from exposure to these ambient concentrations.

Thank you again for your comments. If you wish to discuss these comments more or if you have further questions on the report, please contact Barbara Fry at (916) 322-8276.

Sincerely,

Ronald J. Ames for

William V. Loscutoff, Chief
Toxic Pollutants Branch
Stationary Source Division

Chevron U.S.A. Inc.
575 Market Street, San Francisco, California • Phone (415) 894-2242
Mail Address P O Box 7643 San Francisco CA 94120 7643

W. T. Danker
Manager, Environmental Programs
Environment, Safety, Fire and Health

August 22, 1984

California Air Resources
Board Report - Part A
A Review of Benzene Uses,
Emissions and Public Exposure

William V. Loscutoff, Chief
Toxic Pollutants Branch
Air Resources Board
P. O. Box 2815
Sacramento, California

Dear Sir:

We have reviewed the subject report, and appreciate the opportunity to comment during the early stages of the review process. Our comments, listed below, represent the combined thoughts of our Manufacturing, Fuels Research, and Environmental Health organizations.

Page II-1, Paragraph 1 - The first sentence describes benzene as a hydrocarbon naturally occurring in crude oil and present in gasoline and diesel oil. Because of the high boiling range of diesel oils (90% greater than 350° F) there is no significant amount of benzene (176° F boiling point) present in these products.

Page II-1, Paragraph 2 - This paragraph describes Chevron's El Segundo Refinery as the only benzene producer in California. Recently, Chevron shut down its benzene production facility in El Segundo. The plant has been "mothballed" and will remain shut down indefinitely.

Page II-2 - The second paragraph states that the evaporative benzene emissions from gasoline marketing are estimated based on an EPA factor of 2.4 wt% benzene in the total hydrocarbon emissions from marketing sources. The 2.4 wt% factor appears to be high by approximately a factor of two, which will result in over estimating these emissions. In fact, the 2.4 wt% factor appears to be in conflict with the EPA and SAE factor of 1.2 wt% benzene in evaporative emissions from automobiles quoted on page II-4 of this report. Numbers in the 1 wt% range have also been reported by Mueller in a March 1984 API report entitled "The Analysis of Benzene Emissions from Vehicles and Vehicle Refueling".

Page II-3 - The concluding sentence in the paragraph at the top of the page states that, "Additional testing of benzene emissions from refineries and asphalt plants should be performed prior to considering control measure development for these sources". We certainly agree with this statement, particularly as it would apply to emissions from combustion sources. We do wonder, however, whether the relative volume of emissions from refinery and asphalt plants (less than 1% of the total inventory) would justify this effort.

Page II-4 - In the first paragraph, the staff uses factors of 6.5 and 4.2 wt% benzene in the total hydrocarbon exhaust from catalyst and non-catalyst vehicles respectively. Mueller's API report indicates no significant difference in benzene emissions between catalyst and non-catalyst cars, with the average concentration of benzene in the total hydrocarbon exaust close to 3.5 wt%. The use of these higher benzene emission factors will lead to errors in estimating both current and future emission inventories. More specifically, Figure II-1, Projected Benzene Emissions from Motor Vehicles, would have a noticeably different shape. We estimate the minimum shown will occur at a lower overall emission level and at a date later than 1990. In addition, the resulting up turn or increase in emissions will occur at a much slower rate.

Page II-4 - The second paragraph concludes by stating that additional motor vehicle testing is needed to refine the benzene emission estimates for motor vehicles. We agree and strongly support the need for additional vehicle emission testing. In fact, members of our Fuels Research group are actively involved in a major testing effort currently being initiated by the Coordinating Research Council. This study is aimed specifically at resolving many of the remaining unanswered questions about how benzene and aromatic concentrations in gasoline affect benzene concentrations in tailpipe exhaust.

Page E-13, Section IV. - "Limitations to Analysis" - Item No.2 states that "Indoor benzene concentrations may not be directly related to ambient concentrations. This study makes no attempt to examine indoor exposure". We feel this is a serious limitation to the overall objective of the Air Resources Board/Department of Health Services effort to evaluate benzene as a potential toxic air contaminant, particularly as it may relate to potential future control strategies. Since individuals spend approximately 70% of their time indoors, it follows that it should be important to know both the level and source of this exposure before drawing any final conclusions on the need to control benzene as a toxic air contaminant.

If you have any questions or comments, please contact Mark W. Nordheim of our Environment, Safety, Fire and Health Staff at (415) 894-6107.

Sincerely,

W. T. Danker

MWN:ig

AIR RESOURCES BOARD
1102 Q STREET
P.O. BOX 2815
SACRAMENTO, CA 95812

September 12, 1984

Mr. W. T. Danker, Manager
Environmental Programs
Chevron U.S.A., Inc.
P. O. Box 7643
San Francisco, CA 94120-7643

Dear Mr. Danker:

Subject: Comments on Part A of the Draft Benzene Report

Thank you for your comments and suggestions on the draft Part A of the benzene report. Your letter and this response will become part of Appendix B of the final report. We will send you a copy of the final report. Briefly, our response to your comments are as follows:

1. Page II-1, Paragraph 1 - We recognize that there is very little benzene in diesel fuels and this fact is reflected in the emission inventory. We assume there are no evaporative benzene emissions from the use of diesel fuels and estimate that benzene from diesel exhaust contributes only three percent of the total vehicular benzene emissions.

2. Page II-1, Paragraph 2 - Thank you for informing us that Chevron's El Segundo refinery has shutdown benzene production. The report will be corrected to reflect the closure.

3. Page II-2 - We agree the 2.4 wt. percent factor for benzene evaporative emissions from gasoline marketing is too high. We are revising this emission estimate to 300 tons per year using a 1 wt. percent factor.

4. Page II-3 - A decision whether or not to test for benzene emissions from refineries and asphalt plants will be made during the control measure development phase.

5. Page II-4 - We believe that the API estimtes for the benzene content in catalyst vehicles exhaust are too low for California because of differences in the aromatic contents of fuels tested versus those typically used in California. The API report has a factor of about 3.5 wt. percent benzene in the exhaust from catalyst vehicles. Approximately 25 percent of the test data are for vehicles burning fuels with low aromatic contents (13.7-17.9 wt. percent). Most of the

remaining data in the API report are from vehicles burning gasoline with aromatic contents from 26 to 36 wt. percent. ARB studies in 1980[1] and 1981[2] and a recent study[3] in progress show the average aromatic content in California's unleaded fuels is about 43 wt. percent.

After recalculating the average wt. percent benzene in total hydrocarbon exhaust from catalyst vehicles burning fuels with 38-54 wt. percent aromatics, we are revising the 6.5 wt. percent factor to 4.1 wt. percent benzene. This makes the average wt. percent benzene from catalyst vehicles similar to that for non-catalyst vehicles. Decreasing the average wt. percent benzene for catalyst vehicles changes the projected benzene emissions in Figure II-1. The minimum emissions are projected to occur in 1992 rather than 1990 and the increase in emissions occurs at a slower rate.

6. Page II-4 - We are pleased to learn that a motor vehicle testing program is being initiated. We would appreciate receiving a description of the tests in progress and the test results when the study is complete.

7. Page E-13, Section IV - "Limitations to Analysis" - We believe that indoor air exposures to toxic air contaminants may be an important factor to consider in the risk management phase during which our Board will consider adoption of toxic control measures. However, during the risk assessment (substance identification) phase, AB 1807 requires the Department of Health Services to consider ambient concentrations and risk of harm to public health from exposure to these ambient concentrations.

Again, thank you for your comments. If you have any questions, please contact Barbary Fry at (916) 322-8276.

Sincerely,

Donald J. Ames for

William V. Loscutoff, Chief
Toxic Pollutants Branch
Stationary Source Division

References

1. California Air Resources Board, 1980, 1980 Hydrocarbon Composition of Gasolines in Los Angeles, HS-10-LHC, Haagen-Smit Laboratory, El Monte, CA.

2. California Air Resources Board, 1981, 1981 Hydrocarbon Composition of Gasolines in Los Angeles, HS-17-LHC, Haagen-Smit Laboratory, El Monte, CA.

3. Peoples, 1984, Study in progress.

State of California

Memorandum

To : William V. Loscutoff, Chief
Toxic Pollutants Branch
Air Resources Board
P.O. Box 2815
Sacramento, CA 95812

Date : August 15, 1984

Place : Sacramento

From : **Department of Food and Agriculture**

Subject: Draft Report on Benzene to the Scientific Review Panel

Thank you for sending the Department a copy of the "Draft Report on Benzene to the Scientific Review Panel: Part A - a Review of Benzene Uses, Emissions and Public Exposure" for our comments.

We have reviewed the draft and have no additions or changes.

Lori Johnston

Lori Johnston, Assistant Director
Pest Management, Environmental
Protection & Worker Safety
(916) 322-6315

URNAME
SO-106

To : Lori Johnston, Assistant Director
Pest Management, Environmental
Protection & Worker Safety
Department of Food and Agriculture
1220 N Street
Sacramento, CA 95814

Date : September 12, 1984

Subject: Your Comments on Part A of the Draft Benzene Report

From : Air Resources Board

D.J. Ames for

William V. Loscutoff, Chief
Toxic Pollutants Branch
Stationary Source Division

Thank you for reviewing the draft Part A of the benzene report to the Scientific Review Panel (SRP). We are pleased that you have no additions or changes to the report.

Your response and this letter will be included in Appendix B of the final report which we plan to submit to the SRP on September 14. We will send you a copy of the final report. Please contact me at 322-6023 if you have any comments or questions.

Donald R. Buist
Director
Automotive Emissions and
Fuel Economy Office
Environmental and Safety
Engineering

Ford Motor Company
The American Road
Dearborn, Michigan 48121

August 27, 1984

Mr. William V. Loscutoff, Chief
Toxic Pollutants Branch
Air Resources Board
P.O. Box 2815
Sacramento, California 95812

Dear Mr. Loscutoff:

This letter is in response to your July 19, 1984 request for written comments on a California Air Resources Board draft staff paper titled "Benzene Report to the Scientific Review Panel: Part A — A Review of Benzene uses, Emissions and Public Exposure" dated July, 1984. Much of the information in the draft Staff paper appears correct. However, there are a few areas where we wish to comment on and provide additional information, as detailed below.

In Section II.B., (Current and Projected Stationary and Mobile Source Emissions), the average weight percent benzene of total hydrocarbon exhaust emissions is listed as:

Catalyst	6.5%
Non-Catalyst	4.2%

The catalyst percentage, 6.5% in particular, looks too high based on the EPA data on 46 vehicles in your reference 17, page II-9. Figure 1 is a plot of that data and suggests that the average percentage of benzene emissions is rather constant over model years 1975 to 1982 between about 2.6 and 3.9 percent. Similar results were reported in a March, 1984 study by Mueller Associates, Incorporated for the American Petroleum Institute using a different data set. The 6.5% figure is too high unless the non-leaded fuels in California are unusually rich in aromatics compared to those available elsewhere to cause a higher rate of benzene emissions.

As indicated in Figure 1, the benzene emissions from catalyst vehicles are of the order of 3.2% of total hydrocarbons. However, the effect of this lower emission level from catalyst cars on the estimated vehicular percentage contribution to total benzene tonnage emissions is small due to the relatively large vehicle population in Los Angeles and the relatively low estimated stationary source contribution. On the other hand, CARB's projection of a significant rise in benzene emissions after 1990 "when the number of cars using non-leaded fuel increases" would require a downward revision because it was based on a level of benzene emissions from catalyst vehicles significantly higher than that from non-catalyst cars.

Another concern related to the issue of the percent benzene emissions involves the information in Appendix E of the draft staff paper, "Ambient Monitoring Data and Methods of Air Quality Modeling." The equation on page E-8 of Appendix E would indicate a CO/benzene molar ratio of about 533, assuming the constant term is significantly different from zero, its value (0.51 ppb) represents the background benzene emissions and the value of the slope (1.875 ppb/ppm) may be compared with the CO/benzene molar ratio of vehicle emissions. The EPA data mentioned earlier and listed in Table 1, indicates an average CO/benzene molar ratio of 875. If evaporative and refueling benzene emissions are taken as 1/3 of exhaust benzene emissions, the measured CO/benzene molar ratio would drop to 656 as the expected CO/benzene ratio. Because this figure is 23% above the 533 level suggested by the regression equation in Appendix E, the benzene contribution from vehicle sources in Los Angeles may not be as high as the 93% figure listed on page II-3 of the draft staff report. Rather, an 81% contribution is suggested (100 * 533/656). By contrast, a 44 to 53% contribution in 1978 is indicated by EPA data for the United States as reported by R. M. Dowd, et al., (APCA paper 84-102.5, June, 1984).

Other estimates are also possible. For example, in Table 3 of Appendix E, the CARB report shows the predicted (based on the benzene-CO correlation equation) annual benzene levels at various air quality monitor stations. For 1982 the geographical average annual benzene level in California would be about 3.7 ppb.. Because the benzene level due to non-vehicular sources might be 0.5 ppb, the predicted vehicular contribution would be (3.7-0.5)*100/3.7=86%. This percentage value would be somewhat lower if the true CO/benzene ratio due to vehicular and related sources were 656 instead of 533 as discussed above.

Thus, the Appendix E regression equation would predict a lower contribution from vehicular sources than the estimated value based on inventory. A knowledge of the errors for the estimate of the slope and the adjustment factor would be necessary to ascertain the significance between the predicted and estimated values. For example, the adjustment factor would have to be as high as 1.53 to match the 93% contribution value estimated in the draft report. Although such an adjustment factor is higher than expected, further study would be required to improve the accuracy of these estimates.

Also in Appendix E (p. E-2), it is stated that "fourth quarter data are generally not representative of annual averages for any pollutants and would probably over-estimate annual averages of benzene" (data for September-December, 1983 were used in CARB's correlation). This implies a prior knowledge of the seasonal change of the pollutants of interest. Since no reference is given, CARB's data on benzene levels (CARB report/Table E-1) have been summarized by the month of the year as shown in Table 2. There seems to be indeed a significant increase in the benzene level during the fall-winter season. If up-to-date data for 1984 confirm this observation, further study of the underlying factors may reveal some interesting aspects regarding benzene emissions in the South Coast Air Basin (SCAB) area. Because the climate in this area is mild all year around, the fuel composition is not expected to change very much during the year. In addition, it is unlikely that the on-road vehicle population would show a dramatic seasonal change.

It is of interest to note also that the data at El Monte (15 Km east from Downtown L.A.) show several instances of sustained high benzene level for a period of two or three days during December, 1983. Because only at El Monte were data monitored five days a week, the high benzene instances found at Downtown Los Angeles and Dominquez stations may also represent benzene levels above 10 ppb for longer than 24 hours. These instances of high benzene levels may indicate episodes of recurrent loss of control of benzene emissions at some point sources.

We hope that these comments will be useful to you and your staff as they evaluate benzene uses, emissions, and public exposure.

Sincerely,

D. R. Buist

JWS.3

Table 1

CAR#	Model Year	MAKE	control system	fuel benzene	fuel aromatics	fuel toluene	FTP CO	CO/benzene Ratio	NOX	FID HC	GC HC	MEASURED BENZENE	avg % benz	mg/mi benzene	CO/Benzene molar ratio
9	1975	FORD/PINTO	OXY/AIR/EGR	1.76	32.11	5.56	30.36	270	2.59	3.53	4.49	2.58		113	732
15	1975	PLY/VALIAN	OXY	1.76	32.11	5.56	15.97	254	2.85	1.52	1.94	3.16		61	789
32	1975	OLDS/CUTLA	OXY/EGR	1.76	32.11	5.56	50.98	291	2.28	5.27	7.31	2.59	2.683	175	813
10	1976	MERC/MONAR	OXY/AIR/EGR	1.76	32.11	5.56	2.56	130	4.56	0.87	1.12	1.75		38	342
13	1976	OLDS/STARF	OXY/EFE/EGR	1.76	32.11	5.56	29.87	223	3.48	2.81	3.51	3.71		130	433
18	1976	OLDS/REGEN	OXY/EGR	1.76	32.11	5.56	35.73	305	1.38	2.18	2.74	4.37		117	852
6	1976	TOYOTA/CEL	OXY/AIR/EGR	1.96	45.18	20.25	13.75	263	3.29	0.85	1.15	4.55	3.57	52	733
11	1977	AMC/HORNET	OXY/AIR/EGR	1.76	32.11	5.56	71.81	315	3.13	6.11	6.99	3.23		226	877
14	1977	BUICK/SKYH	OXY/EFE/EGR	1.76	32.11	5.56	12.84	283	3.95	1.48	1.98	3.88		59	543
20	1977	CHEV/CHEVE	OXY/EGR	1.76	32.11	5.56	19.83	399	1.53	1.67	2.11	2.36		50	1112
24	1977	DATSUN/F-1	AIR/EGR	1.76	32.11	5.56	13.28	318	4.86	1.92	2.33	1.84	2.488	43	844
17	1978	PONT/PHOEN	OXY/EFE/EGR	1.76	32.11	5.56	38.61	339	4.22	1.93	2.37	3.92		93	919
22	1978	PLY/VOLAR	OXY/EGR	1.76	32.11	5.56	23.17	341	4.19	1.83	2.16	3.15		68	938
23	1978	DATSUN/200	OXY/EGR	1.76	32.11	5.56	12.66	342	6.27	1.52	1.78	2.88		37	954
2	1978	FORD/LTD/V	OXY/AIR/EGR	1.96	45.18	20.25	13.23	373	1.38	0.73	1.09	2.24		36	1038
5	1978	FORD/MUSTA	OXY/FI	1.96	45.18	20.25	47.57	164	3.74	4.70	6.68	4.33	3.348	289	459
16	1979	TOYOTA/COR	OXY/CCO/EGR	1.76	32.11	5.56	15.98	271	2.88	1.58	2.01	2.93		59	737
25	1979	FORD/FAIRM	OXY/AIR/EGR	1.76	32.11	5.56	7.79	152	3.12	2.22	2.99	1.71		51	423
31	1979	MAZDA/RX-7	TR/AIR	1.76	32.11	5.56	5.81	139	1.81	1.25	1.56	2.67		42	389
1	1979	CHEV/CHEVE	OXY	1.96	45.18	20.25	27.84	350	0.91	1.23	1.90	5.48		108	728
4	1979	PLY/VOLARE	OXY/EGR	1.96	45.18	20.25	44.88	175	3.24	2.88	3.58	4.42	3.882	141	744
7	1980	VW/SCIRROC	OXY/FI/EGR	1.76	32.11	5.56	6.88	346	2.48	0.46	0.58	3.53		18	941
19	1980	BUICK/ELEC	OXY/AIR/EFE/EGR	1.76	32.11	5.56	18.36	438	1.26	0.77	0.89	2.71		24	1178
24	1980	MAZDA/GLC	OXY/AIR/EGR	1.76	32.11	5.56	25.89	549	0.86	1.09	2.31	2.84		47	1533
35	1980	OLDS/CUTLA	OXY/AIR/EGR	1.76	32.11	5.56	31.84	372	2.10	2.88	2.64	3.24		86	1038
37	1980	CHEV/CITAT	OXY/AIR/EGR	1.96	32.11	5.56	5.11	381	1.64	0.36	0.53	2.53		13	1063
39	1980	FORD/FAIRM	TVC/OXY/EGR	1.76	32.11	5.56	6.99	89	2.45	1.75	1.99	3.93		78	249
46	1980	CHYS/LEBAR	OXY/EGR	1.76	32.11	5.56	9.66	587	0.53	0.37	0.49	3.36	3.849	14	1637
14	1981	MAZDA/626	OXY	1.76	32.11	5.56	0.68	87	0.74	0.19	0.35	1.96		7	244
27	1981	CHEV/CHEVE	CAT/EGR	1.76	32.11	5.56	9.35	232	1.10	0.82	1.14	3.53		48	648
28	1981	MERC/LYNX	TVC/OXY/AIR/EGR	1.76	32.11	5.56	7.68	550	0.74	0.64	0.88	1.72		14	1537
29	1981	VW/JETTA	TVC/OXY/FI/EGR	1.76	32.11	5.56	5.26	241	1.49	0.53	0.72	2.88		28	728
33	1981	FORD/ESCOR	TVC/AIR/EGR	1.76	32.11	5.56	10.14	561	0.89	0.91	1.16	2.79		32	1565
36	1981	PONTIAC/T-	TVC/AIR/EGR	1.76	32.11	5.56	9.52	347	0.77	0.57	0.77	3.37		24	1023
38	1981	CHEV/CITAT	TVC/AIR/EGR	1.76	32.11	5.56	6.95	386	0.98	0.37	0.52	3.46		18	1078
41	1981	CHEV/CHEVE	TVC/EGR	1.76	32.11	5.56	10.24	359	0.56	0.83	1.03	3.84		48	722
42	1981	CHEV/CITAT	CAT/EGR	1.76	32.11	5.56	1.83	263	1.34	0.19	0.29	2.48		7	733
44	1981	AMC/CONCOR	TVC/FEC	1.76	32.11	5.56	11.39	784	0.48	0.61	0.76	2.14		14	1970
3	1981	CHEV/CITAT	TVC/OXY/AIR/EGR	1.96	45.18	20.25	15.51	284	3.29	1.36	1.67	3.27		55	792
8	1982	MAZDA/RX-7	TVC/OXY/AIR	1.76	32.11	5.56	4.82	179	0.93	0.29	0.37	6.87	3.114	22	499
21	1982	OLDS/DELTA	TVC/OXY/AIR/EGR	1.76	32.11	5.56	5.81	258	0.85	0.84	1.18	1.35		15	721
30	1982	CHEV/CHEVE	TVC/OXY/AIR/EGR	1.76	32.11	5.56	5.33	237	1.88	0.51	0.61	3.48		22	441
40	1982	CHEV/CITAT	TVC/AIR/EGR	1.76	32.11	5.56	3.33	414	0.82	0.23	0.35	2.23		8	1154
43	1982	CHYS/LEBAR	TVC/EGR	1.76	32.11	5.56	7.52	237	0.85	0.33	0.41	7.74		32	441
45	1982	FORD/MUSTA	TVC/AIR/EGR	1.76	32.11	5.56	8.24	399	3.58	0.48	0.63	4.82		21	1112
							1.32	377	0.56	0.18	0.29	1.39	3.518	4	1852
			Average ----)					314				3.23			879

Table 2 - Seasonal Variation of Benzene Level

Period	All Four Stations Mean	S. D.	No. Obs.		DOLA and Riverside (1) Mean	S. D.	No. Obs.	
Sept/83	2.9	1.3	24	(0)	3.6	1.9	8	(0)
Oct/83	6.1	2.2	34	(3)	6.1	2.9	8	(1)
Nov/83	6.1	2.3	35	(2)	5.9	2.3	10	(0)
Dec/83	7.3	4.2	23	(5)	5.9	3.4	7	(0)
Jan/84	7.9	2.8	30	(6)	7.3	2.9	10	(2)
Feb/84	6.5	2.2	29	(3)	6.5	2.4	9	(1)
Mar/84	4.2	1.8	34	(0)	4.1	1.3	9	(0)

(1) Both CO and benzene were monitored at these two stations.

(2) Number of parenthesis denotes observations of benzene levels equal to or greater than 10 ppb. The breakdown of such observations by station is as follows: 13/El Monte, 4/DOLA, 3/Dominquez and 0/Riverside.

JWS.3A

Figure 1

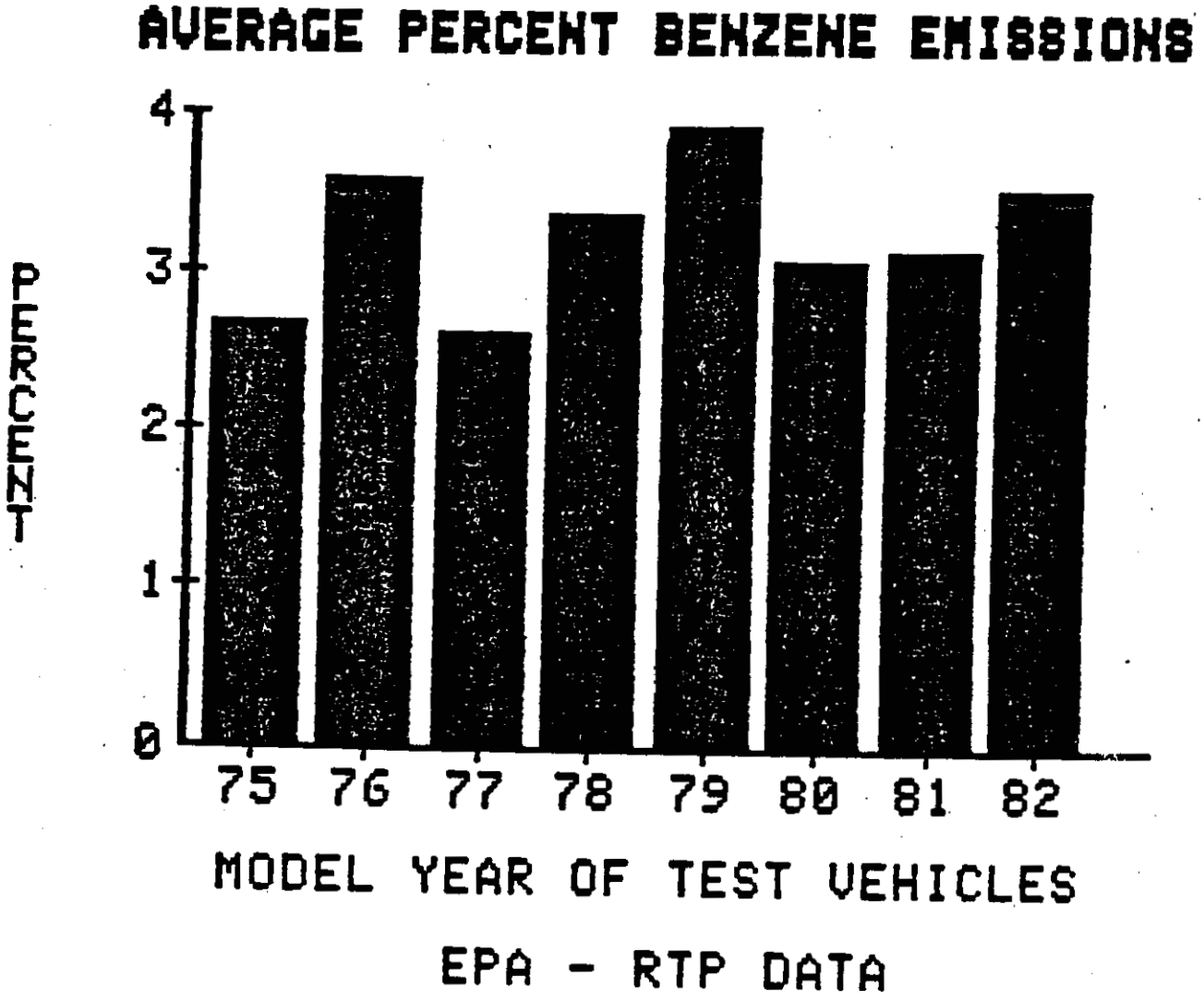
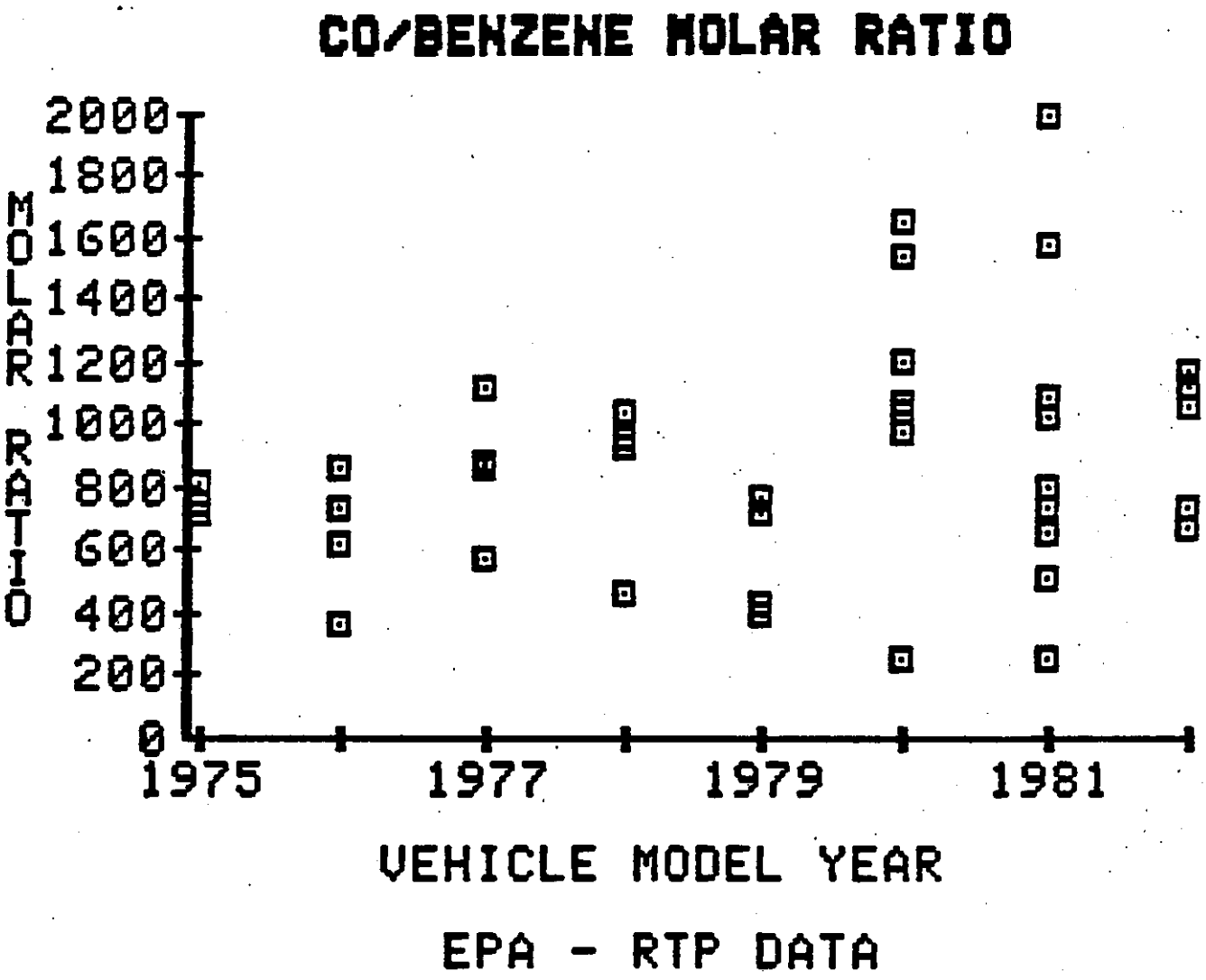

AVERAGE PERCENT BENZENE EMISSIONS
PERCENT
4
3
2
1
0
75
76
77
78
79
80
81
82
MODEL YEAR OF TEST VEHICLES
EPA - RTP DATA

Figure 2


CO/BENZENE MOLAR RATIO
2000
1800
1600
1400
1200
1000
800
600
400
200
0
MOLAR RATIO
1975
1977
1979
1981
VEHICLE MODEL YEAR
EPA - RTP DATA

AIR RESOURCES BOARD
1102 Q STREET
P.O. BOX 2815
SACRAMENTO, CA 95812

MADE READY
PROOF -
D.C.-166
PART 2

September 12, 1984

Mr. D. R. Buist, Director
Automotive Emissions and Fuel
Economy Office
Environmental and Safety Engineering
Ford Motor Company
The American Road
Dearborn, MI 48121

Dear Mr. Buist:

Subject: Comments on Part A of the Draft Benzene Report

Thank you for your letter of August 27, 1984, regarding our draft Benzene Report to the Scientific Review Panel, Part A. It and this letter will appear in Appendix B of the final version. We will send you a copy of the final report. Our responses are presented under three headings corresponding to your major points.

Benzene in Vehicle Exhaust

Several people commented as you did that all the available data taken together do not show a significant difference between catalyst and non-catalyst equipped cars in the fraction of exhaust hydrocarbon that is benzene. We have re-examined the data and have changed the benzene fraction for catalyst vehicles. The values for benzene fractions are as follows: catalysts - 4.1 percent, non-catalyst - 4.2 percent. These numbers are based on data from the original references and exclude some data taken for unleaded fuels with aromatic contents too low to represent gasoline in California. Our emission projections will be revised according to the new values.

Contribution of Vehicles to Total Benzene Inventory

The changes described above plus a change in calculation of evaporative emissions yield a benzene inventory that is 83 percent from on-road vehicle exhaust and 93 percent from exhausts plus fuel evaporation. As you point out, an independent estimate of vehicles' contribution to the inventory can be made by considering the ratio of CO to benzene in both the ambient air and in vehicular exhausts (plus knowing the benzene fuel evaporation and the CO from non-vehicular sources). However, the ratio of CO to benzene in exhausts is critical. It should be estimated only from data from vehicles representing

the emission characteristics of cars on the road in California and burning fuels similar to gasoline in California. Because some of the vehicles in reference 17 did not meet those qualifications, the molar ratio of 875 that you cite may not be applicable for California.

For the purpose of the health effects evaluation by the Department of Health Services and review of the Department's evaluation by the Scientific Review Panel, a more refined emission inventory is not necessary. However, we will refine the inventory in our work to develop control strategies. At that time, we will take care to reconcile the inventory with an approach like the one of your suggestion.

Seasonality of Ambient Benzene

We are aware of the trend to higher ambient benzene concentrations during the winter. It is expected because the air is stabler then, and dispersion is less effective. This is witnessed by elevated concentrations of CO and lead in the winter. Also, because benzene is photochemically reactive it should have a slightly longer chemical lifetime during the winter.

Again, thank you for your comments. If you have any questions please contact Barbara Fry at (916) 322-8276.

Sincerely,

Donald J. Ames

William V. Loscutoff, Chief
Toxic Pollutants Branch
Stationary Source Division

IT CORPORATION

August 10, 1984

Mr. William B. Loscutoff, Chief
Toxic Pollutants Branch
California Air Resources Board
P. O. Box 2815
Sacramento, CA 95812

Dear Bill:

CARB STAFF DRAFT "BENZENE REPORT TO THE SCIENTIFIC REVIEW PANEL"

I have been out of the office for four weeks, so my comments on the draft Benzene Report are later than I would have liked. I hope they reach you in time to be considered in your revisions.

1. Additional References - The March, 1984 issue of "Risk Analysis", which was just sent out at the end of July, 1984, contains several letters to the editor about benzene. These are by van Raalte, et al (p. 1), Irvine (p. 3), Gaffey (p. 5), Chandler (p. 7) and Infante, et al (p. 9). The March, 1984 issue is Volume 4 of the journal.

Obviously, your report could not have included these letters. I'm not sure they are even relevant, although they should be of interest to the DOHS health effects report writers.

2. Statistical Treatment of Correlation Coefficient - I believe there is a misunderstanding about statistical significance of the correlation coefficient cited on page IV-2. The footnote interprets a 0.01 significance level as indicating there is one chance in 10,000 that the correlation coefficient calculated (0.82 in the example) would happen by chance.

I think the correct meaning is that a 0.01 level indicates one chance in 100. The error comes about because many people equate "probability" with something erroneously called "percent probability". Probability has dimensionless units bounded by zero and one. The incorrect term of "percent probability" usually means percentage, bounded by zero and one hundred, with units of "percent".

I seriously doubt that your data gave a correlaion coefficient of 0.82 with 0.0001 probability of a false positive. I think the significance level was 0.01 probability, or one percent.

Further, you should bear in mind that a correlation coefficient of 0.82 is not as impressive as it appears. The amount of variation explained by the correlation effect is not r - the correlation coefficient, but r^2 - the coefficient squared. Taking r=0.82, then r^2=0.67. Thus, about two-thirds of the relationship is explained by correlation, but one-third is not. This becomes more startling if one compares the r and r^2 values for downtown Los Angeles, where r=0.59 (or 0.67 if temperature is also considered). Then r^2 =0.35 (or 0.45 if temperature is also considered). I will pursue this below.

3. Choice of CO as a Benzene Surrogate - I believe the model you chose for the CO-benzene correlation may not be the most suitable. If the model is to be used to predict benzene concentrations, it needs to do so over the range of plausible CO concentrations that can be measured. Your model predicts benzene levels of 0.5 ppb at zero CO levels. Most of the predicted values for benzene lie in the 3 to 6 ppb levels, so the baseline zero CO level of 0.5 ppb is somewhere between one sixth and one twelfth of the predicted values. However, if CO is supposed to be a surrogate for benzene from mobile sources, this is far too large a built-in "assumption".

The model needs the temperature relationship, as shown by your own data for downtown Los Angeles - one of only two stations where you had actual measurements of both CO and benzene. Another obvious correlate would be altitude, since the relation between vehicle CO and altitude (Denver is a good example) is strong. This is significant in some parts of the state.

Finally, I think you need to develop more correlation data at locations other than the South Coast Air Basin - particularly, you need data for the San Francisco area, the Sierra Nevada, and the San Joaquin and Sacramento valleys, and for some range of seasons - winter and summer. Only then can you hope to use CO measurements as a surrogate.

I suggest that what you have now is pretty good data to suggest that ambient benzene levels in the SCAB range from 1 to 10 ppb with 5 ppb as good a measure of central tendancy as any. This is certainly going to be as accurate as any dose-response data that DOHS will be able to provide, from what I have seen (see the Infante letter referred to above).

4. Exposure Population Estimate - I think the approach outlined in the report for estimating population exposure is good. If the CO contours can be interpolated between stations, if the CO-benzene correlations are close enough, and if the population estimates are good, then CO data can predict exposure. I believe one needs to do a careful estimate not only of the mean benzene concentration in a population "cell" but of the variance over this region. Again, a better model relating CO to benzene seems needed.

Finally, I wonder why the 1979 SCAG population data were used when 1980 census estimates are available. The 1979 SCAG estimates have to be less accurate, since they are based, fundamentally, on 1970 census data and SCAG's attempts at updating.

Please feel free to contact me if you have questions or comments on this letter. For your information, I expect to be out of the office again September 7 to October 1 this year.

With best regards,

Nick

R. Nichols Hazelwood, Ph.D.
Project Manager
Environmental Affairs

RNH/sp

STATE OF CALIFORNIA
GEORGE DEUKMEJIAN, Governor

AIR RESOURCES BOARD
1102 Q STREET
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SACRAMENTO, CA 95812

August 17, 1984

Dr. R. Nichols Hazelwood
Project Manager, Environmental Affairs
IT Corporation
23456 Hawthorne Blvd., Suite 220
Torrance, CA 90505

Dear Dr. Hazelwood:

Subject: Your Comments on the Draft Benzene Report

Thank you for your comments on Part A of the draft report on benzene. We appreciate the thoroughness with which you reviewed the draft. We have also prepared some responses to your comments that I'd like to share with you. I am responding to them under the titles you have in your letter.

1. Additional References - We will quote the citations to the Department of Health Services.

2. Statistical Treatment of Correlation Coefficient - the correlation of ambient benzene against ambient CO (117 data pairs) was calculated with standard statistical software. Our modeling staff verifies the result that if the two variables are completely independent ($\rho=0$), the probability that a sample size of 117 would yield a sample correlation coefficient equal to or greater than .82 is .0001 or .01 percent probability.

   Regarding the coefficient .82, we understand the concept that 30% of the variation in the benzene measurements were not attributable to variations in the CO measurements. However, our modeling staff tells us that the result is quite good for this type of analysis. The poor result (.59) obtained if only data from downtown L.A. (DOLA) are included is not of consequence because the coefficient .82 is obtained from all CO-benzene pairs analyzed together without regard to their origins. Since only about 15% of the data pairs are from DOLA, the smaller correlation coefficient derived from DOLA data alone is not surprising.

3. Choice of CO as a Benzene Surrogate - Regarding your concern that the model predicts benzene levels of .5 ppb at zero CO levels, the data entered into the correlation do not extend down to zero CO.

Extrapolation to CO values below the range of CO values in the correlation would be improper and was not done in our analysis.

We did not include a temperature variable as a surrogate for benzene "breathing" emission data because, as Table 2 in Appendix E shows, its effect on the correlation would have been marginal. The DOLA site provided only 15% of the CO-benzene data pairs, whereas the other site providing actual CO data (El Monte) provided over half. Temperature had little affect on the correlation of El Monte data alone (or on the Dominguez or Riverside stations' data alone).

We did not include an altitude variable in the model because the SCAB is essentially flat over the areas where the vast majority of people live. Our purpose was solely to extend the information from the four monitors to the entire basin, not beyond. We do not intend that the correlation be applied outside the SCAB. However, we recognize the value of generating a model using more than one quarter's data and including data from locations other than the South Coast Air Basin. Before control measures are considered for benzene emissions, a great deal more data representing seasonal variations and other locations should be available. We are in the final stages of developing a statewide toxic air contaminant monitoring network. This network will include monitoring stations in the San Francisco Area and Central California in addition to expanding the number of stations in the Los Angeles area.

4. Exposure Population Estimate - We believe that the level of modeling of benzene concentrations versus CO concentrations provided in the report is appropriate to estimate spatial variations. More resolution would require a greater density of CO monitoring sites, which out of practicalities will not be.

   In addition, the 1979 SCAG data on population density has been routinely used for air quality modeling in the SCAB. The 1980 census data are not yet available to us in machine-usable form. Our modeling staff indicate that in the meantime the 1979 data are adequate for calculating an estimate.

Thank you again for your comments. If you wish to discuss these comments more or if you have further questions on the report please contact me at (916) 322-6023.

Sincerely,

Bill

William V. Loscutoff, Chief
Toxic Pollutants Branch
Stationary Source Division

Mobil Oil Corporation

8225 GALLOWS ROAD
FAIRFAX, VIRGINIA 22031

August 21, 1984

Mr. William V. Loscutoff, Chief
Toxic Pollutants Branch
Air Resources Board
P. O. Box 2815
Sacramento, California 95812

CALIFORNIA AIR RESOURCES BOARD
DRAFT REPORT ON BENZENE TO THE
SCIENTIFIC REVIEW PANEL

Gentlemen:

We have reviewed the California Air Resources Board (CARB) report " A Review of Benzene Uses, Emissions and Public Exposure" and offer the following comments for the Board's consideration.

- The value of 2.4 weight percent benzene in total hydrocarbon emissions from gasoline marketing sources stated on page II-2 appears to be high. In EPA's August 8, 1984 Federal Register notice on "Regulatory Strategies for the Gasoline Marketing Industry," the average amount of benzene in liquid gasoline is given as 1.3% on page 31708. We would expect the benzene on the total hydrocarbon emissions to be slightly less than this percentage. In addition, the 2.4% number is inconsistent with the evaporative emissions from automobiles on page II-4 of the CARB document, which is stated as 1.2% total evaporative hydrocarbons. These evaporative emissions consist of two components: (1) diurnal emissions which consist of only the lighter components that would evaporate from a vehicle tank at ambient temperature and (2) hot soak emissions which are essentially a boiling-off of the full range gasoline in a vehicle carburetor, after the engine is turned off. Of these two components, the hot soak emissions would have the higher benzene content which would be equal to the benzene content in the liquid gasoline. The diurnal emissions would be lower, and more analogous to typical gasoline marketing emissions. Therefore, we would expect benzene emissions from gasoline marketing emissions to be about 1% the total hydrocarbon emissions. The benzene evaporative emissions from these sources should be listed as 305 tons per year instead of 730 tons per year.

- Another significant flaw that we find in it is an overestimation of the benzene content of vehicle exhaust. CARB estimates that benzene is 6.5% of the hydrocarbons in exhaust for catalyst-equipped cars. In a recent API survey of published information on 78 cars, the average was found to be 3.4% for oxidation catalysts and 4.0% for three-way catalysts. For non-catalyst cars, CARB estimates 4.2%; API found 3.5%. Enclosed for the Board's review is a copy of the API report "Analysis of Benzene Emissions From Vehicles and Vehicle Refueling", March 1984 detailing the data on the 78 vehicle survey.

- A major concern is the analytical approach taken by Haagen-Smit Laboratory. The data they report is as low as 0.01 ppb with 90 percent accuracy. We are not aware of any analytical technique that is accurately capable of measuring such a low level, especially considering the sampling approach that is used. However, we would need to review the detailed analytical methods before making a definite judgement on the accuracy or precision of the reported data.

- We are concerned over the fact that all of the benzene detected in CARB's limited monitoring program were assumed to result from anthropogenic sources. CARB did not compare their data with the benzene levels found in background areas upwind of the sampling area. Neither did CARB include data on the ambient benzene concentrations over pristine areas such as oceans and forests. In addition, we question whether four sampling points were sufficient to adequately quantify ambient exposure levels over such a large region. These deficiencies should be corrected before any regulatory strategies can be considered.

We appreciate the opportunity to submit our comments for the Board's consideration. Should you have any questions concerning these comments I can be contacted by telephoning 703/849-4191.

Sincerely,

T. C. Lyons
Manager, Environmental Affairs

8018P

AIR RESOURCES BOARD
1102 Q STREET
P.O. BOX 2815
SACRAMENTO, CA 95812

September 12, 1984

Mr. T. C. Lyons
Manager, Environmental Affairs
Mobil Oil Corporation
3225 Gallows Road
Fairfax, VA 22037

Dear Mr. Lyons:

Subject: Comments on Part A of the Draft Benzene Report

Thank you for your comments on the draft Part A of the benzene report. Your letter and this response will become part of Appendix B of the final report. We will send you a copy of the final report. I am responding to your comments in the same sequence in your letter.

1. We agree the 2.4 wt. percent factor for benzene evaporative emissions from gasoline marketing is too high. We are revising this emission estimate to 300 tons per year using a 1 wt. percent factor.

2. We agree that the draft report overestimated the benzene content of catalyst vehicle exhaust. However, we believe that the API report estimates for benzene content in the exhaust of catalyst vehicles are too low for California, because of differences in the aromatic contents between the gasoline API used versus that typical of California gasoline.

   The API report has a factor of about 3.5 wt. percent benzene for catalyst vehicles exhaust. Approximately 25 percent of the API test data are for vehicles burning fuels with low aromatic contents (13.7-17.9 wt. percent). Most of the data in the API report are from vehicles burning aromatic fuels ranging from 26-36 wt. percent. ARB studies in 1980[1/] and 1981[2/] and a recent study[3/] in progress show the average aromatic content in California's unleaded fuels is about 43 wt. percent. After recalculating the average wt. percent benzene in total hydrocarbon exhaust from catalyst vehicles burning fuels with 38-54 wt. percent aromatics, we are revising the 6.5 wt. percent factor downward to 4.1 wt. percent benzene. This makes the average wt. percent benzene from catalyst vehicles similar to that for non-catalyst vehicles.

ARB and API used the same data to estimate non-catalyst factors of 4.2 wt. percent and 3.5 wt. percent respectively. API's recalculation of the original data resulted in a lower wt. percent factor. We are retaining the 4.2 wt. percent factor for non-catalyst vehicles.

3. We verified with your staff by telephone that your concern with the analytical approach was for Oak Ridge National Laboratory (ORNL) rather than Haagen-Smit as stated in your letter. The status report we reviewed for the ORNL indoor air study does not include details of the analytical methods. You may wish to contact them for further information.

4. The benzene emission inventory in Part A contains benzene emission estimates from all sources that staff could quantify. We would appreciate receiving any additional benzene emission estimates you may have.

   The intent of including the ambient benzene monitoring data in Part A is to give the Department of Health Services (DHS) an approximation of the ambient levels to which Californians are exposed. AB 1807 requires the DHS to consider risk of harm to public health in their health evaluation report. We agree a more comprehensive emission inventory and ambient exposure assessment is needed prior to the Board's consideration of toxic control measures.

Thank you again for your comments. If you wish to discuss these comments more or if you have further questions on the report, please contact Barbara Fry at (916) 322-8276.

Sincerely,

Donald J. Ames for

William V. Loscutoff, Chief
Toxic Pollutants Branch
Stationary Source Division

References

1. California Air Resources Board, 1980, 1980 Hydrocarbon Composition of Gasolines in Los Angeles, HS-10-LHC, Haagen-Smit Laboratory, El Monte, CA.

2. California Air Resources Board, 1981, 1981 Hydrocarbon Composition of Gasolines in Los Angeles, HS-17-LHC, Haagen-Smit Laboratory, El Monte, CA.

3. Peoples, 1984, Study in progress.

4. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans, Vol. 29, May 1982.

OCAW
Oil, Chemical & Atomic Workers
International Union, AFL-CIO

International Offices:
255 Union Blvd., Lakewood, CO 80228
303/987-2229
Mail: P.O. Box 2812, Denver, CO 80201

EXPRESS MAIL

August 28, 1984

Mr. William V. Loscutoff, Chief
Toxic Pollutants Branch
Air Resources Board
P.O. Box 2815
Sacramento, CA 95812

Dear Mr. Loscutoff:

Thank you for the opportunity to comment on the Department of Health Services' report on Benzene (Part B). This report has been reviewed by the health and safety staff of the Oil, Chemical and Atomic Workers International Union. We find that this is a good study that appropriately considers the health risks to persons exposed to benzene, whether from the workplace or the environment.

We agree completely with the position of the Department of Health that there is no known safe threshold for benzene exposure so that it should be treated as if it had no threshold.

We were also glad to see the Department take a prudent position on benzene risks from atmospheric emissions. The Union would only recommend that the Department review the two most recent benzene studies which serve to further underscore its carcinogenicity. These are:

1) "Statistical Analysis of Hematology Data From the Chronic Test of Benzene." By Program Resources, Inc., P.O. Box 12794, Research Triangle Park, NC 27709, 5/31/84

2) NTP Technical Report on the Toxicology and Carcinogenesis Studies of Benzene, NIH Publication #84-2545, Draft 7/84

We also took the liberty to review Part A, "A Review of Benzene Uses, Emission and Public Exposure", prepared by the staff of the Air Resources Board.

We would agree with the Air Resources Board that "additional testing of benzene emissions from petroleum refineries and asphalt plants should be performed prior to considering control measure development for these sources".[1] We would urge that this testing be done without delay so that any necessary control measures can be required and instituted in a timely manner.

Thank you for submitting these two documents for review.

Sincerely,

Dan C. Edwards

Dan C. Edwards, Director
Health and Safety Department

SK/DCE/mb
cc: Robert Wages, V-P, OCAW
Jack Foley, Director, District #1
Thomas Lind, Int'l Representative
Robert Boudreau, Int'l Representative

---

[1] Since the two studies cited in the report offer only rough approximations of benzene emissions from refineries and asphalt plants, it is reasonable to want more precise measurements.

AIR RESOURCES BOARD
1102 Q STREET
P.O. BOX 2815
SACRAMENTO, CA 95812

September 12, 1984

Mr. Dan C. Edwards, Director
Health and Safety Department
Oil, Chemical and Atomic Workers
P. O. Box 2812
Denver, Colorado 80201

Dear Mr. Edwards:

Subject: Comments on Part A of the Draft Benzene Report

Thank you for your comments on the draft Part A of the benzene report. We will transmit your comments on Part B to the Department of Health Services. Your letter and this response will become part of Appendix B of the final report. We will send you a copy of the final report.

We appreciate your desire for immediate testing of benzene emissions from petroleum refineries and asphalt plants. At this time we do not have a specific schedule for benzene source testing. We expect to conduct some testing of benzene sources during the control measure development phase once benzene is identified as a toxic air contaminant.

Thank you again for your comments. If you wish to discuss these comments more, please contact Barbara Fry at (916) 322-8276.

Sincerely,

Donald J. Ames for

William V. Loscutoff, Chief
Toxic Pollutants Branch
Stationary Source Division

UNIVERSITY OF CALIFORNIA, DAVIS

BERKELEY • DAVIS • IRVINE • LOS ANGELES • RIVERSIDE • SAN DIEGO • SAN FRANCISCO SANTA BARBARA • SANTA CRUZ

DIVISION OF MEDICAL SCIENCES
DEPARTMENT OF INTERNAL MEDICINE
SECTION OF PULMONARY MEDICINE

SCHOOL OF MEDICINE
DAVIS, CALIFORNIA 95616

July 27, 1984

Dr. William V. Loscutoff, Chief
Toxic Pollutants Branch
Air Resources Board
P. O. Box 2815
Sacramento, CA 95812

Dear Dr. Loscutoff:

RE: Draft Report on Benzene, Part A

Thank you for the opportunity to comment on this document. My only question concerns the implied comparison with indoor levels of benzene from the EPA TEAM study in Elizabeth and Bayonne, New Jersey (IV-4). I do not understand the meaning of the last sentence of the third paragraph: "Thus, personal air measurements....may explain the high benzene levels..." Was something omitted in this draft? Also, Elizabeth and Bayonne are proximal to (and generally downwind from) a major oil refinery complex (Exxon's Bayway refinery, Phillips Petroleum, and others). Might that proximity have influenced indoor benzene levels? It is unfortunate that the only available study was not performed in a more typical area, though perhaps the chosen sites might accurately model the California situation in the Pinole/Hercules area.

Sincerely,

Jerold A. Last
Northern California
Occupational Health Center,
University of California,
Davis, CA

JAL:sjm
cc: Marc Schenker, M.D., NCOHC
Noreen Dowling, PSRDP

102 O STREET
P.O. BOX 2815
SACRAMENTO, CA 95812

September 12, 1984

Mr. Jerold A. Last
Northern California Occupational
Health Center
University of California, Davis
Davis, CA 95616

Dear Mr. Last:

Subject: Comments on Part A of the Draft Benzene Report

Thank you for your comments on our discussion of the EPA indoor air study in Part A of the draft benzene report. Your letter and this response will become part of Appendix B of the final report. We will send you a copy of the final report.

You expressed some confusion with the sentence, "Thus, personal air measurements in smokers' homes may explain the high benzene levels found in the EPA study." The EPA TEAM study indicates: 1) benzene is more prevalent in smokers' homes than in non-smokers' homes; and 2) 45 percent of the sample population were smokers. However, the report does not identify the specific sources of indoor benzene concentrations. Thus, we hypothesized that personal air measurements in the 30 ppb range may be from smokers' homes.

Also, you asked if nearby oil refineries influenced indoor benzene levels in the EPA study. This study includes a statistical analysis correlating simultaneous indoor and outdoor (backyard) benzene samples. The correlation coefficient for indoor and outdoor benzene samples was 0.35. This means 88 percent of the variations in the indoor benzene concentrations were not attributable to variations in the outdoor benzene concentrations. Thus, it appears the benzene emissions from nearby oil refineries did not greatly influence the indoor benzene concentrations.

Thank you again for your comments. If you wish to discuss these comments more or if you have further questions on the report, please contact Barbara Fry at (916) 322-8276.

Sincerely,

Ronald J. Ames for

William V. Loscutoff, Chief
Toxic Pollutants Branch
Stationary Source Division

UNIVERSITY OF CALIFORNIA, SANTA CRUZ

BERKELEY • DAVIS • IRVINE • LOS ANGELES • RIVERSIDE • SAN DIEGO • SAN FRANCISCO SANTA BARBARA • SANTA CRUZ

ENVIRONMENTAL HEALTH & SAFETY SANTA CRUZ, CALIFORNIA 95064

August 7, 1984

William V. Loscutoff, Chief
Toxic Pollutants Branch
Air Resources Board
PO Box 2815
Sacramento, CA 95812

Re: Draft Report On Benzene To The Scientific Review Panel - Part A

Dear Mr Loscutoff:

Part A of the subject report has been reviewed. Comments are made on the preliminary text along with some suggestions.

1. Page II-1, paragraph 2: If the 14,000 tons of benzene independently produced annually is a "minor fraction" of the total benzene content in gasoline, what is the total tonnage of benzene available in distributed gasoline annually? Also, how many gallons of gasoline are used per month or annually by outlets in the area of concern?

2. Page II-3, "Mobile Emission Sources": Since motor vehicles contribute about 93% of the estimated benzene emissions in California, figures on gasoline consumption vs benzene output could yield an overall effectiveness figure for vehicle systems relative to benzene used in the combustion process.

3. Sampling is obviously needed with more locations near heavily used roadways. Sampling at such high point areas with a height differential could yield valuable information on benzene concentrations vs height. If the concentrations are higher with decreasing height, children would be the recipients of higher doses when in sidewalk traffic.

4. Meteorological considerations is important to benzene concentrations particularly in an area such as the San Fernando Valley. Perhaps some data from "Project Basin" may be useful in future determinations.

5. Since the EPA has recently indicated that lead will be largely omitted from gasoline, can we expect that even more benzene will be used to maintain or increase octane ratings?

Overall, Part A of the report is well done and includes much information of value to those with concern for human safety. Part B on benzene health hazards should be even more informative on human safety. It is hoped that the comments on Part A offer some constructive suggestions. I hope to review Part B of the report when it is issued.

Cordially,

James C. Lang
EH&S Officer

STATE OF CALIFORNIA
GEORGE DEUKMEJIAN, Governor

AIR RESOURCES BOARD
1102 Q STREET
P.O. BOX 2815
SACRAMENTO, CA 95812

September 12, 1984

Mr. James C. Lang
Environmental Health and
Safety Officer
University of California, Santa Cruz
Santa Cruz, CA 95064

Dear Mr. Lang:

Subject: Comments on Part A of the Draft Benzene Report

Thank you for your comments and suggestions on the draft of Part A of the benzene report. Your letter and this response will become part of Appendix B of the final report. We will send you a copy of the final report. Briefly, our response to your numbered comments are as follows:

1. We estimate the total benzene content of gasoline sold in California in 1983 to be 511,000 tons. Thus, the 14,000 tons of benzene independently produced in 1983 was about 3 percent of the total benzene content in gasoline. Benzene is no longer produced in California with the 1984 closure of Chevron's El Segundo benzene plant.

   We estimate that about 5.3 billion gallons of gasoline are consumed annually in the South Coast Air Basin.

2. The ratio of benzene emissions to gasoline consumed is approximately 0.003 lbs. benzene emitted per gallon gasoline consumed using a 1983 consumption of 11.2 billion gallons and estimated vehicle benzene emissions of 15,000 tons.

3. We agree sampling with a height differential near heavily used roadways could provide useful exposure information. However, our intent for this report was to give the Department of Health Services an approximation of the annual average ambient benzene concentration experienced by persons in the SCAB. We expect to gather more detailed exposure information during the consideration of toxic air contaminant control measures following the identification of benzene as a toxic air contaminant.

4. ARB staff are directly involved in the "Project Basin" study and plan to use these data when the study is completed. We expect the study to be completed in the spring of 1985.

5. The overall aromatic content of leaded fuel has increased with decreasing lead in the fuel. Analysis of low lead fuels is needed to determine whether or not the benzene content has increased with increasing aromatic content. However, even if the benzene content has not increased, benzene exhaust emissions are expected to increase with increasing aromatics (toluene, xylene) in the fuel. We plan to investigate benzene emission trends in much greater detail during the development of control measures.

Thank you again for your comments. If you wish to discuss these comments more or if you have further questions on the report, please contact Barbara Fry at (916) 322-8276.

Sincerely,

Donald J. Ames for

William V. Loscutoff, Chief
Toxic Pollutants Branch
Stationary Source Division

Western Oil and Gas Association
727 West Seventh Street, Los Angeles, California 90017
(213) 627-4866

August 31, 1984

BY MESSENGER

William V. Loscutoff, Chief
Toxic Pollutants Branch
Air Resources Board
Post Office Box 2815
Sacramento, California 95812

Re: Benzene Report to the Scientific Review Panel, Part A -- A Review of Benzene Uses, Emissions and Public Exposure

Dear Mr. Loscutoff:

The Western Oil and Gas Association ("WOGA") appreciates the opportunity to review your draft report on benzene and to offer comments prior to its submission to the Scientific Review Panel ("SRP"). Our primary concern is that the best data available be used to assess the relationship between sources of benzene and public exposure so that a realistic appraisal of the potential to reduce exposure levels can be made.

We are currently in the process of gathering information on ambient benzene concentrations in the South Coast Air Basin and will make this information available to you when our study is completed. However, we do not expect this information to be available for several months. In the interim, we have a few general comments on the Part A report. Some of our comments are based on studies that are currently in process and have not been finalized. More detailed comments will follow at a later date.

We will address three issues in these comments. Those issues are: (1) the estimates of benzene emissions from motor vehicles; (2) the adequacy of the database used to calculate ambient concentrations, and (3) the failure to address indoor air pollution. We will begin with emissions from motor vehicles.

Estimates of Benzene Emissions from Motor Vehicles are Overstated.

To estimate benzene from motor vehicle exhaust, emission factors were used based on studies by the Environmental Protection Agency ("EPA") and the Society of Automotive Engineers ("SAE"). Factors of 6.5 and 4.2 weight % benzene in the total hydrocarbon exhaust from catalyst and noncatalyst vehicles,

respectively, were used. A recent American Petroleum Institute ("API") report entitled "The Analysis of Benzene Emissions from Vehicles and Vehicle Refueling" found no significant difference in benzene emissions between catalyst and noncatalyst-equipped cars. Furthermore, the API report calculates the average concentration of benzene in the total hydrocarbon exhaust at close to 3.5 weight %.

In Figure II-1 (Projected Benzene Emissions from Motor Vehicles), a sharp upturn in benzene emissions in tons per year is predicted to begin around the year 1990 and continue through the year 2000. This estimated increase is affected by the emission factors used. If the emission factors in the API study are substituted, the overall emissions will be lower and the rate of increase after 1990 will be much slower.

Inadequacy of the Data Base

We are concerned with the representativeness of the ambient benzene measurements made in the South Coast Air Basin and the conclusions drawn from these data. To begin, as we understand your monitoring program, benzene levels were actually obtained from only four monitoring sites. It appears that all of these sites were located very close to major freeways and/or heavily traveled streets. Appendix E to the staff report explains that:

> "The estimates apply to areas not immediately around large point sources of benzene. Estimating the locally high concentrations near sources requires different data and modeling techniques than those described here. The sources are mostly not in residential areas. Because residential population data were used to estimate the populace's exposure to benzene, neglecting such locally high concentrations does not introduce serious error."
>
> (Appendix E, p. E-1.)

Appendix E recognizes the fact that ambient concentrations in the areas surrounding stationary sources may be unrepresentative. We think that the same point can be made with regard to the air around freeways because the majority of the population lives a greater distance from freeways than the location of the measurement sites. For this reason, we question drawing broad conclusions from these ambient measurements.

The estimates and monitor readings should reflect, as close as possible, the actual benzene level of the air that most people breathe. Thus, while the measurements used by your staff may be accurate, the number of measurements appears to be insufficient and should have included measurements inside homes, office buildings, department stores and other areas where the public has frequent access. Such an approach would more properly determine the true population exposure to benzene. This brings us to our major concern which is the failure to address indoor air quality.

Indoor Benzene Levels Cannot be Ignored.

Appendix E to the report presents the details of the methodology used to develop estimates of annual average concentrations of benzene in the South Coast Air Basin. The Appendix states that: "indoor benzene concentrations may not be directly related to ambient concentrations. This study makes no attempt to examine indoor exposure." (Appendix E, p. E-13.) This is a serious deficiency in the Part A report because current research is showing that indoor benzene levels are significant and must be evaluated in determining what, if any, controls on benzene emission sources should be required.

The report states that "very few data on benzene concentrations are available and no data are available for California." (p. IV-4.) This is only partially true. Research Triangle Institute ("RTI"), under contract to EPA, has completed an extensive data collection effort involving over 600 individuals in Los Angeles and Contra Costa Counties. As was done by RTI in its earlier studies for EPA in Elizabeth and Bayonne, New Jersey (the "EPA study"), indoor overnight air samples and comparative outdoor overnight ambient air benzene concentrations were studied. We are informed that all data collection in California has been completed and that RTI is currently conducting an analysis of the data. According to EPA, the findings should be available by December of this year. If the findings from the California studies are in any way similar to those for the New Jersey studies, this information must be addressed.

With regard to the EPA study, your analysis appeared to ignore a number of significant findings. Specifically, the study found that (1) there is no relationship between ambient indoor benzene concentrations and nearby outdoor air; (2) the indoor ambient benzene concentrations are significantly greater than outdoor concentrations; and (3) there does not appear to be any direct relationship between exposure and dosage.

With regard to the first point, relationship between indoor and outdoor benzene levels, you correctly note that there are various indoor sources of ambient benzene, most importantly, tobacco use. Other indoor sources of benzene include appliances, heating, air conditioning and unvented heaters.

With regard to indoor benzene levels we know that indoor concentrations are significantly greater than outdoor levels. The EPA study, based on a probability sample of 97 homes, found that indoor ambient benzene concentrations were between 2.3 or 3.5 times greater than outdoor concentrations, depending upon whether the comparison was based on the arithmetic mean or median value. It should be noted that even greater differences were found in a study conducted for the Consumer Product Safety Commission (the "CPSC study") by the Oak Ridge National Laboratory ("ORNL") which was also reviewed by your staff.

With regard to the relationship between exposure and dosage, data developed by RTI for the EPA study also shows that the relationship is, at best, extremely complicated. Figure VII-22 of the RTI report shows a natural logarithemic plot of breath versus daytime personal air measurements. While the Spearman correlation of .17 for all measureable values is statistically significant, it demonstrates that there is no direct relationship between the daytime exposure (as measured by daytime personal air) and dosage (as measured by breath concentrations). It may well be that ambient benzene dosage received by individuals is far more a function of individual behavior, particularly smoking, than to exposure to ambient benzene in the air.

Turning now to your evaluation of the CPSC study's interim report on concentrations of volatile organic compounds in indoor and outdoor air, we have the following comments. The statement that this "report discusses only a limited data from one house" is incorrect. Forty houses were studied. Furthermore, the major conclusions of the study should have been discussed. Those conclusions were:

1. A greater number of the volatile organic chemicals were present indoors than outdoors (ten or less were observed outdoors and over 150 indoors).

2. The indoor levels of volatile organic chemicals are generally ten-fold greater than outdoor levels.

3. The reported potential health effects of the identified volatile organic chemicals include carcinogenic, mutagenic, embryotoxic and allergenic effects, as well as irritation of mucous membranes and damage to the central nervous system. An open question remains as to which of these effects may be manifested at the levels found. While there may be problems in the way in which the CPSC study was conducted, this information cannot be discounted altogether.

The importance of indoor air quality findings involves more than the fact that indoor benzene levels are higher than outdoor benzene levels. The current literature on "time budgets" indicates that the majority of persons spend over 70 percent of their time indoors. In fact, research on time budgets has revealed that urban residents generally spend about 90 percent of their time indoors, with one study finding that even young middle-aged men spend no more than an hour a day on average, outdoors.*/ As a result, most people's exposure level is dominated by indoor air, not outdoor air.

While it is true that data on indoor air quality are limited, the data that are available have staggering implications. Soon data will be available on indoor versus outdoor air quality in California. For this reason, the indoor air quality studies cannot be ignored because they have a direct bearing on the types of controls that should be adopted and how effective any control can be.

In conclusion, we ask that our concerns be incorporated into the report or, alternatively, that this letter be sent to the SRP with the report. With regard to the issue of indoor air quality, we strongly recommend that a great deal more attention be given to the role of exposure to indoor benzene levels.

Sincerely,

Robert Harrison

Robert N. Harrison
Assistant General Manager

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*/ Hinckle, L. E., and S. H. Murray. "The Importance of the Quality of Indoor Air." In "Symposium on Health Aspects of Indoor Air Pollution," 57 Bulletin of the New York Academy of Medicine 10, 828 (December 1981).

STATE OF CALIFORNIA
GEORGE DEUKMEJIAN, Governor

AIR RESOURCES BOARD
1102 Q STREET
O. BOX 2815
ACRAMENTO, CA 95812

September 12, 1984

Mr. Robert H. Harrison
Assistant General Manager
Western Oil and Gas Association
727 W. Seventh Street
Los Angeles, CA 90017

Dear Mr. Harrison:

Subject: Comments of August 31, 1984, on Part A of the Draft Benzene Report

Thank you for your comments on Part A of the benzene report to the Scientific Review Panel. Your letter and this response will become part of Appendix B of the final report. We will send you a copy of the final report. Our responses follow under the headings you have in your letter.

Estimates of Benzene Emissions from Motor Vehicles Overstated

We have reviewed our calculations based on the API study that you cited and will revise the figures for benzene in total exhaust hydrocarbons as follows: non-catalyst - 4.2 percent, catalyst - 4.1 percent. The emission projections will be revised accordingly.

These values differ from those obtained through a simple averaging of all API data. The API data taken on catalyst-equipped cars include many from runs using unleaded fuels with aromatic contents far below those typical of gasoline consumed in California (43 percent by weight, according to our data). To estimate emissions from catalysts, we used only API data taken on fuels with aromatic contents between 38 wt. percent and 54 wt. percent.

ARB and API used the same data to estimate non-catalyst factors of 4.2 wt. percent and 3.5 wt. percent, respectively. API's recalculation of the original data resulted in a lower wt. percent factor. We are retaining the 4.2 wt. percent factor for non-catalyst vehicles.

Inadequacy of the Data Base

We realize that the four monitoring stations as a group may be too near major roadways to typify most residential receptors. (However, two of them are also

criteria pollutant stations and thus are located according to guidelines for obtaining representative data.) Nevertheless, any near-road bias in the benzene concentrations at the stations should be removed by using CO measurements at 31 other monitoring stations as surrogate benzene measurements. The average value across the basin derived by that technique is, appropriately, 20 percent lower than the average measurement among the four benzene monitors.

Indoor Benzene Levels Cannot be Ignored

You state that indoor benzene levels are significant and cannot be ignored in determining benzene exposure and in developing control measures. We agree that indoor air exposures to toxic air contaminants may be an important factor to consider in the risk management phase during which the Board will consider adoption of toxic control measures. However, during the risk assessment (substance identification) phase, AB 1807 requires the Department of Health Services to consider ambient concentrations and risk of harm to public health from exposure to these ambient concentrations.

In regard to the CPSC study, the interim report provided benzene data only for one house although the study included forty houses. We are hopeful that the final report will include benzene data for all forty houses.

We are pleased to learn that you are gathering information on ambient benzene concentrations in the South Coast Air Basin. We would appreciate receiving a description of the study in progress and the results when the study is completed.

Thank you again for your comments. If you wish to discuss these comments more or if you have further questions on the report, please contact Barbara Fry at (916) 322-8276.

Sincerely,

Donald J Ames for

William V. Loscutoff, Chief
Toxic Pollutants Branch
Stationary Source Division

STATE OF CALIFORNIA
GEORGE DEUKMEJIAN, Governor

AIR RESOURCES BOARD
1102 Q STREET
P.O. BOX 2815
SACRAMENTO, CA 95812

July 27, 1984

Dear Sir or Madam:

Subject: Department of Health Services' Report on Benzene (Part B)

In my June 20, 1984, letter informing you that Part A - "A Review of Benzene Uses, Emissions, and Public Exposure" of the benzene report for the Scientific Review Panel (SRP) was available for review, I indicated that the Department of Health Services (DHS) portion of the report, Part B - "A Review of Benzene Health Hazards," would not be available for review until the final report is submitted to the SRP. However, on July 25, 1984, we received the final version of Part B from DHS. We now expect to submit the full report to the SRP in about 30 days and are making Part B available prior to its formal submittal to the SRP. I am also making it available now so that when we formally submit the report to the Panel we can also provide them with any written comments you may have on Part B.

If you would like to obtain a copy of the Part B report, please call our Public Information Office at (916) 322-2990 or send your request to the attention of:

Public Information Office
Re: Benzene Report - Part B
California Air Resources Board
P. O. Box 2815
Sacramento, CA 95812

In order for your comments to be included in our submittal to the SRP, we are requesting that comments on the Part B report be submitted to us by August 30, 1984. Written comments should be sent to:

William V. Loscutoff, Chief
Toxic Pollutants Branch
Air Resources Board
P. O. Box 2815
Sacramento, CA 95812

We are also updating our mailing list. If you wish to remain on the list, please return the enclosed form by August 30, 1984. If we do not hear from you by that date, we will assume you wish to be deleted from our mailing list.

Sincerely,

Peter D. Venturini, Chief
Stationary Source Division

Enclosure

cc: Alex Kelter
Assemblymember Sally Tanner

STATE OF CALIFORNIA
GEORGE DEUKMEJIAN, Governo

AIR RESOURCES BOARD
1102 Q STREET
P.O. BOX 2815
SACRAMENTO, CA 95812

September 12, 1984

Dear Sir or Madam:

Subject: Your Comments on the Department of Health Services' Report on Benzene (Part B)

Thank you for your comments on Part B of the benzene report for the Scientific Review Panel (SRP). Your comments have been forwarded to the Department of Health Services for review. Also, your comments will be appended to the final benzene report which will be submitted to the SRP in a few days.

Sincerely,

Donald J. Ames for

William V. Loscutoff, Chief
Toxic Pollutants Branch
Stationary Source Division

AMERICAN LUNG ASSOCIATION
of CALIFORNIA

August 17, 1984

William V. Loscutoff, Chief
Toxic Pollutants Branch
Air Resources Board
P.O. Box 2815
Sacramento, Ca. 95812

Dear Mr. Loscutoff:

The Health Effects of Benzene, Part B of the Report on Benzene, is a good and reasonable document based on data available. We have no additional information for the Scientific Review Panel.

The possible health effects of benzene from exposure to indoor air is of concern. The point was raised in Part A of the Report but not addressed. It was considered beyond the scope of this document which responds to the statutory direction of AB 1807. We believe indoor exposure to benzene may be a more significant problem. We recommend that it be addressed by the Department of Health Services because there is a public health responsibility to do so, even without a specific legislative mandate.

Thank you for the opportunity to review the Report.

Yours truly,

Gladys Meade

Gladys Meade
Environmental Health Director

cc: Dean Sheppard, M.D.
California Thoracic Society

GM/br

ARCO Petroleum Products Company
515 South Flower Street
Los Angeles, California 90071
Telephone 213 486 8750

David A. Smith
Consultant
Environmental Regulatory Compliance

August 30, 1984

William V. Loscutoff, Chief
Toxic Pollutants Branch
Air Resources Board
Post Office Box 2815
Sacramento, California

Dear Mr. Loscutoff:

Attached are brief ARCO Petroleum Products Company (APPCo) comments on the California Air Resources Board preliminary draft report entitled, "Part A - A Review of Benzene Uses, Emissions and Public Exposure." APPCo personnel also contributed to and fully support the comments submitted to you by the Western Oil and Gas Association (WOGA) on Part A and the associated Department of Health Services Part B report entitled, "Health Effects of Benzene."

In particular, we wish to emphasize WOGA's point that the DOHS did not present the "range of risks to humans resulting from current or anticipated exposure" of benzene required by the Health and Safety Code Section 39660(c). A range of risk determination requires the use of various assumptions and methods to evaluate risks at certain dose levels. DOHS failed to do this. This omission is exemplified in the Department's dismissal of data from human studies which have been used by all other governmental agencies in assessing human benzene exposure risks. It is these types of problems that make us believe the Part B report is seriously deficient.

If you wish to discuss any of the attached comments on Part A, please call me at the above phone number. Please call Dr. Charles Lapin at 213/486-3825 if you have questions with regard to Part B which you wish to discuss with us.

Sincerely,

D. A. Smith
Consultant, Environmental/Health Planning

DAS/bf
Attachment

cc: Dr. C. A. Lapin

California Chamber of Commerce

August 29, 1984

Mr. William V. Loscutoff, Chief
Toxic Pollutants Branch
Air Resources Board
P.O. Box 2815
Sacramento, CA 95812

Dear Mr. Loscutoff:

Thank you for the opportunity to comment on the report entitled "Health Effects of Benzene, Part B".

A task force comprised of representatives from the California Environmental Health Group and the Chemical Industry Council of California has reviewed the benzene report. The attached comments express this group's concerns.

As you may know, the California Environmental Health Group (CEHG), was organized by the California Chamber of Commerce to achieve industry's concurrence on issues concerning the state's development of a cancer policy.

Our review essentially agrees that benzene should be listed as a toxic airborne substance in California. However, our task force strongly disagrees with the report's approach to risk assessment, and thus, the conclusions that derive from that approach. It is our view, that the role of the Department of Health Services (DHS) in this process is to scientifically assess the effects of benzene exposure, using appropriate risk assessment models. This report wanders off into opinion and selective assumptions which give it a distinct bias rather than the objective fact finding posture of scientists.

We believe the Science Review Panel will be sufficiently concerned with the quality of the benzene report to return it to the DHS so that it may remove its many subjective comments and to broaden its information concerning risk assessment models.

Sincerely,

John T. Hay
President

JTH:jc
Enclosure

1027 10th Street, 4th Floor · P.O. Box 1736 · Sacramento, CA 95808 · (916) 444-6670

Comments on the Benzene Health Assessment Document

Prepared by a task force of the

Chemical Industry Council of California

in association with the

California Environmental Health Group

The following comments on Part B, HEALTH EFFECTS OF BENZENE are primarily directed at the approach to risk assessment applied by the Department of Health Services(DHS) rather than to the interpretation of the data applicable to the specific substance. While we question some of the data interpretations, detailed technical criticisms would require more time than has been allowed for comment.

We strongly support the use of the risk assessment technique in the regulatory process. We acknowledge that the term, "risk assessment" is ill-defined and that no universally accepted standards exist for the risk assessment process. We further acknowledge that this is a newly devised and rapidly developing technique in which virtually all elements are clouded with uncertainty.

Irrespective of these shortcomings, we believe that the risk assessment technique offers the best available basis for fulfilling risk management responsibility.

In that context, we offer these comments with the hope that they will contribute to the improvement and clarification of the risk assessment process so that it will develop into a valuable tool for the use in the management of hazardous substances.

Our comments are divided into four subject areas for ease of discussion. These areas are not discrete and some overlap in comment necessarily occurs.

A. Separation of the Risk Assessment and Risk Management Functions

1. Background

- AB1807(Tanner) - Chapter 1047, September 23, 1983; pioneered the statutory mandate of the risk assessment process in regulatory affairs. A primary provision of this law is the functional separation of risk assessment and risk management.

  While the inclusion of this principle pre-dated by some months the publication of the National Research Council's(NRC) report entitled, Risk Assessment In The Federal Government: Managing The Process, the subject was discussed extensively by all interested California parties prior to its acceptance. The adoption of that

principle into the regulatory process was a primary recommendation of the NRC Committee.

- In the same report, the NRC committee debated at length the propriety of organizationally separating these responsibilities by placing the authority for each in different agencies.

  Not having the benefit of the NRC Committee's thinking, and because of California's particular organizational structure, responsibility for risk assessment was assigned to the Department of Health Services, and that for risk management to the California Air Resources Board and (in the case of pesticides) to the Department of Food and Agriculture.

  A major factor in that choice was the desire to encourage, to the maximum extent possible, a clear separation of scientific determinations from societal judgments so that the latter could be based on the best available scientific knowledge. The benzene assessment document indicates that the goal was not fully realized.

- The DHS benzene report represents the initial attempt at implementation of AB1807. Contrary to the goal of this legislation, the benzene document intermingles scientifically established fact with policy considerations.

  Just such a pitfall is warned against in the NRC report (page 142):

  > "Organizational arrangements that separate risk assessment from risk management decision-making will not necessarily insure that the policy basis of choices made in the risk assessment process is clearly distinguished from the scientific basis of such choices."

  A review of the DHS benzene report reveals a recurring pattern of an admixture of scientific fact and risk management policy considerations without a clear distinction made between the two.

2. Specific Comment

- Explicit examples of risk management policy considerations included in the document are (emphasis added):

  * "Since the threshold dose for the human population should be the threshold dose for the most sensitive individual; this dose may be so low as to be effectively zero."(Page 49)

  * "The ARB is encouraged to use the assumptions stated above for regulatory purposes."(Page 80) (emphasis added)

- Many examples of implied policy statements can be found throughout the document. Inclusion of such statements not only confuse the uninitiated reader but clearly infringes on the risk management prerogative. Advocacy of specific risk management policies would best be reserved for the public hearing provided for in §39666(a) of AB1807.

B. Inferential Bridges

1. Background

- In the assessment of the risk from exposure to a suspected human carcinogen for regulatory purposes, it is necessary to adopt assumptions at many points in the process because the cause of cancer and the operative mechanisms are unknown. The NRC report justifies the use of these "inferential bridges" as necessary to provide a complete data base from which the risk assessment proceeds.

2. Specific Comments

- The benzene document proceeds from a single set of selected assumptions (both stated and implied) about the causation and mechanism of cancer, then presents selected data which support those assumptions.

  In the case of the benzene assessment, there can be no argument about any of the individual "inferential bridges" adopted by DHS. Each represents a logical assumption in the light of current scientific knowledge.

  Because this subject is esoteric, alternative assumptions of equal scientific validity should be presented in parallel. This would make clear to the non-specialist reader that differing valid conclusions can derive from the same data.

- A second concern with the DHS document is the lack of clearly stated assumptions and science policy decisions. Scientific tradition dictates that the reporter make clear to the reader the distinction between a statement of established scientific fact and an assumption adopted by the author as an "inferential bridge" (see previously cited NRC report).

  In the May 22, 1984 Federal Register, the Office of Science and Technology Policy(OSTP) published Chemical Carcinogens; Notice of Review of the Science and Its Associated Principles. Principle #29 states:

  > "While several considerations often enter the risk assessment process, it is most important to maintain a

clear distinction among facts (statements supported by data), consensus (statements generally held in the scientific community), assumptions (statements made to fill data gaps), and scientific policy decisions (statements made to resolve points of current controversy)."

The final paragraph of Chapter 6.II.D of the OSTP document states:

"Finally, it is important in the characterization of human cancer risk to summarize briefly any judgments or assumptions that may have entered into the risk assessment process to insure that they are clearly differentiated from scientific fact.(1)"

The DHS' method of presentation appears to be in conflict with this principle. The assumptions upon which the assessment is based are vaguely stated and scattered throughout the report. Identified examples of stated or implied assumptions include (emphasis added):

* "In a case such as benzene, where general biological evidence does not strongly suggest a threshold, the staff of DOHS recommends treating the substance as if it had no threshold." (Pages 1/2, Exec. Summ.)

* "Chromasomal abnormalities may occur at lower levels than previously thought and may represent a state which carries an increased risk of cancer." (Page 2, Exec. Summ.)

* "...the staff of the DHS considers that benzene should be treated as a substance without a carcinogenic threshold."(Page 2, Exec. Summ.)

* (Re:low dose extrapolations) "Such extrapolations depend on many assumptions, each with its own uncertainties." (Page 2, Exec. Summ.)

* "Since employed people tend to be healthier than the general population, we would expect to see less disease and death in a group of workers. Therefore, use of the general population as the control will overestimate the number of cases of disease we would expect to see in the workers and thus obscure our ability to detect a small increase in the workers' rate of disease."(Page 43)

* "But the processes of carcinogenesis appear to be qualitatively different from those in classical toxicology."(Page 46)

* "This scenario, so different from classic toxicologic

processes, makes a threshold less likely for carcinogenesis."(Page 46)

* "Therefore, since we cannot know which of the possible carcinogenic mechanisms are already operating and contributing to background incidence, we will assume that no additional exposure, however small, may be considered free of risk."(Page 47)

* "For this reason, the staff of the DHS as a general rule assumes that an identified carcinogen has no threshold and does not distinguish between "genetic" (directly acting on DNA) and "epigenetic" (not directly acting on DNA) carcinogens for the purposes of identification or dose-response assessment."(Page 47)

* "However, this model produces a threshold by requiring that the carcinogen be instantaneously deactivated, which is unlikely."(Page 48)

* "If this were true, chromosomal damage due to low-level exposures to benzene could cause cancer."(Page 51)

* "Because of the inability to completely resolve many of the criticisms of the CAG benzene risk assessment, the staff of DHS has elected to base its risk assessment on data available from recent animal bioassays (NTP 1983) although for purposes of comparison the staff of DHS will cite the Rinsky re-evaluation of the Infante study used in the CAG assessment."(Page 56)

* "Although it could be argued that these chronic toxicological insults from high doses of benzene could be responsible for the carcinogenic response to benzene, the staff of DHS believes that the evidence supporting this theory (cytotoxicity) is insufficient and at present there does not appear to be convincing scientific or public health grounds to justify incorporating the cytotoxicity theory in the risk assessment process."(Page 71)

* "In the absence of decisive empirical evidence as to the best scaling factor, the staff of DHS has adopted the convention of scaling the dose rate by body surface area, a procedure routinely used by pediatricians for calculating medical doses for babies and children."(Page 73)

* "Except when relevant pharmacokinetic data on both humans and animals and data which allow a time-to-tumor type model are available, the staff of the DHS prefers the multistage model."(Page 79)

* "To account for the possibility of dose additivity to background carcinogens, the staff of the DHS recommends using the linearized 95% upper confidence level."(Page 85)

- The Executive Summary of the DHS document (which is all that many individuals are likely to read) presents a collage of scientific fact, assumptions, and scientific policy decisions without a distinction of which is which. This may (or may not) develop a large misinformed constituency for the document.

- Pages 1 through 30 properly contain, in the main, a citation of scientific data, most of which enjoys science community consensus.

  In contrast, Pages 31 through the first half of 35 consist solely of a summary of the controversial principles (science policy decisions) contained in the original draft of the California Carcinogen Policy. Contrary principles based on equally valid scientific data are either not presented or are dismissed with only superficial justification. No clear distinction is made between fact and assumption.

- A second glaring example of policy considerations following scientific data begins with the last paragraph on page 85 and continues through the end of page 87.

C. AB1807 Mandate For Conducting The Health Assessment

1. Background

- AB1807 sets out the requirements for DHS in conducting an evaluation prior to proposing the designation of a substance as a toxic air contaminant. In addition to the general requirements that DHS shall consider all available scientific data (§39660(b)), it shall also assess the availability, and quality of data on health effects, including potency, mode of action and other relevant biological factors of the substance (§39660(c). Finally, AB1807 specifies the manner in which results of the evaluation are to be reported (§39660(c), second paragraph). This important provision dictates a variety of requirements and requires careful consideration. Because of its importance, the second paragraph of §39660(c) is included in its entirety:

  > "The evaluation shall also contain an estimate of the levels of exposure which may cause or contribute to adverse health effects and, in the case where there is no threshold of significant adverse health effects, the range of risk to humans resulting from current or anticipated exposure."(emphasis added)

- The intent of this subsection is two-fold; first, to differentiate

between the clearly identifiable levels of a toxic air contaminant which cause or contribute to adverse health effects and those in which the level of causation is less ascertainable, i.e., no threshold of effect.

Secondly, in the case where the levels causing or contributing to an adverse effect are not clearly ascertainable, the intent is to define a range of risk to humans from current or anticipated exposure where the risk of an adverse health effect is determined to be significant.

The following table illustrates how these provisions would apply in the case of benzene.

Adverse Health Effect = Leukemia

Threshold?	Level causing or contributing to adverse health effects	Is there significant risk of adverse health effects	What is the range of risks?
YES	DHS Report	Not Applicable	Not Applicable
NO	Not Applicable	DHS Report	DHS Report

The DHS health evaluation circumvents the scientific analysis mandated by AB1807 by imposing policy decisions which will make it difficult for risk managers to understand (1) whether or not a threshold exists, (2) whether or not the risk of adverse health effects of benzene are significant and (3) the range of those risks to humans.

* Determination of a threshold for adverse effects.

  The DHS report does not directly address this question. Instead, it discusses thresholds as they relate to data interpretation and extrapolation models. The report effects a strong policy bias within DHS to deny thresholds for carcinogens. For example, the report's discussion of thresholds is based on the premise on page 45:

> "There is a theoretical reason to believe, however, that the carcinogenic effect of benzene or indeed of any carcinogen could convey a low probability of causing cancer at very low doses. A small probability applied to a large population can produce an unacceptable number of cancers, hence the concern with the possible 'no threshold' properties of carcinogens like benzene."

This statement of policy, again a function of risk management not of science, colors the discussion of the conceptual mechanisms to explain the observed no effect threshold in several detailed epidemiology studies as well as the animal bioassays.

Unlike other substances where we must rely solely on animal data, the health effects of benzene exposure have been studied extensively in human populations. In the case of benzene, we need not rely solely on an extrapolation from animal to man, but rather can observe a threshold of significant effects in those populations.

With this knowledge, experimental data can be properly applied to fairly extrapolate a practical or operational threshold to a value which takes into consideration individuals more sensitive than workers, and which incorporates a sufficient margin of safety to correct for insufficient resolving power of epidemiology. This approach is consistent with the Federal OSTP GUIDELINES which recommends in Principle #25:

> "Decisions on the carcinogenicity of chemicals in humans should be based on considerations of relevant data, whether they are indicative of a positive or negative response and should use sound biological and statistical principles. This weight of evidence approach can include consideration of the following factors and should give appropriate weight to each on a case-by-case basis:
>
> (a) findings from long-term animal studies
>
> (b) results from epidemiological studies."

DHS, in the final analysis, ignores human epidemiology opting instead for linear extrapolation of the incidence of preputial gland tumors found only in rodents. The Department supports this position by establishing a standard not included in statute for deciding whether a threshold can be determined. The report states, "...the staff of DHS as a general rule assumes that an identified carcinogen has no threshold..."(page 47) and "To argue for a threshold, the staff of DHS would require strong positive evidence that benzene acts only through mechanisms which ought to have a threshold."(emphasis added) (page 1) or" compelling arguments" (page 2).

AB1807 includes no such criteria, instead it prescribes

either an "...estimate of the levels of exposure which may cause or contribute to adverse health effects and in the case where there is no threshold of significant adverse health effects, the range of risk to humans."(emphasis added)

- Significant adverse health effects

  * The question of whether benzene exposures pose a significant risk of adverse health effects, at least in worker populations, was closely examined by the U.S. Supreme Court in the OSHA Benzene Standard Case (Industrial Union Department, AFL-CIO v. American Petroleum Institute, 8 OSHA 1586). Although that case dealt with a different law and its focus was on a standard proposal to reduce worker exposure from 10 to 1 ppm of benzene, the court's reasoning in applying the term 'significant risk' as the prerequisite for more stringent regulation of benzene by OSHA, is certainly germane to the review of the health effects assessment under AB1807.

    In the OSHA case, many of the same worker epidemiologyy studies and extrapolations presented in the DHS report were examined. Yet the court, in reviewing all the evidence, could not find an OSHA showing of a significant risk of leukemia for workers exposed to 10 ppm of benzene over a 50 year working lifetime. This is an exposure approximately 35,000 times greater than the 0.1 ppb exposure at which DHS has estimated a 17 in a million risk and nearly 7,000 times greater than the ARB has estimated to be the exposure of the entire California population.

  * The DHS report has attempted, through one conservative assumption piled on top of another, to convince the ARB that the public in California exposed to 4.6 ppb will experience 233 excess cancer deaths.This is a projective precision which probably exceeds the limits of technology.

  * The conservative assumptions responsible for these risk estimates are (emphasis added)

    > A policy decision to use the Krump Multi-Stage Model) to extrapolate carcinogenic response data from high dose to low dose, and directly from animals to man (with slight corrections for body size).
    >
    > There are other models available for this purpose which equally fit the data in the observable range. At a minimum, a range of estimates using alternative models as required by AB1807, should have been tested.
    >
    > Principle #26 of the OSTP Guidelines states,

"No single mathematical procedure is recognized as the most appropriate for low dose extrapolation in carcinogenisis."

* Rejection of alternative theories compromised the selection of models with different slope or a functional threshold.

At a minimum, DHS should have described how these approaches would have affected the range of risks estimate. Rejection of one such approach, 'the pharmacokinetics model', on the basis that metabolites must be "instantaneously deactivated" for it to to be plausible (page 48), is not supported by science or logic.

The metabolic pathway presented on page 7 indicates that benzene is metabolized into a generally accepted carcinogenic moiety. - benzene oxide/epoxide - which subsequently is further metabolized into various non-carcinogenic species including phenol or conjugated with glutathione and tissue macro molecules.

These biochemical processes provide ample justification to seriously consider a theory which postulates a finite conversion rate of benzene to oxide/epoxide and with rapid deactivation to non-carcinogenic species. Unless one dogmatically accepts the 'one-hit theory', substantial evidence exists to support a functional threshold based on this pharacokinetic approach.

Recent work in this area, not referenced in the DHS document has just come to our attention. This was done by E. J. O'Flaherty and M. Andersen and will be published in November 1984 by the National Science Foundation in State Of The Art In Risk Assessment. A pre-publication copy is attached for your information.

Salient conclusions from this work are:

"The most important single application of pharmacokinetic principles is to quantitation of the relationship between applied or administered dose and effective or delivered dose, defined as the concentration or amount of toxic agent reaching the receptor sites. Administered dose is rarely congruent with effective dose. Over narrow ranges, especially at low doses, effective dose may be proportional to applied dose. But as dose (or exposure) increases, the likelihood that applied and effective dose are not proportional increases also. Specifically, within the range

of the maximum tolerated dose (MTD) and the ½ MTD, doses that are routinely used not only in carcinogenic bioassays, but also in the evaluation of other kinds of toxicities, careful and thorough studies with a variety of compounds have shown that effective and administered dose are not linearly related. Dose dependence of metabolism has been demonstrated for vinyl chloride (Watanabe et al., 1976, 1978), for 1,1-dichloroethylene (McKenna et al., 1978a, b; Andersen et al., 1979), for methylene chloride (Ott et al., 1983), for styrene (Ramsey and Andersen, 1984; Andersen et al., 1984), and for trichloroethylene and perchloroethylene (Buben and O'Flaherty, 1984), among others. The pervasiveness of dose-dependent pharmacokinetic behavior at exposures large enough to be toxic is now well established. Its consequence is that high-dose data, such as those usually obtained in animal studies, cannot be extrapolated directly into the low-dose range. Unless the pharmacokinetic basis of the relationship between administered and effective dose is understood and is incorporated into the extrapolation process, extrapolation from high to low doses is not biologically defensible."(emphasis added)

* Use of delivered dose (page 45) as the basis for risk assessment adds additional conservation to the risk estimate because about 50% of benzene administered has been shown to be exhaled even when the route of administration is by gavage. Also, this focus on delivered dose misses the point cited above regarding benzene metabolism and effective dose.

* Other compounding assumptions: 95% upper confidence level data plugged into models, most sensitive species/most sensitive organ.

- Range of risks

* As has been discussed above, AB1807 requires DHS to present the range of risk when no threshold is found for significant adverse health effects. Although DHS mentions alternative theories (but not alternative risk assessment procedures) it merely discredits them and presents only a single estimate of risk. This approach appears to be inconsistent with the AB1807 requirements and objective scientific analysis intended for scientific peer review.

Further, OSTP Guideline #27 states,

"...quantification of the various sources of uncertainty involved can be as important as the projection of the risk estimate itself."

This implies the desirability for the presentation of a range of risks rather than a single value as presented in the DHS document.

* DHS has used a single mathematical model and applied it to the findings of several different animal bioassys and epidemiological studies (See Table VI-5, Pages 73/75 and Figure VI-2, Page 84).

  Because each mathematical model derives from a variety of facts, consensus, and assumptions (inferential bridges), the selection of a single model automatically introduces biases. Scientific policy decisions are implicitly adopted by this approach.

  The resulting quantification of risk is valid only if the assumptions are valid. Application of other assumptions of equal scientific validity would result in markedly different conclusions.

* It would be more appropriate, in response to the AB1807 mandate for the presentation of a range of risks, to apply several models which fit the data to the same study populations and to depict the range of risks represented by those applications. This would provide valuable insights into the validity of the theoretical life time risks.

  In the case of the DHS assessment, if the stated theoretical lifetime risk at an exposure level of 0.1 ppb (page 85) is applied in the strictest sense to the Infante/Rinsky et al. population, more cancer deaths (by several orders of magnitude) would appear to be generated than were actually observed for all causes of death in the study population. It would be helpful to see the results of this same application of theoretical risks derived from the use of other models.

* The presentation of these kinds of data to the individuals statutorily responsible for risk management would facilitate arrival at a more realistic judgement concerning the actual likely risk from exposure to the substance. This is, after all, the primary purpose of the risk assessment process.

  The benzene document presents no alternative assessments based on different assumptions. Thus, the individuals responsible for risk management will be left with a single choice of policy. This is contrary to the AB1807 mandate that a range of risks be presented when inadequate evidence

of a threshold is encountered.

D. Manner of Data Interpretation Presentation

- In a number of instances the document presents data in a way which tends to place undue emphasis on equivocal data without making it clear that the corollary is equally likely. In the document this is done by the use of the words 'may' and 'might' to precede an interpretation following the presentation of a fact.

  Examples of this type of ambiguity include (emphasis added):

  * "Toxic doses may retard fetal development.(Page 30)"

  * "There is some evidence that high and prolonged exposure to benzene may affect menstrual and reproductive function."(Page 30)

  * "...the staff of DHS does wish to point out that a larger epidemiological study might indeed implicate benzene in the causation of cancer at sites other than the hematopoietic system."(Page 42)

  * "While not wishing to put too much emphasis on significance testing in this particular study, staff does wish to emphasize that a larger epidemiological study might indeed implicate benzene in the causation of cancer at other sites than hematopoetic(sic) system."(Page 82)

- Other examples of variations on this fallacy include the citing of non-significant statistical data to support preconceived assumptions while dismissing statistically significant data when they do not support the 'pattern'. In some instances, there is the citation of non-significant statistical data followed by a "this may prove, etc.", without a concomitant, "may not prove".

- In other instances where alternative assumptions are presented, they are dismissed with such phrases as "which is unlikely" even when such assumptions are accepted by a significant segment of the scientific community.

- Examples of these fallacy are found on Pages 38, 39, 42, 63, 81 and 82. An interesting example is a statement regarding the association between aplastic anemia and leukemia in which "are said to" on page 25 becomes "are" on page 35. A reading of these pages with this perspective in mind will provide adequate examples.

NSF: State of the Art in Risk Assessment

VI. Pharmacokinetic Methods in Risk Assessment

Ellen J. O'Flaherty, Ph.D.

and

Mel Anderson, Ph.D.

Nov. 1984
(pre-publication)

Pharmacokinetics is an independent area of specialization in the sense that it can be discussed independently of other aspects of dose-response assessmen in humans and animals. But pharmacokinetic techniques have utility only to t extent that they can contribute to resolution of dose-response relationships in animals and in humans and to biologically reasonable species-to-species conversions of dose-response relationships. Pharmacokinetic principles can also facilitate conversions among equivalent doses when route and duration of exposure differ, and can contribute to definition of conditions under which such conversions are not justifiable.

The most important single application of pharmacokinetic principles is to quantitation of the relationship between applied or administered dose and effective or delivered dose, defined as the concentration or amount of toxic agent reaching the receptor sites. Administered dose is rarely congruent with effective dose. Over narrow ranges, especially at low doses, effective dose may be proportional to applied dose. But as dose (or exposure) increases, the likelihood that applied and effective dose are not proportional increases als Specifically, within the range of the maximum tolerated dose (MTD) and 1/2 MTD, doses that are routinely used not only in carcinogenicity bioassays but also in the evaluation of other kinds of toxicities, careful and thorough studies with a variety of compounds have shown that effective and administered dose are not linearly related. Dose dependence of metabolism has been demonstrated for vinyl chloride (Watanabe et al., 1976, 1978), for 1,1-dichloroethylene (McKenna et al., 1978a, b; Andersen et al., 1979), for methylene chloride (Ott et al., 1983), for styrene (Ramsey and Andersen, 1984; Andersen et al., 1984), and for trichloroethylene and perchloroethylene (Buben and O'Flaherty, 1984), among others. The pervasiveness of dose-dependent pharmacokinetic behavior at expo-

sures large enough to be toxic is now well established. Its consequence is that high-dose data, such as those usually obtained in animal studies, cannot be extrapolated directly into the low-dose range. Unless the pharmacokinetic basis of the relationship between administered and effective dose is understood and is incorporated into the extrapolation process, extrapolation from high to low doses is not biologically defensible.

Two examples of the kinds and magnitudes of errors that can be introduced if extrapolations are carried out without regard for kinetic behavior will be shown and briefly discussed. In the first, production of an active metabolite is capacity-limited at high doses; in the second, exposure to active agent increases disproportionately at high doses.

Vinyl chloride, which is associated in humans with development of the rare tumor, hepatic angiosarcoma, also causes hepatic angiosarcoma (as well as other tumors) in rats. The prevalence of angiosarcoma in vinyl chloride-treated rats reaches a maximum at intermediate vinyl chloride dose rates and does not increase further with further increases in vinyl chloride dose rate (Maltoni and Lefemine, 1975) (Figure 1a). When Gehring et al. (1978) expressed prevalence as a function of the rate of biotransformation - that is, of the rate of formation of an active metabolite - the plateau in the dose-response curve disappeared (Figure 1b). The dashed extrapolation line in Figure 1a shows clearly that extrapolation from even the low-dose range of the administered dose-response curve tends to underestimate the slope of the true dose-response relationship. Extrapolation from the high-dose range leads to gross overestimation of the carcinogenicity of low doses of vinyl chloride.

Urethane (ethyl carbamate), a compound that is not known to be tumorigenic in humans, produces multiple pulmonary adenomas in mice. In this case, the

dose-effect relationship (Figure 2a) shows an increasing incremental rise with dose (Sichak and O'Flaherty, 1984). The active moiety in urethane adenogenesis has not been unequivocally established. However, when tumor incidence, expressed as a function of the area under the curve of urethane concentration in the blood versus time, a measure of effective dose, the relationship between dose and effect is linear (Figure 2b). In this case, linear extrapolation of effect out of the high-administered-dose range would have underestimated the adenogenicity of low doses of urethane.

In Figures 1 and 2, the relationships between administered and effective doses are different, and the expressions of effective dose (rate of metabolism, and area under the concentration curve) are different. Practical techniques for incorporation of pharmacokinetic information into evaluation of dose-response relationships can be resolved into techniques for addressing two questions: (1) What is the effective dose - that is, how is it to be measured? and (2) What is the relationship of administered to effective dose? These questions can be inextricably interrelated in practice: for example, it may be necessary to establish the best measure of effective dose empirically, as that measure that best resolves anomalies in the applied dose-response curve. But for clarity and simplicity of presentation, the two questions will be addressed separately here.

1. Appropriate Measures of Effective Dose

There is no universally applicable measure of effective dose. To begin with, whether the critical effect is most closely associated with peak concentration at the receptor sites, integrated total exposure of receptor sites to the chemical, or some intermediate measure such as integrated total exposure to concentrations above a threshold value, is often not known. All that can b

stated with certainty a priori is that appropriate dose correlates of effect will be effect-dependent. For example, it is generally agreed that the effective dose of a genetically-acting carcinogen is the integrated total exposure of the receptor sites to reactive molecules, whether parent or metabolite. On the other hand, the acute toxicity of a rapidly-acting toxicant such as cyanide is much more closely related to peak concentrations in blood and tissues.

The urethane example of Figure 2 can be extended to illustrate the effect dependence of the appropriate measure of exposure. The LD50 of urethane in mice is about 2 g/kg, approached by the doses shown in Figure 2. Manipulation of the urethane elimination rate in order to alter the relationship between area under the concentration curve and applied (intraperitoneal) dose leaves the acute lethality of urethane unchanged even though these manipulations result in shifts in urethane adenogenicity. Presumably this distinction occurs because acute lethality is associated with peak (initial) concentration, which is unaffected by alteration in the urethane elimination rate, while adenogenesis is associated with an expression of total exposure that is dependent on elimination rate.

In the absence of specific knowledge as to the measure of exposure that is the primary determinant of toxicity in a particular case, biologically justifiable procedures for estimation of useful dose correlates of toxicity can be outlined. The procedures recommended here have at least reasonable likelihood of success; that is, it is reasonable to expect them to lead to successful resolution of anomalous applied dose-response curves in a significant percentage of cases. Nonetheless, the regulator cannot afford to lose sight of the fact that there is no substitute for reliable experimental or epidemiological information

Some of the procedures recommended here for estimation of effective dose are model-independent, but others are based on very simple pharmacokinetic models. These models are based on the assumptions that metabolism is describable by single expression (that is, that there is only one metabolic pathway or that all parallel pathways have identical kinetic characteristics); that only one metabolic pathway is associated with significant toxicity; and that elimination kinetics are either first-order or Michaelis-Menten. The appropriateness of these simple models has already been established for a number of compounds, and it appears reasonably certain that the models will be shown to possess broad utility. But at the same time, it is absolutely certain that these simple pharmacokinetic models are not accurately descriptive of the pharmacokinetic behavior of all chemicals. For example, methylene chloride is metabolized in rats by multiple parallel pathways, at least two of which are saturable and are potentially capable of generating toxicologically active intermediates or metabolic end products (DiVincenzo and Hamilton, 1975; Anders et al., 1977; McKenna et al., 1982). Complex metabolic behavior such as this can sometimes be adequately described by simple models. For example, careful analysis of the vinyl chloride dose-carcinogenicity relationship in rats suggests that both depletion of glutathione, presumably involved in metabolite elimination, and capacity-limited production of carcinogenic metabolite may contribute to the form of the vinyl chloride dose-angiosarcoma relationship (Watanabe et al., 1977). Nonetheless, this relationship is satisfactorily described by a single expression of Michaelis-Menten form (Gehring et al., 1978). Such simplifications are not always successful, however. The anomalous dose-response curve for ethylene dichloride lethality in rats can be only partially resolved by incorporating a term for saturability of metabolite production. Differential effects

of microsomal enzyme inducers and inhibitors on ethylene dichloride lethality suggest that the rate of production of ethylene dichloride metabolites correlates well with ethylene dichloride toxicity only within limited dose ranges and in the absence of treatments altering the rate of active metabolite elimination (Andersen et al., 1980).

Acute Exposure

Unless acute lethality is the dominant concern, it is probably most reasonable to relate expected effect after acute exposure to the amount of active agent reaching the receptor sites. More practically, this translates into the amount of active agent moving through the blood. (The assumption of proportionality between concentration in blood or plasma and concentration at receptor sites is not always well founded. However, distribution is not as likely to be a source of dose dependency as is elimination). The total amount moving through the blood is the integral of concentration in blood over time:

$$\int_{t=0}^{t=\infty} C(t)dt, \qquad (1)$$

where C(t) is the concentration at time t and the integration is carried out from t = 0 to t = ∞.

Equation (1) represents the total area under the concentration curve, AUC_{∞}. If disposition kinetics are not dose-dependent, AUC_{∞} is directly proportional both to dose and to the half-life, $t_{1/2}$, of the compound:

$$AUC_{\infty} = \frac{(D)(t_{\frac{1}{2}})}{(V)(.693)} = \frac{D}{(k_e)(V)} \quad , \qquad (2)$$

where V is the volume of distribution and k_e is the rate constant for elimination. Equation (2) applies whether the toxicant is administered "instantaneously" (intravenously) or is absorbed by a first-order mechanism (orally or by inhalation). D is the bioavailable dose, which, except in the case of intravenous administration, may be only a fraction of the administered dose. Since this fraction is ordinarily not known except from a comparison of (AUC_{∞})oral with (AUC_{∞})i.v., the experimentally determined area under the curve is usually calculated directly from the concentration data rather than by using Equation (2). The calculation can be carried out by summing the areas of the trapezoids formed by connecting sequential concentration data points by straight line segments and extending perpendicular line segments from each of these points to the concentration axis. The area from the last concentration point to infinite time is calculated as C/k_e, where C is the concentration at the last sampling time.

Even if disposition kinetics are dose-dependent, AUC_{∞} is the appropriate measure of integrated effective dose, although it is no longer proportional to administered dose. An explicit equation relating AUC_{∞} to dose has been derived for the Michaelis-Menten model (Wagner, 1973):

$$AUC_{\infty} = \frac{D}{(V)(V_m)} \left(\frac{D}{2V} + K_m\right), \qquad (3)$$

where V_m is the maximum elimination rate achieved when all active elimination sites are occupied, K_m is the half-saturation constant or the concentration at which elimination rate = $- V_m/2$, and D and V are as previously defined. This equation can be used whenever the applicability of Michaelis-Menten kinetics has

been verified. Generally, however, it probably is most defensible simply to calculate the area under the experimental concentration curve. This procedure is not model-dependent, so that it may be used whenever integrated effective exposure is the dose referent of choice.

In principle, the area under the curve of concentration of a chemically stable active metabolite may be used as the measure of effective dose of the metabolite. In practice, such measurements are likely to be less useful for environmental toxicants than for drugs. The principal features of the metabolic profiles of drugs are known, and drug metabolites are often sufficiently chemically stable to circulate in the blood. Indeed, prodrugs are designed specifically to produce stable active metabolites. In contrast, the metabolic patterns of environmental contaminants are usually not fully known, and metabolites, particularly highly active ones, are likely to be chemically unstable and, therefore, not measurable in the blood. This point will be discussed further below.

Chronic Exposure

When an exposure is extended in time to a point at which it can no longer be called acute, even calculation of applied dose is subject to some controversy. Traditionally, when exposure is intermediate in duration, Haber's Law has been used. This procedure, a concentration x time or dose rate x time calculation, gives total exposure to an environmental contaminant. When acute doses are given repeatedly at widely-spaced intervals, as in daily oral gavage of an experimental animal, the number of doses times the daily dose has been used as an equivalent measure of total dose (Decad et al., 1981). Over periods of time that are short relative to the half-life of the compound, these estimates may be appropriate. However, to use this type of calculation is to overlook the fact

that body burdens of a chemical do not increase indefinitely with increasing length of exposure. As a consequence of the action of elimination mechanisms, the body burden reaches a steady state after a period of time dictated by half-life of the compound, and in the absence of factors acting to alter the volume of distribution or the half-life does not increase further even though exposure continues at the same rate. It should therefore not be surprising that careful examination of published toxicity data has shown that the long-term no-effect dose rate of a chemical can be predicted with reasonable assurance from the short-term no-effect dose rate (McNamara, 1976). A committee of the Society of Toxicology stated in 1974 that, "with the exception of carcinogenesis and certain rare neurological effects, there is little, if any additional information obtained on the character of toxic effects that are not detected within three months of testing with animals." Those few effects whose appearance is delayed tend to be effects with long induction periods rather than effects whose occurrence requires prolonged exposure to the toxicant. Thus, steady-state concentration in the blood is a better measure of effective dose than is any kind of area under the blood concentration curve during chronic exposure.

In fact, the relationship of steady-state concentration C_{ss} to basic pharmacokinetic parameters demonstrates that C_{ss} is exactly analogous to the AUC_{∞} measured after a single dose. When disposition mechanisms are not dose-dependent,

$$C_{ss} = \frac{DR}{(k_e)(V)} = \frac{(DR)(t_{\frac{1}{2}})}{(V)(.693)} , \qquad (4)$$

where DR is dose rate, expressed as rate of absorption into the systemic circulation, and V and k_e are as previously defined. Equation (4) has the same form as Equation (2). For the Michaelis-Menten model, with a single capacity-limited elimination mechanism,

$$C_{ss} = DR\left(\frac{K_m + C_{ss}}{(V)(V_m)}\right) = \frac{DR}{(V)(V_m)}\,(K_m + C_{ss}), \qquad (5)$$

as long as DR does not exceed V_m. Equation (5) is analogous, although not identical, to Equation (3).

Steady-state concentration can be measured directly in the blood. If exposure is continuous, such as in an inhalation exposure to steady state, concentration measurement presents no theoretical difficulty. If, however, exposure has been intermittent rather than continuous - for example, if a test chemical has been given repeatedly to animals by daily gavage, or if a contaminant is present in food - the average concentration $\bar{C}$ during the dose interval τ is equivalent to C_{ss}. $\bar{C}$ in the nth dose interval is defined as (Wagner et al., 1965)

$$\bar{C}_n = \frac{1}{\tau}\int_{t_n}^{t_{n+1}} C(n,t)\,dt, \qquad (6)$$

It can be shown (Van Rossum and Tomey, 1968) that when steady state has been reached, provided that disposition is not dose-dependent the value of the integral in Equation (6) is $D/(k_e)(V)$ where D is the repeated dose, so that the average concentration at steady state is

$$C_{ss} = \frac{1}{\tau} \cdot \frac{D}{(k_e)(V)} = \frac{DR}{(k_e)(V)} \qquad (7)$$

Thus, while C_{ss} is the appropriate measure of effective exposure during continuous exposure to steady state, when an experimental design involves repeated administration of a test compound whose kinetics are not dose-dependent, AUC from t_n to t_{n+1} at steady state may be used as a surrogate for C_{ss} since the two are directly proportional. This technique is of little more than academic interest, however, since the value of AUC from t_n to t_{n+1} at steady state is seldom if ever known. Measurements such as these are not routinely undertaken by the experimentalist. It is unlikely that important inaccuracies or bias would be introduced by substituting for either $\bar{C}$ or AUC from t_n to t_{n+1} the concentration measured in blood at some convenient constant time after administration of the repeated dose as the measure of effective dose.

Like AUC_{∞}, C_{ss} and $\bar{C}$ at steady state are independent of any kinetic model. The major restriction on their appropriate application is that all toxicologically critical compartments must have reached a steady-state relationship with the blood within the time period of measurement.

The regulator is frequently concerned with toxicants whose concentration cannot be measured. Sometimes analytical problems preclude direct measurement of concentration, but more often the active moiety is simply inherently unmeasurable. Many environmental toxicants are not direct acting. These agents are converted to toxic or reactive metabolites. Most often, the chemical identity of the active metabolite has not been firmly established, and often it is not even known with certainty whether more than one metabolite is active. It would be impractical to undertake identification and quantitation of active

metabolites of all, or even of the majority of potential environmental toxicants. Furthermore, in some cases the toxicologically active metabolites may be so reactive that they do not leave the tissue, or perhaps even the intracellular site, where they were formed. Their very existence is intrinsically undemonstrable by standard analytical methods, and must be inferred from indirect evidence such as the chemical identity of metabolic end products (see, for example, Miller and Guengerich (1982)). Gillette (1974 a,b) has presented a perspective on the kinetics and toxicity of these short-lived, chemically reactive species, which have the potential to bind covalently to cellular macromolecules. For compounds that generate such reactive metabolites, a surrogate measure of effective dose must be sought.

Pharmacokinetic principles provide the basis for defining two surrogate measures of effective dose that have been successfully utilized when an undetermined or analytically undemonstrable metabolite was believed to be the toxic agent. Use of these effective-dose surrogates is appropriate only when the criteria outlined below have been met. It should be clear that a dose surrogate need not be equal in magnitude to the effective dose, nor even be expressed in the same units. It must, however, be proportional to effective dose.

One of the two measures that have successfully been used as surrogates for effective dose is the rate of formation of active metabolites, or, more accurately, the rate of loss of parent compound. This technique is based on the assumptions that (1) The critical effect is associated with total exposure to active metabolites rather than with peak concentrations, (2) The rate of formation of the critical metabolite(s) is proportional to the rate of disappearance of the parent chemical and (3) Elimination of the critical metabolite(s) is first-order.

The requirement that the critical effect be associated with total integrated exposure is almost certain to be met by highly reactive molecules, but may not be met by chemically unreactive molecules - that is, by agents that act by combining reversibly with receptor sites. For the latter group of toxicants, slow production of metabolite over an extended time period may not be toxicologically equivalent to rapid metabolite production with achievement of high concentrations in body fluids at early times after administration, even though integrated exposure may be the same in the two cases. As discussed briefly above, the proper dose correlates of toxicity will be effect-specific for reversibly-acting agents. For this group of toxicants, toxicity, metabolic, and pharmacokinetic data must be interpreted and correlated with particular care.

When exposure is either continuous or chronic to steady state and the three conditions above have been met, then it can be predicted by analogy with Equation (4) that total exposure to metabolite should be proportional to the rate of metabolite appearance. Effective dose should be proportional to exposure as long as the enzyme systems catalyzing transformation of toxicant to active metabolite(s) are not near saturation, but may approach constancy at high exposure where the rate of active metabolite production has reached its maximum value.

Measurement of the rate of loss of parent compound is less readily applicable to data from an acute study, for two reasons. First, the rate of metabolism is not constant during the period of elimination of a single dose, as it is at steady state. Commonly, the rate of metabolism after a single dose varies either directly with concentration (first-order metabolism) or in accordance with Michaelis-Menten kinetics (from a maximum of Vm down into the first-order

concentration range). If there is only one metabolite and the parent compound is retained long enough that virtually all of it is transformed, the rate of transformation is not important. However, if there is more than one metabolite or if the parent compound is excreted directly as well as being metabolized, rates of transformation can be very important since the concentration dependencies of competing elimination mechanisms control the relative amounts of different metabolites produced. Second, other disposition nonlinearities may control metabolism and toxicity. For example, methylene chloride readily enters the fat. After a single dose, it is released slowly from fat and reenters the blood, from which it is redistributed to tissues including metabolizing tissues. Thus, methylene chloride and its metabolites persist in the body for time periods much longer than would be expected on the basis of their elimination half-lives alone (Ratney et al., 1974 or Stewart et al., 1976).

Nonetheless, experience has shown that the rate of loss of the administered compound from the blood over a limited time period can be a useful and toxicologically relevant surrogate for effective dose. This was the technique used by Gehring et al. (1978) to resolve the vinyl chloride dose-carcinogenicity curve (Figure 1), and by Andersen et al. (1979) to resolve the 1,1-dichloroethylene dose-lethality curve.

The second measure that has successfully been used as a surrogate for effective dose is total excretion of stable end products of metabolism. This technique is suitable for use when (1) All stable end products originate either directly or indirectly from the toxic intermediate (there may, of course, be only one end product, in which case this criterion is met automatically), or else all parallel metabolic pathways have the same Vm and Km values, and (2) The

critical effect is associated with total exposure. Under these conditions total stable end products of metabolism represent the "dose" of active metabolite; th amount and possibly the chemical identity of the reactive precursor are inferr from the amounts and chemical identities of excreted metabolites.

Because it is based on cumulative excretion and does not have time as one of its dimensions, this technique is appropriate for use either with acute or with chronic data. When it is applied to chronic data, total stable metabolites excreted within a dose interval or within a unit of time at steady state are related to dose rate.

It is worth repeating that both the elimination rate and the total excreted metabolite surrogates are subject to the same limitation: that effective dose is presumed to be an amount rather than a concentration.

2. The Relationship of Administered to Effective Dose

The principal source of dose-dependent kinetic behavior is the intrin capacity limitation of most elimination mechanisms including all biotransformation mechanisms and a number of renal and hepatic excretion mechanisms as well. This intrinsic dose dependence is the direct consequence of constraints on the number of metabolizing enzyme molecules or of membrane transport proteins responsible for active biliary excretion or for renal tubular secretion and active reabsorption. While there are other causes of dose-dependent kinetics, capacity-limited elimination is the only one that will be explicitly dealt with here.

The familiar Michaelis-Menten equation describes the behavior of the simplest capacity-limited system, in which physical combination of a single

substrate molecule with a single carrier protein or enzyme molecule is prerequisite to excretion or biotransformation:

$$v = \frac{dC}{dt} = -\frac{(V_m)(C)}{Km + C} \quad . \tag{8}$$

where dC/dt is the reaction velocity v or the rate of change of concentration at the active site, and V_m and K_m are as previously defined.

In spite of the extreme and, in many respects, unrealistic simplicity of the reaction scheme that gives rise to the Michaelis-Menten equation, the overall rates of biotransformation and transport mechanisms often turn out to be describable by equations of the Michaelis-Menten form. This is presumably due to the fact that of the many sequential steps making up an elimination process, a single step is rate-limiting. As long as requisite cofactors are present in excess, the activity of the overall elimination process usually approximates Michaelis-Menten behavior.

Even though the rate of elimination may be related to the amount of substrate present at biotransformation or transport sites by Michaelis-Menten kinetics, the actual rate of elimination in vivo may not display Michaelis-Menten behavior. This is because under certain conditions, the rate of arrival of substrate at the elimination sites is lower than the rate at which the elimination mechanism is able to metabolize or excrete the chemical. These conditions are most likely to be met for high-affinity elimination processes, as will be shown.

Elimination, or clearance, takes place in many organs. Since the liver is the dominant site of metabolic elimination, the equations in this section are written in notation appropriate to clearance by the liver.

Two hepatic clearances can be defined. One, the intrinsic clearance Cl_{int} (Wilkinson and Shand, 1975), relates the rate of hepatic elimination to the concentration of the chemical at the elimination site. It is based directly on the Michaelis-Menten equation:

$$Cl_{int} = - \frac{v}{C_l} = - \frac{V_m}{K_m + C_l} , \qquad (9)$$

where C_l is the concentration of the chemical in liver tissue fluid. Cl_{int} is the volume of liver tissue fluid that is cleared of the chemical per unit time. It represents the ability of the liver to eliminate the chemical in the absence of any flow restrictions.

Clearance, as it is customarily measured, relates the rate of hepatic elimination to the concentration of the chemical in the blood entering the liver, C_{in}. Since $v = Q (C_{in} - C_{out})$, where C_{in} is the concentration of the chemical in hepatic arterial blood, C_{out} is its concentration in hepatic venous blood, and Q is hepatic perfusion rate,

$$Cl = - \frac{v}{C_{in}} = \frac{Q(C_{in} - C_{out})}{C_{in}} . \qquad (10)$$

The way in which measured clearance is related to factors such as hepatic perfusion rate and intrinsic clearance is determined by the way in which C_l is related to C_{in} and C_{out}. Two models of hepatic extraction have been proposed. In the well-stirred model (Rowland et al., 1973), the liver is considered a

single well-stirred compartment in equilibrium with (venous) blood leaving the liver, so that $C_l = C_{out}$. In the parallel-tube model (Brauer, 1963), the liver is seen as a bundle of parallel tubes along which the concentration of toxicant declines steadily from C_{in} to C_{out}. The two models predict different dependencies of measured clearance on intrinsic clearance and blood flow (Pang and Rowland, 1977). There is experimental support for both models, although the well-stirred model appears to be somewhat better supported by published experimental data (Nies et al., 1976; Wilkinson, 1976). Because of this and because the two models predict the same limiting behavior when either $Q >> Cl_{int}$ or $Cl_{int} >> Q$, the simpler, well-stirred model will be used to illustrate this limiting behavior.

In the well-stirred model, $C_l = C_{out}$. If C_l is substituted for C_{out} in Equation (10) and the equation rearranged to give Cl in terms of Cl_{int},

$$Cl = Q \left(\frac{Cl_{int}}{Q + Cl_{int}}\right) \qquad (11)$$

When $Q >> Cl_{int}$, Equation (11) reduces to

$$Cl = Cl_{int}$$

When $Cl_{int} >> Q$, Equation (11) reduces to

$$Cl = Q.$$

These relationships, and their consequences, are illustrated in Figure 3 for two capacity-limited elimination mechanisms, one high-affinity (low K_m) and one low-affinity (high K_m). Since the two mechanisms have the same V_m value, at any given substrate concentration C_l less than saturating the high-affinity mechanism will dominate the low-affinity mechanism (Figure 3) (see also the defini-

tion of Cl_{int}; Equation (9)). For the high-affinity mechanism, in fact, there exists a significant range of concentrations within which the elimination mechanism can clear liver fluid of the chemical more rapidly than the chemical can be transferred from blood to liver fluid (e.g., $v' > v$ and $Cl'_{int} > Cl$). In this low concentration range, hepatic perfusion is rate-limiting. At sufficiently high concentrations of the chemical in perfusing blood, however, the elimination mechanism is saturated, $v > v'$ (and $Cl > Cl'_{int}$), and elimination is capacity-limited. This type of behavior is one example of "flip-flop" kinetics, in which one of several interrelated steps is rate-limiting in one concentration range while another becomes rate-limiting in another concentration range. Flip-flop kinetics of elimination have been observed for styrene (Andersen et al., 1984) and for most of the low-molecular-weight, volatile halogenated hydrocarbons, such as the chlorinated ethylenes and methylene chloride (Filser and Bolt, 1979; Andersen, 1981). The exception appears to be perchloroethylene, for which V_m is extremely low.

Perchloroethylene is an example of the other extreme of dependence of clearance on blood flow and on intrinsic clearance, in which the rate of transfer of the chemical from blood to liver fluid is more rapid at all concentrations than is the rate of removal of the chemical from liver fluid by the elimination mechanism (Figure 3; $v > v''$ and $Cl > Cl''_{int}$). Elimination is capacity-limited at all concentrations, and the chemical displays Michaelis-Menten kinetics throughout the entire dose range.

Effective dose should reflect the form of concentration dependence of the rate-limiting step in the metabolism and excretion sequence. This may be an elimination step or, if a metabolite is active, it may be formation of the met

bolite. Clearly, the way in which a capacity-limited process affects the relationship between administered and effective dose will depend on whether the critical process controls formation or elimination of the active moiety.

Elimination is Rate-Determining

When elimination is rate-determining for the active moiety, either parent or metabolite, then effective dose is to be expected to increase more rapidly than administered dose as the critical elimination mechanism approaches saturation. Of course, if substrate concentrations are much lower than K_m or if elimination is not capacity-limited, then administered and effective dose are proportional throughout the entire dose range.

If elimination is Michaelis-Menten in form, then effective dose should increase as the sum of two dose terms, one linear and one quadratic (Equation (3) and Equation (5)). This is the behavior shown by urethane (Figure 2), for which, however, elimination is close to saturation throughout the entire experimental dose range, so that the quadratic term is dominant and the linear term is not apparent.

On the other hand, if elimination displays flip-flop kinetics, then the administered dose-effective dose relationship should have two linear segments with a short transition region, as illustrated by Ramsey and Andersen (1984) (Figure 4) in the simulated dependence of styrene steady-state blood concentration on styrene concentration in inhaled air.

Formation Is Rate-Determining

When formation is rate-determining, the effective dose should approach a constant maximum as the administered dose or dose rate increases beyond the

point at which the critical formation mechanism is saturated. Provided that mechanisms for elimination of the active intermediate do not themselves approach saturation, further increments in administered dose should not cause additional increments in toxicity. This is the behavior shown by vinyl chloride (Figure 1).

In this case too, the shape of the administered dose-effective dose relationship should reflect whether the approach to saturation is dictated by Michaelis-Menten or by flip-flop kinetics. (Andersen (1981) has pointed out that the shape of the vinyl chloride inhalation dose-metabolism curve (Watanabe et al., 1978) is not inconsistent with perfusion limitation at air concentrations from 1 to 100 ppm, even though the inhalation dose-hepatic angiosarcoma curve (Maltoni and Lefemine, 1975) is satisfactorily described by a Michaelis-Menten expression for air concentrations from 50-10,000 ppm).

The distinction between flip-flop and Michaelis-Menten behavior when formation of active metabolites is rate-limiting is well illustrated by perchloroethylene and trichloroethylene. Both of these compounds generate hepatotoxic metabolites. Rats were given repeated daily doses of trichloroethylene or perchloroethylene by gavage for six weeks, and total metabolism was measured and expressed as total 24-hr excretion of stable metabolites in urine (Buben and O'Flaherty, 1984). Metabolism of both compounds proved to be capacity-limited, but they displayed distinctly different kinetic behavior. Elimination of trichloroethylene was perfusion-limited at low dose rates (Figure 5a), while elimination of perchloroethylene was capacity-limited at all dose rates (Figure 5b). The dose dependence of hepatoxicity of both compounds mirrored the dose dependence of metabolism, plateauing at high dose rates but

directly proportional to lower dose rates of trichloroethylene and displaying Michaelis-Henten kinetics throughout the entire range of perchloroethylene dose rates. As a result of the congruence of the dose-effect and dose-metabolism curves for both compounds, the relationship between magnitude of effect and total urinary metabolite is linear in both cases (Figure 6).

Thus, the amount of metabolism of both trichloroethylene and perchloroethylene is directly related to their hepatotoxicity, irrespective of whether this metabolism is perfusion-limited at low dose rates (trichloroethylene) or capacity-limited at low dose rates (perchloroethylene).

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Figure 1. (a) Vinyl chloride concentration, ppm in air, versus hepatic angiosarcoma prevalence in rats (Maltoni and Lefemine, 1975); log-probit scales. The solid line is the line of best fit; the dashed line is a linear extrapolation. (b) Rate of vinyl chloride metabolism (Watanabe et al., 1978) versus hepatic angiosarcoma prevalence in rats (Gehring et al., 1978); log-probit scales.

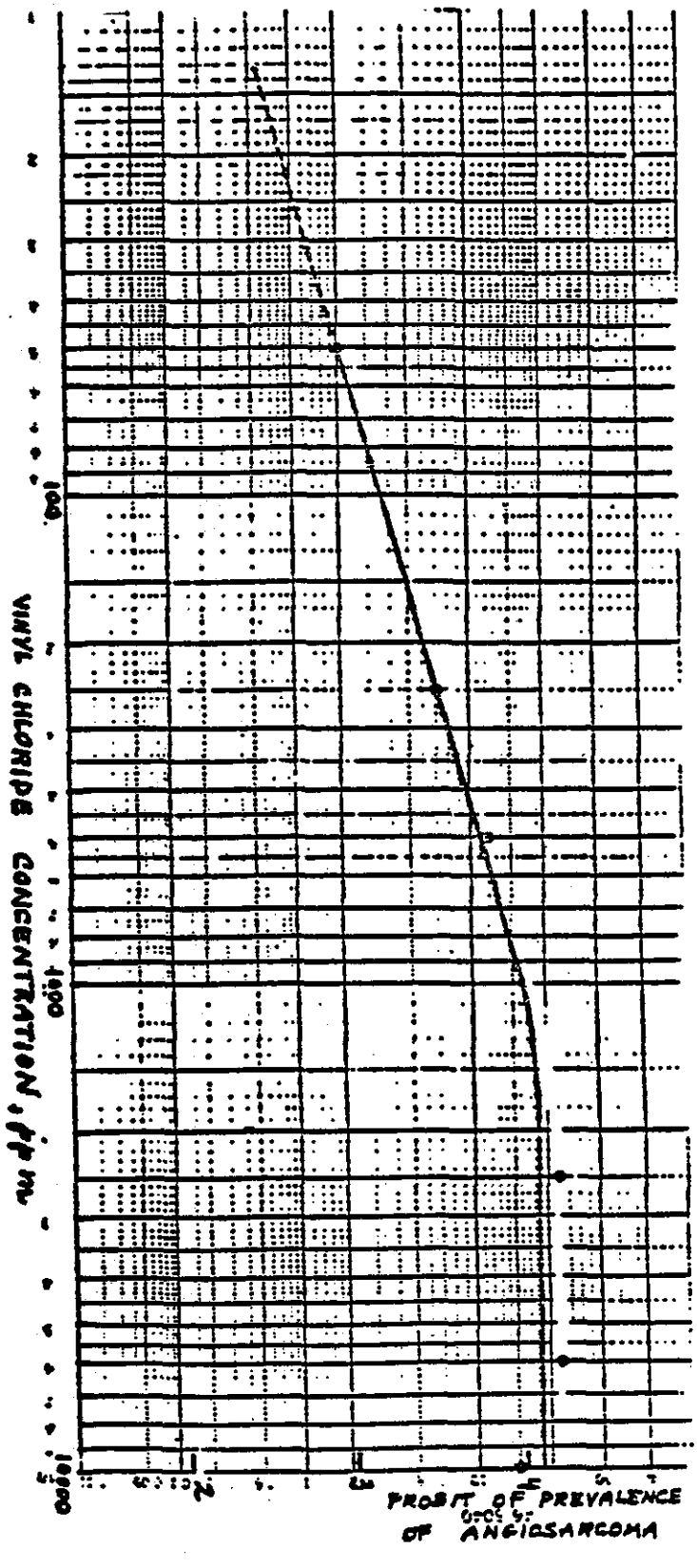
Figure 1. (a) Administered urethane dose versus pulmonary adenoma prevalence in mice. (b) Urethane concentrations in the blood, integrated over time (AUC_{∞}), versus pulmonary adenoma prevalence in mice. From Sichak and O'Flaherty, 1984, with permission.

Figure 3. (a) Dependence of rate of extraction on concentration in blood entering the tissue and of rate of metabolism on concentration in tissue fluid. Metabolism is shown for two enzymes, for both of which $V_m = 5.0$. (b) Dependence of the three corresponding clearances on referent concentrations.

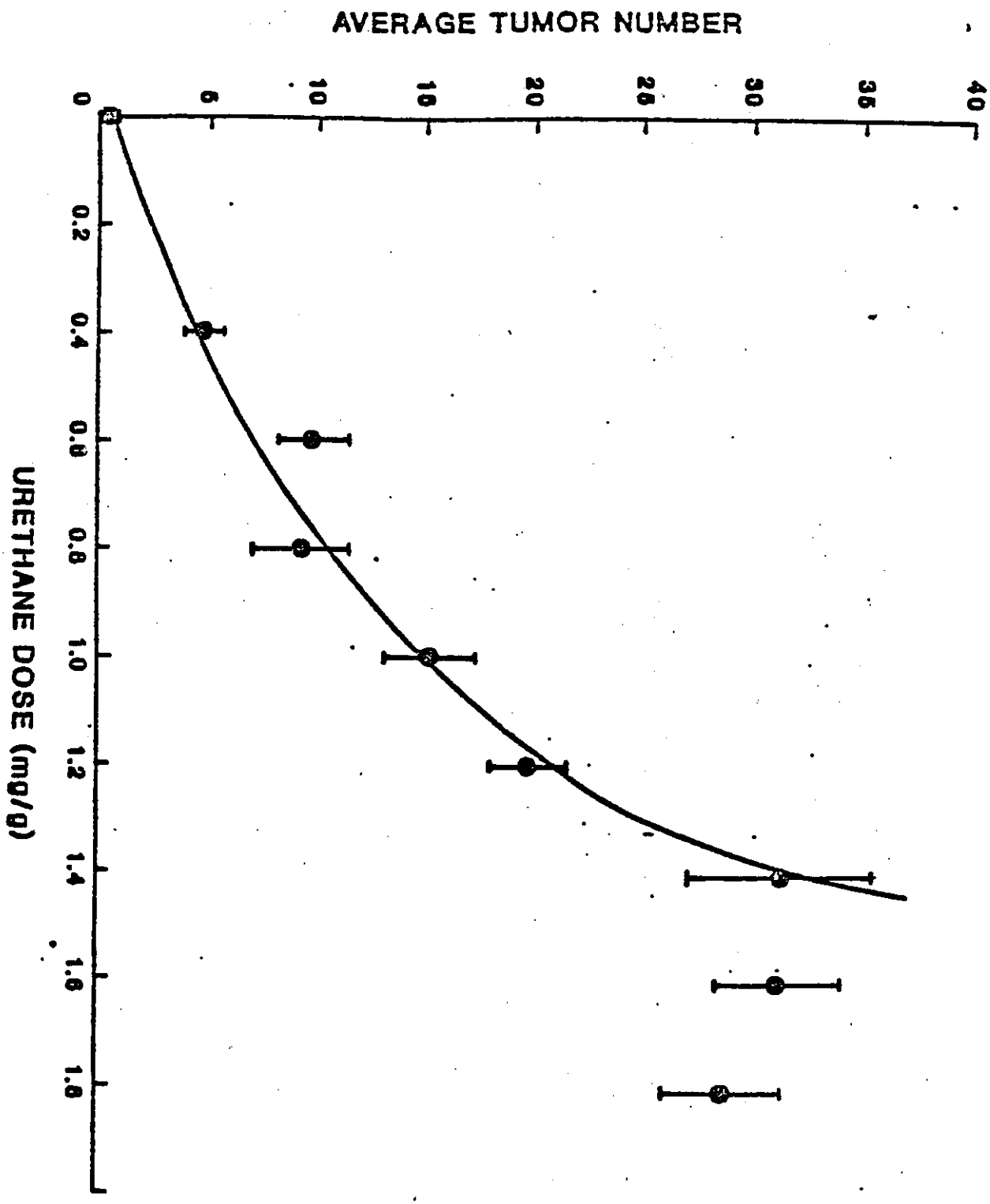
Figure 4. Simulated styrene concentrations in arterial blood of mice, rats, and humans versus styrene concentration in inhaled air. Light lines are blood concentrations after inhaling styrene continuously for 6 hr. Heavy line is blood concentration after inhaling styrene continuously for 400 hr to reach steady state concentrations. From Ramsey and Andersen, 1984, with permission.

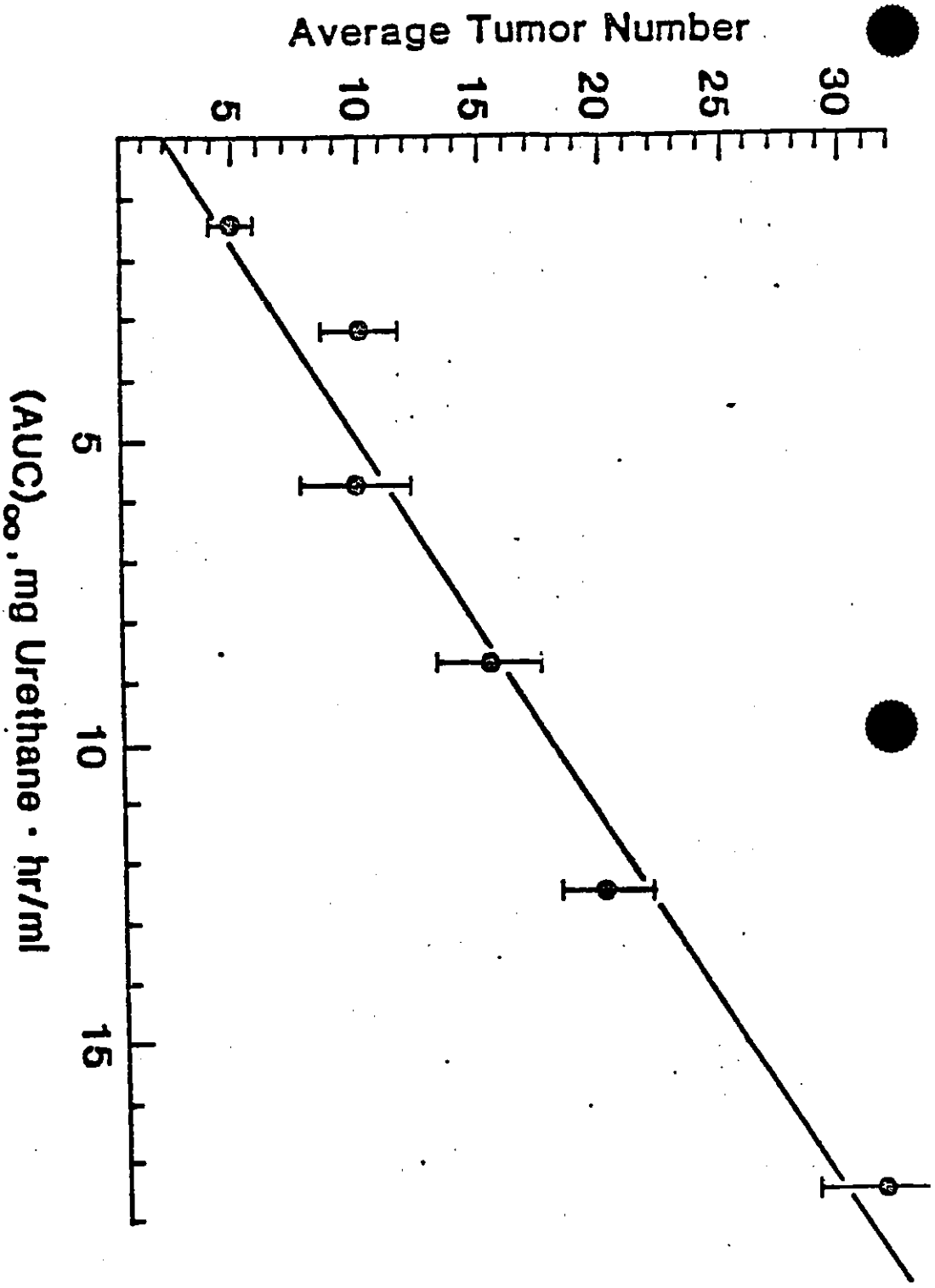
Figure 5. (a) Total urinary metabolites excreted within 24 hours of administration of a repeat oral dose of trichloroethylene to mice. Most points represent means of data from 7-9 mice. SEM is shown. (b) Total urinary metabolites excreted within 24 hours of administration of a repeat oral dose of perchloroethylene to mice. Most points represent means of data from 9-11 mice. SEM is shown. From Buben and O'Flaherty, 1984, with permission.

Figure 6. (a) Liver weight to body weight ratio in mice after 6 weeks of daily oral administration of trichloroethylene, 5 days/week, as a function of 24-hour urinary metabolite excretion. (b) Liver weight to body weight ratio in mice after 6 weeks of daily oral administration of perchloroethylene, 5 days/week, as a function of 24-hour urinary metabolite excretion. From Buben and O'Flaherty, 1984, with permission.

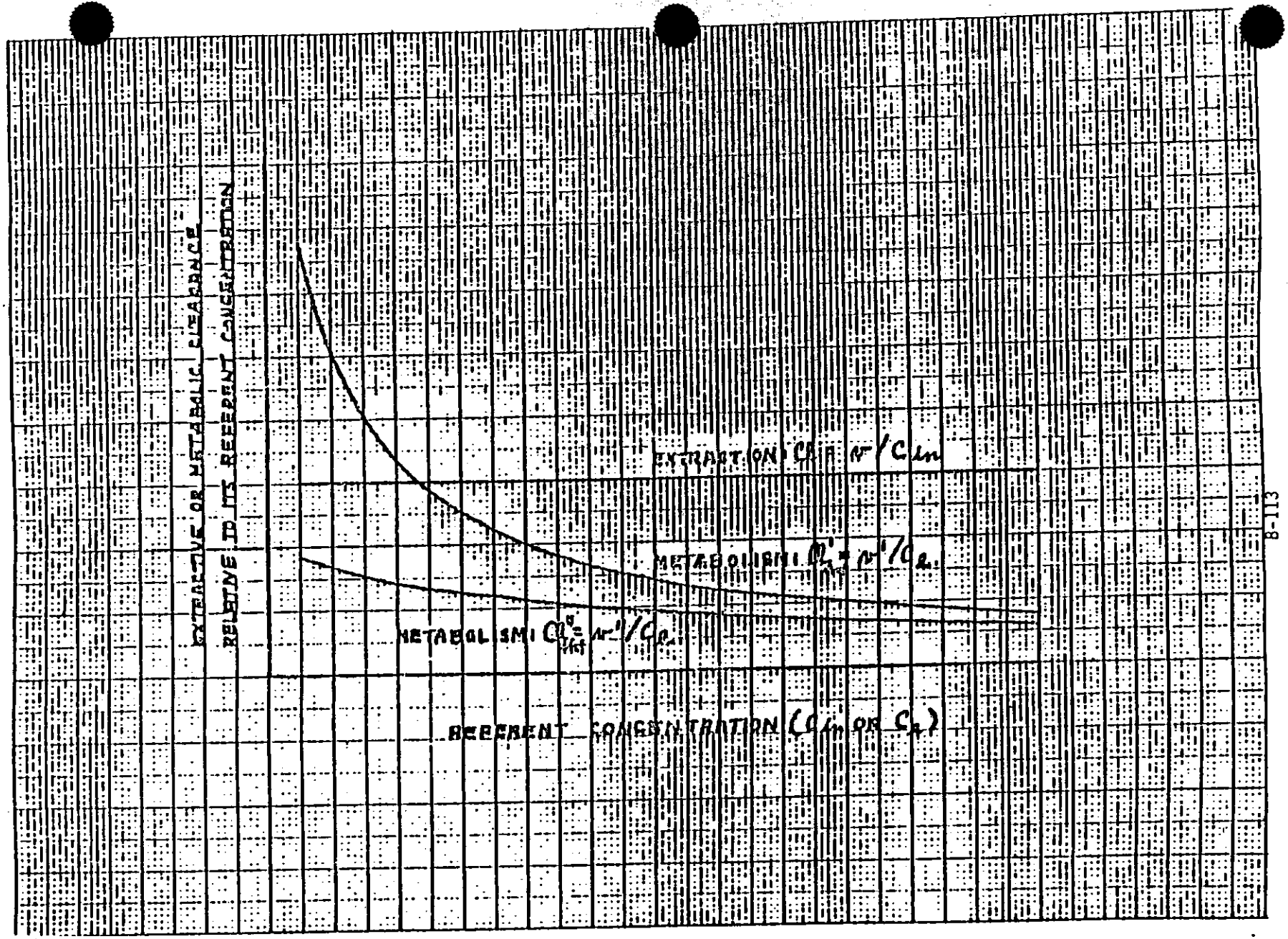

VINYL CHLORIDE CONCENTRATION, ppm
100
1000
10000
PROBIT OF PREVALENCE OF ANGIOSARCOMA

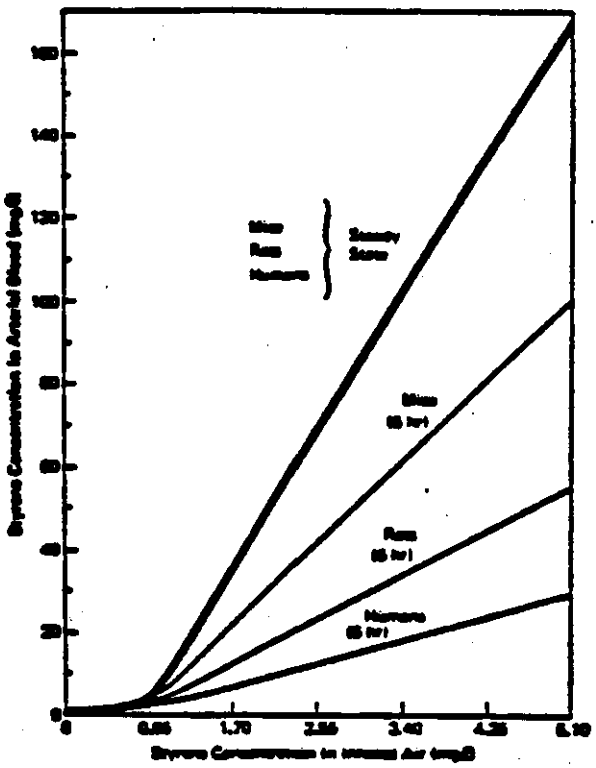
RATE OF VINYL CHLORIDE METABOLISM, mg/kg/hr
PROBIT OF PREVALENCE
OF ANGIOSARCOMA
45 8040

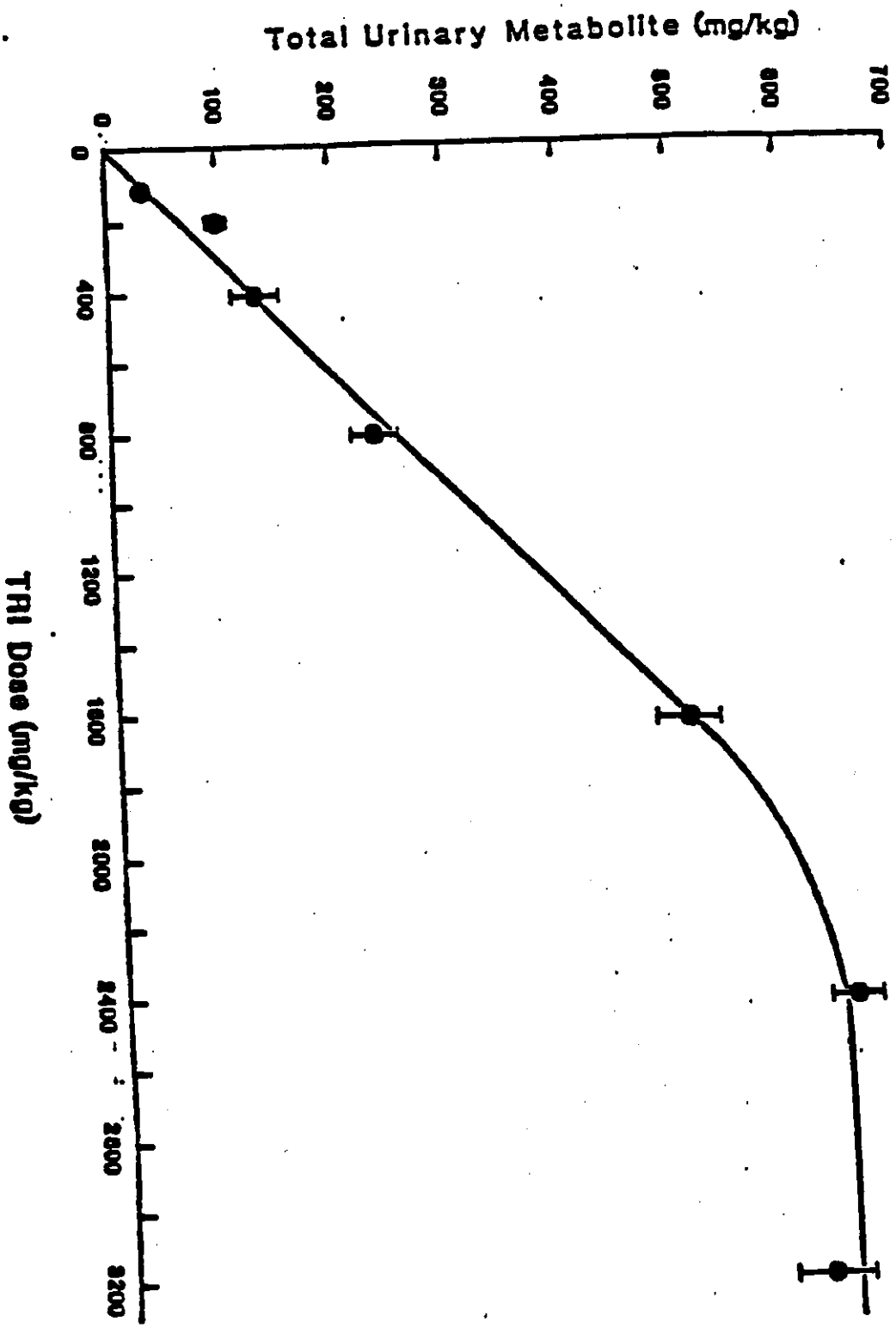

AVERAGE TUMOR NUMBER
0
6
10
16
20
26
30
36
40
URETHANE DOSE (mg/g)
0
0.2
0.4
0.6
0.8
1.0
1.2
1.4
1.6
1.8

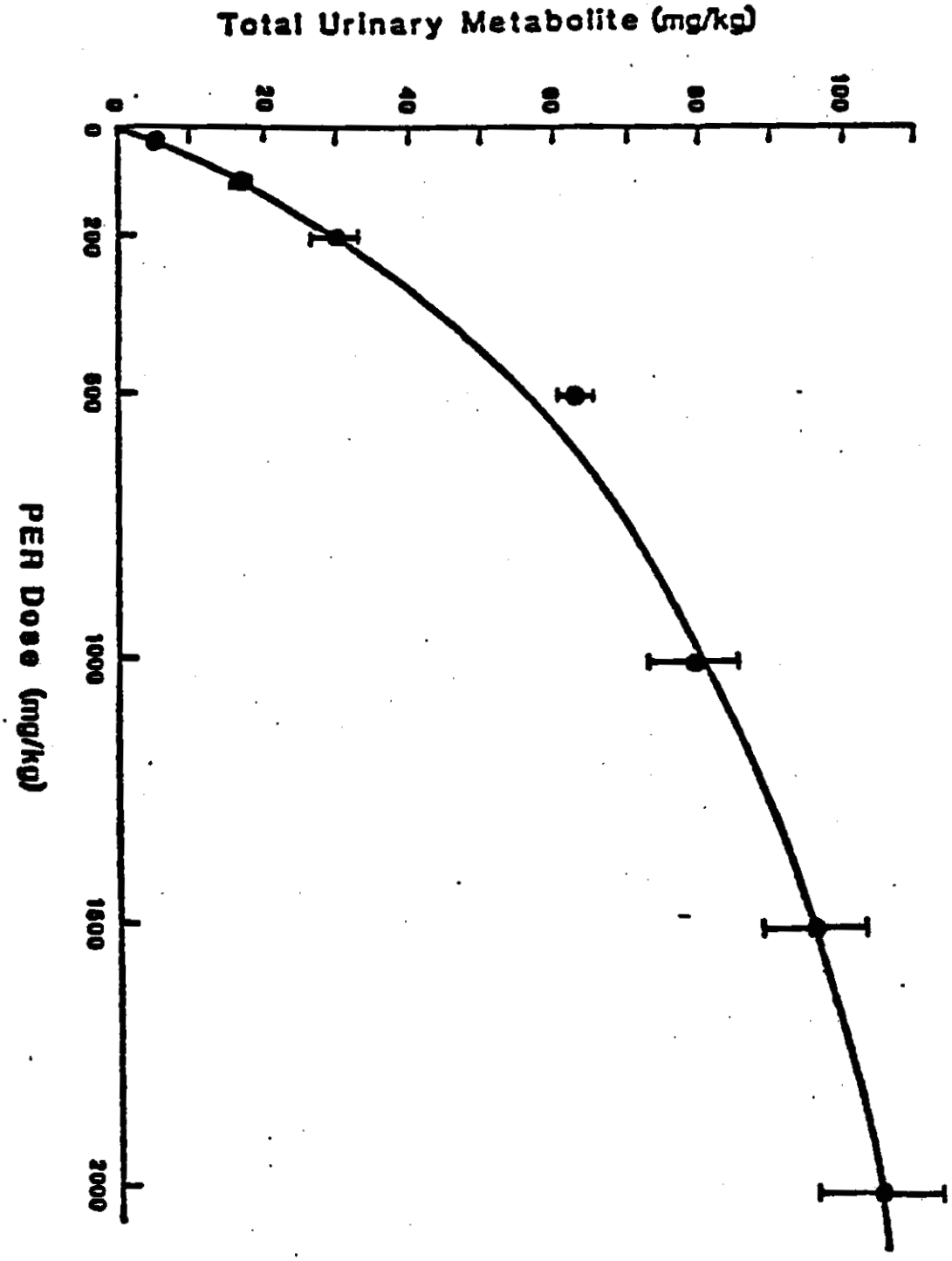

Average Tumor Number
5
10
15
20
25
30
(AUC)∞, mg Urethane · hr/ml
5
10
15

RATE OF EXTRACTION OR METABOLISM
RELATIVE TO ITS REFERENT CONCENTRATION
REFERENT CONCENTRATION (Cin OR Ca)


EXTRACTION OR METABOLIC CLEARANCE
RELATIVE TO ITS REFERENT CONCENTRATION
EXTRACTION
METABOLISM
METABOLISM
REFERENT CONCENTRATION (Cin OR CR)




Total Urinary Metabolite (mg/kg)
0
100
200
300
400
500
600
700
THI Dose (mg/kg)
0
400
800
1200
1600
2000
2400
2800
3200


Total Urinary Metabolite (mg/kg)
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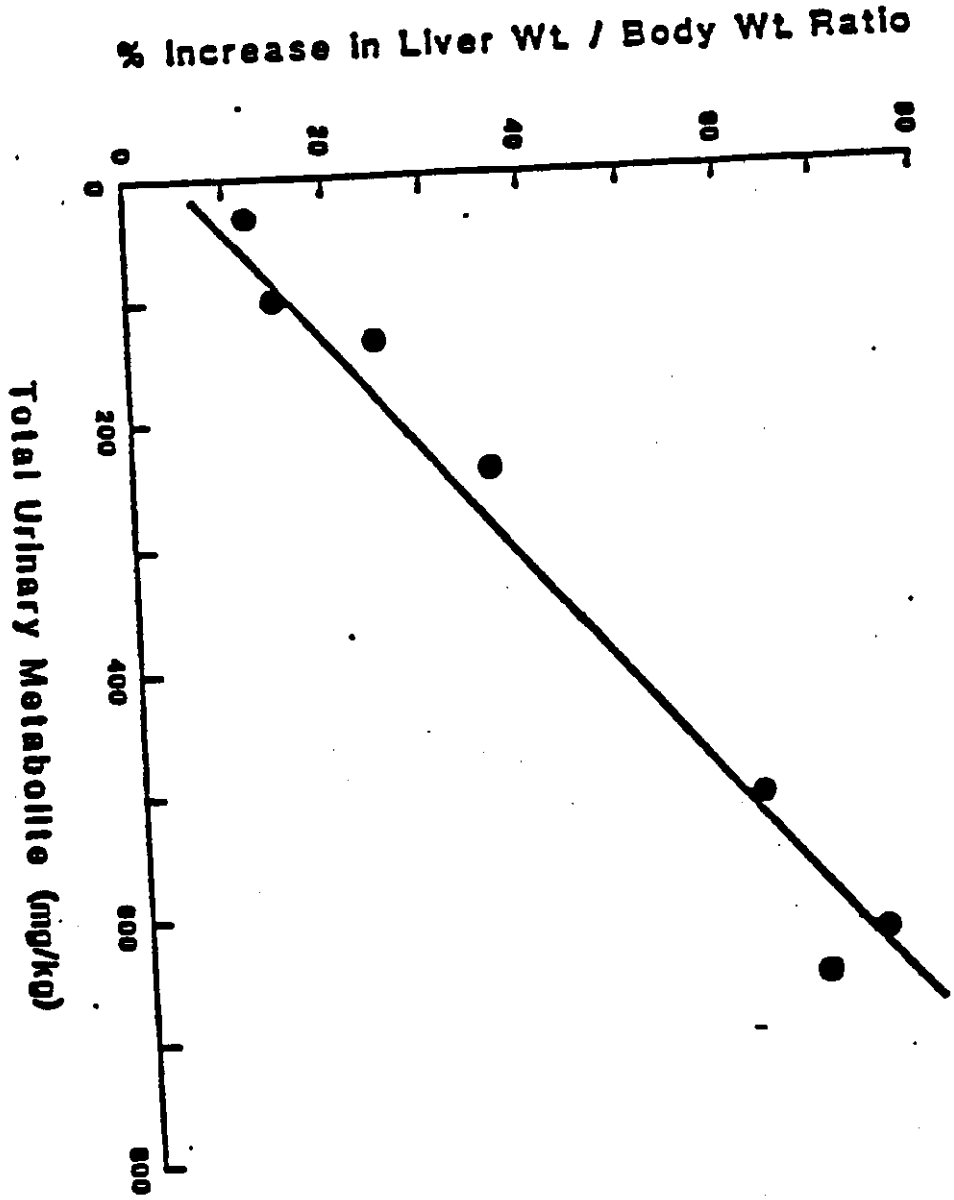
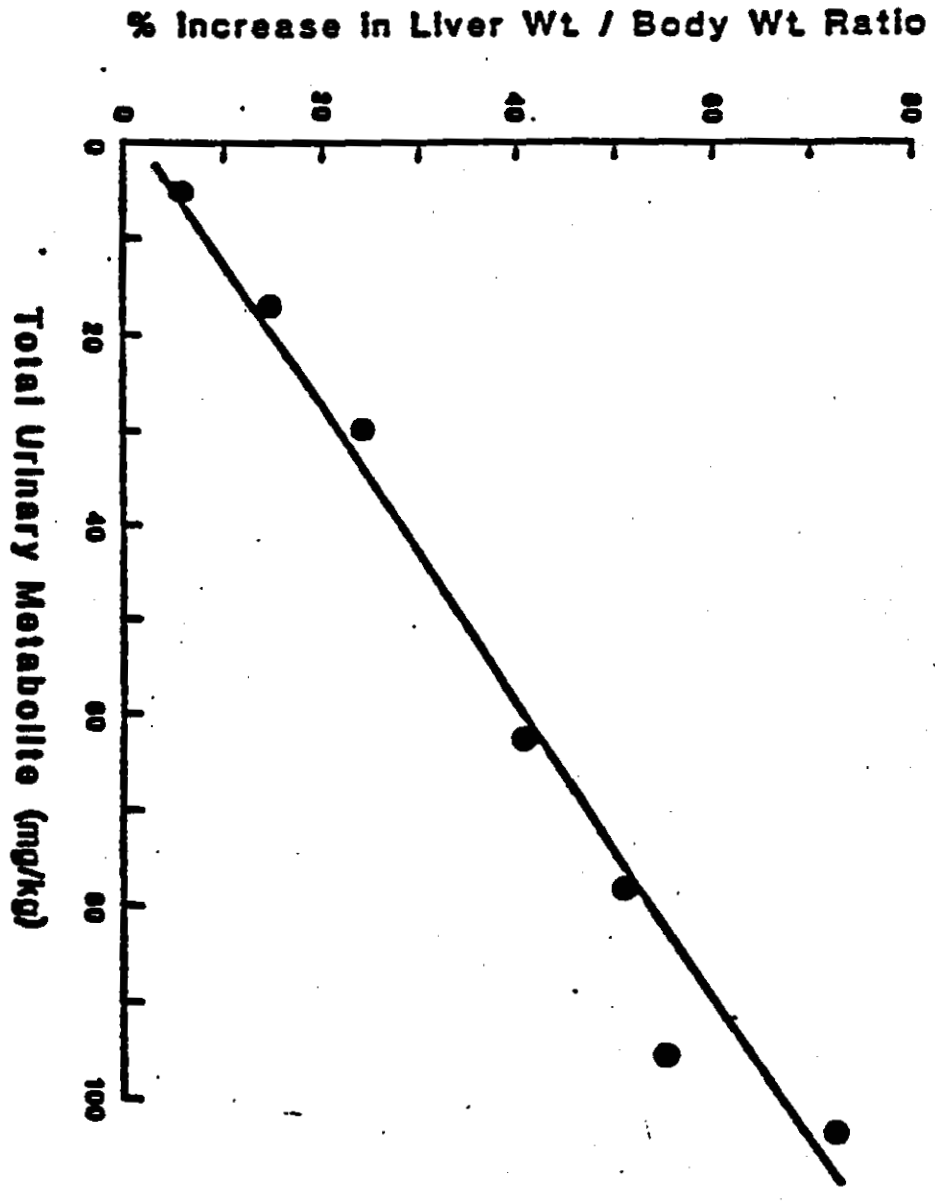
20
40
60
80
100
PER Dose (mg/kg)
0
200
400
1000
1600
2000


% Increase in Liver Wt / Body Wt Ratio
0
20
40
60
80
Total Urinary Metabolite (mg/kg)
0
200
400
600
800


% Increase in Liver Wt / Body Wt Ratio
Total Urinary Metabolite (mg/kg)
0
20
40
60
80
100

California Council for
Environmental and
Economic Balance

August 29, 1984

Mr. William V. Loscutoff
Toxic Pollutants Branch
Air Resources Board
P.O. Box 2815
Sacramento, Calif. 95812

Dear Mr. Loscutoff:

The Council takes this opportunity to comment upon the draft of Part B, "Health Effects of Benzene," prior to its submittal to the Scientific Review Panel.

While the report mentions the uncertainty associated with the assessment of risks of carcinogenicity from exposure to chemical compounds such as benzene, we believe that the document's accuracy and utility as a basis for risk management by the Air Resources Board would be substantially enhanced if it more explicitly acknowledged -- and quantified, where possible -- the various sources of uncertainty in the risk assessment. In this regard, we offer the following specific comments that are consistent with state law (Health and Safety Code Sections 39650-39674) and with the framework drafted by the federal Office of Science and Technology Policy (OSTP) on "Chemical Carcinogens; Review of the Science and Its Associated Principles" (49 FR 21594 et seq).

° Assumptions and Scientific Policy Decisions Should be Explicitly Identified and Summarized

One of the OSTP principles for risk assessment is the importance of maintaining "a clear distinction among facts (statements supported by data), consensus (statements generally held in the scientific community), assumptions (statements made to fill data gaps), and science policy decisions (statements made to resolve points of current controversy)." (49 FR 21599) A committee of the National Research Council has identified 50 separate decision points in a typical risk assessment for carcinogenicity, and found no scientific consensus about how to deal with many of them. The NRC concluded that "Policy considerations inevitably affect, and perhaps determine, some of the choices." (Risk Assessment in the Federal Government, page 33)

Although the risk assessment does in certain cases distinguish explicitly between facts, consensus, assumptions and science policy decisions, it would be useful to the public, to risk management agencies, and probably also to the Scientific Review Panel, if the risk assessment were to include a summary of the judgments and assumptions that entered into the risk assessment process so as to differentiate them from scientific fact.

° Quantification of Sources of Uncertainty and Identification of a Range of Risk

According to the federal OSTP risk assessment principles, "The quantification of the various sources of uncertainty involved in cancer risk assessment can be as important as the projection of the risk estimate itself. The sources that might be addressed include: (a) The statistical uncertainty associated with a given risk estimate; (b) The variability introduced by the selection of a particular low-dose extrapolation procedure; (c) When risk estimation is based on laboratory generated data, the biological variability associated with the use of a particular test organism and its scaling or extrapolation to man." (49 FR 21599) The draft benzene risk assessment apparently quantifies only one of these three sources, i.e. the statistical uncertainty associated with a given risk estimate by calculation of confidence limits.

Although the risk assessment does include in Table VI-5 a range of risks, they are all calculated using a single model. OSTP policy notes that "... the choice of a particular low-dose extrapolation model can have a profound influence on the estimated low-dose risk. Therefore, it has been proposed that an indication of the variability introduced by model selection be obtained by considering the range in the magnitude of low-dose risk estimates associated with the more commonly-employed models." (49 FR 21660) Accordingly, the Council recommends that the risk assessment be expanded to include estimates of human risk based on other models in addition to the multi-stage model. Inclusion of human risk estimates so derived would more accurately describe the actual range of potential human risk as required by state law (Health and Safety Code Section 39660(c)).

The Council believes that these recommended additions to the benzene risk assessment would result in a more complete and accurate representation of the potential human risks posed by exposure to benzene, and a sounder basis for risk management decisions.

Sincerely,

Evelyn F. Heidelberg
Vice President

EFH:pj

cc: Assemblywoman Tanner
Corinne Marshall

Chevron U.S.A. Inc.
575 Market Street, San Francisco, California • Phone (415) 894-2242
Mail Address: P.O. Box 7643, San Francisco, CA 94120-7643

W. T. Danker
Manager, Environmental Programs
Environment, Safety, Fire and Health

August 30, 1984

Department of Health Services
Report on Benzene - Part B
Health Effects of Benzene

Mr. William V. Lascutoff, Chief
Toxic Pollutants Branch
Air Resources Board
P. O. Box 2815
Sacramento. CA 95812

Dear Sir:

Chevron has reviewed the subject report, and we appreciate the opportunity to comment prior to submitting the report to the Scientific Review Panel (SRP). Our comments, listed below, are aimed at making the report a balanced presentation of information that can be used effectively by the SRP and the Air Resources Board, during the decision making process.

1. In its approach to quantifying the carcinogenic risk presented by the exposure to airborne benzene, the DHS appears to mix policy decision with scientific fact. As a matter of "scientific policy", the Department has selected a linear no-threshold model to extrapolate human risk from the most conservative animal data available. The multistage model was preferred by the Department because "it at least is based on some of the theoretical concepts of carcinogenesis." It must be pointed out, however, that there are a number of other risk models, also based on the theoretical concepts of carcinogensis, which would adequately fit the experimental data. Several of these models may be even better predictors of the observed data than the multistage model. We believe it would be more appropriate to apply a range of models to the experimental data. This would allow the assumptions and uncertainties inherent in each model to be fully evaluated so that their limitations are clearly understood throughout the decision making process.

2. We have several concerns regarding the animal data selected by the Department as the basis for its risk calculations. The data

was obtained from a study utilizing oral dosing rather than inhalation, despite the many acknowledged and theoretical differences in the distribution and excretion of benzene following exposure by these routes. While clearly identifying the hematopoietic system and bone marrow as the target organs of benzene's toxicity in both animals and man, the Department selected the incidence of preputial gland tumors as the basis from which to make its risk extrapolations. It is important to note that these tumors have been observed only among males of one specie in one study. In addition, we do not believe there is conclusive evidence that benzene produces tumors in human beings at sites other than those of the hematopoietic and lymphatic systems.

3. We believe that the DHS incorrectly concludes that epidemiological (human) studies are not useful in developing quantitative risk assessments because they lack sufficient statistical power to establish no observed adverse effect levels (or thresholds). While this may often be true, epidemiological studies are useful in establishing upper statistical bounds for cancer incidents at differing levels of human exposure. Such information has been used as the basis for extrapolation of cancer risk at low exposures by the EPA and OSHA in the establishment of their benzene standards.

4. In addressing the concepts of thresholds, we believe the Department has made several unfounded distinctions between carcinogenic mechanisms and those of other toxicological end points ("classic toxicological processes"). These differences are then used in the selection of a linear no-threshold risk assessment model. The potential impacts of physiologic reserve and adaptation on carinogenic responses appeared to have been discounted by the Department despite evidence demonstrating the rates of genetic repair mechanisms, redundant genetic sequences, and immune surveillance in modifying the carcinogenicity of chemicals. The substantial background incidence of cancer in man is interpreted by DHS to demonstrate that human exposure to carcinogens is already well in excess of any possible population threshold for at least some mechanisms. This overlooks, however, the contribution to the background incidence of many spontaneous biological events which need not be related to environmental agents, such as disruption in cell-to-cell communications and errors in DNA replication and repair. The DHS has suggested that the human population is likely to be characterized by a wide distribution of thresholds, such that there would be no absolute lower bound. This hypothesis does not appear supportable in light of the myriad of other traditional toxicological responses for which practical population thresholds have been established.

5. In reviewing the evidence concerning non-genetic mechanisms of carcinogenesis, we believe the DHS has overlooked several lines of supportive evidence, such as the development of bladder tumors following the induction of bladder stones by terephthalates, the induction of lung and mesothelial tumors by natural and man-made fibers having specific physical characteristics, and skin tumor promotion by phorbol esters.

These comments have been prepaired in consultation with Dr. Robert Wilkenfeld, a Toxicologist at the Chevron Environmental Health Center, Incorporated. If you have any questions or comments, please contact Dr. Wilkenfeld at (415) 231-6018 or Mark W. Nordheim of our Environmental, Safety, Fire and Health Staff at (415) 894-6107.

Sincerely,

W. T. Danker

MWN:ig

IT CORPORATION

August 22, 1984

Mr. William V. Loscutoff, Chief
Toxics Pollutants Branch
California Air Resources Board
P. O. Box 2815
Sacramento, CA 95812

Dear Bill:

Subject: DOHS Draft "Health Effects of Benzene"

Thank you for the copy of the DOHS draft of Section B: Health Effects, for your Benzene report. In general, I have two comments:

1. Parts of it, dealing with biology (Sections I through V) are excellent.

2. Parts of it, dealing with aspects of Risk Management (Sections VI and VII) are inappropriate, incomplete, and inaccurate. They should be deleted or redone. Let me be specific: There are three major issues in Sections VI and VII. They are:

   a. Thresholds.

   b. Dose-response Models.

   c. Acceptable Risk Levels.

In each case I feel the DOHS staff has not done a fair and complete job.

Thresholds

The issue of thresholds for carcinogenic action has been debated in many arenas. There are strong emotions on both sides of this issue. The DOHS draft comes down entirely on the "no threshold" side. The references I sent you two weeks ago, on the letters in "Risk Analysis", deal with some other

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views. Further, in my letter to you last week on your Chromium bibliography, I cited three papers on the specific issue of thresholds. Of those, both the Claus and Bolander and Koch papers make specific predictions about thresholds. In Koch's paper, there is a numerical value given for benzene. A quantitative value is readily calculated for Claus and Bolander's approach. I doubt that the dose-response data from either the human epidemiology studies or the animal bioassays cited in the Section B report can statistically rule out the threshold model.

It is fashionable to argue that there is no statistical "proof" of a threshold in these kinds of situations. Most of the "evidence" advanced, including the Congressional OTA study, is simply statistical curve-fitting exercises. If you ask the question "Do the data prove there is a threshold?", the answer is "No." If, on the other hand, you ask "Do the data prove there is no threshold?", the answer again is "No." One can assume either mathematical model, one with the curve forced to go through zero response and zero dose, or another with the curve forced to go through zero response at some positive fixed dose. The statistical evidence is not sufficient to rule out or confirm either model.

I believe the DOHS report needs to deal with this point. The decision to regulate, to set thresholds, and to set air quality standards, is the province of the Board and/or County or Regional Districts. The Health report needs to lay out the information on health effects in a fair and unbiased fashion. If DOHS does not provide complete information to begin with, the Science Review Panel, it seems to me, has no option but to require a thorough rewrite.

Dose-response Models

I, personally, have no major quarrel with the use of the Armitage-Doll multistage model as probably the "best" available. This is based on our present, incomplete knowledge of mechanisms of carcinogenesis. I do not think, however, that the Crump method for calculation gives the kind of results that are best suited for estimating human dose-response relationships. Those issues, however, have to do with the choice of model and the assumption of linear extrapolation of the upper 95 percent confidence limit to zero dose.

Further, the model used does not include the possibility of a threshold, as discussed above. I do not feel that the

model issue is one that can be resolved by a debate among proponents of one or another formula. As I recall, the federal court rejected an OSHA benzene standard in part because all plausible models were not used, and the one chosen gave, in the court's view, a biased result.

Therefore, it seems to me that it is incumbent on DOHS to present results of several models in their extrapolations to low dose. These models should include both threshold and non-threshold cases. I do not believe the calculated 95 percent UCL should be compared with the calculated MLE (see the third paragraph on page 83, and the first paragraph on page 79). This truly is comparing apples and oranges.

Again, sections of the report dealing with these subjects need revision.

Acceptable Risk Levels

The summary, on page 3, and the report, on page 87, discuss the question of what is or is not a "negligible" risk. This is totally inappropriate for DOHS. The selection of actionable risk level is one that your Board must make. The information provided in the paragraphs referred to is only a miniscule fragment of a very complex and extensive literature on the subject. Furthermore, it is not a particularly relevant or illuminating example.

DOHS has been directed by the Governor's Office to delete all items related to Risk Management in its Cancer Policy. I do not think it appropriate to allow this kind of end run. DOHS staff should not be providing recommendations on policy matters to your Board, unless asked specifically.

I believe the CARB staff, perhaps with the aid of a contractor, needs to prepare some data on Risk Management options for the Board. It would be a good idea to have the technical aspects of such a report reviewed by some of the many California experts with extensive professional experience in the areas of risk analysis, assessment, and management. Possibly this could be done with oversight from Dr. Mrak's panel.

Other Specific Comments

The following are listed by page, in no order of priority:

Page 31 last paragraph - "Four major methods are in current use for identification..." On pages 32 and 33, five methods are listed. Is one not a "major" method? Which?

Pages 48-49 - There are a number of arguable statements here about instantaneous deactivations, choice of "most-sensitive individuals", and the use of statistical curve-fitting as evidence. If the revisions I suggest above about threshold are adopted, these pages will be changed. If not, I will provide the Science Review Panel with detailed comments.

Page 80 last sentence - It is not appropriate for DOHS staff to make unsupported recommendations to the Board, at least according to my reading of AB 1807.

Page 82 last paragraph - Again raises the question of "actionable levels" and "de minimus risk", both of which are the Board's province, not DOHS staff's.

Page 85 last paragraph - This points out a need for some estimates of indoor benzene exposure levels in California. Most studies show that people spend nearly all (over 22 hours) of the day indoors, either at home or at work. That being the case, outdoor benzene levels may be meaningless for assessing risk to California's citizens.

Page 99 last paragraph, third line: "Further, each transition (I) is dependent on two constants, a ..." I think "parameters" would be a better choice of words.

Please call if I can clarify or expand on any of these points.

Very truly yours,

Nick

R. Nichols Hazelwood, Ph.D.
Project Manager
Environmental Affairs

RNH:vh

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W. PAUL TIPPETT, *Chairman*
V. J. ADDUCI, *President and Chief Executive Officer*
THOMAS H. HANNA, *Senior Vice President*

August 29, 1984

William V. Loscutoff, Chief
Toxic Pollutants Branch
Air Resources Board
P. O. Box 2815
Sacramento, California 95812

Dear Mr. Loscutoff:

Subject: Department of Health Services Report on Benzene (Part B)

The Motor Vehicle Manufacturers Association of the United States, Inc. (MVMA)* is a trade association whose members represent the major domestic motor vehicle manufacturers. We are responding to your request for comments on the subject report.

As you outline in your letter of July 27, 1984 the subject report unexpectedly became available on July 25, 1984. We received that letter of availability on August 3, 1984, immediately requested the document and received it on August 10, 1984. In order for comments to be included in your submittal to the Scientific Review Panel, the comments were requested by August 30, 1984.

As you know, the subject report is very long, detailed and complex. The document obviously required a great deal of time and effort to develop. Likewise, a proportionate amount of time and effort are required for development of review comments. In addition, it is evident from reading only the executive summary that certain recommendations and numerous assumptions contained in the document, require extensive scientific review and discussion. For these reasons, we are requesting a 60 day extension of the comment period for the subject document.

---

*MVMA members are AM General Corporation, American Motors Corporation, Chrysler Corporation, Ford Motor Company, General Motors Corporation, International Harvester Company, M.A.N. Truck and Bus Corporation, PACCAR Inc, Volkswagen of America, Inc., and Volvo North America Corporation.

We trust that this request will be approved because the Board has exposed a commitment to a sound scientific basis for regulation of toxic air pollutants. A comment period which allows less than adequate time for thorough scientific evaluation would be contrary to the Board's commitment to sound science.

We would appreciate expeditious consideration and reply to our request for an extension of the comment period.

Sincerely,

Fred W. Bowditch

Dr. Fred W. Bowditch
Vice President
Technical Affairs

FWB/s

AIR RESOURCES BOARD
1102 Q STREET
P.O. BOX 2815
SACRAMENTO, CA 95812

September 12, 1984

Dr. Fred W. Bowditch, Vice President
Technical Affairs
Motor Vehicle Manufacturers Association
of the United States, Inc.
300 New Center Building
Detroit, MI 48202

Dear Dr. Bowditch:

Subject: Department of Health Services Report on Benzene (Part B)

Thank you for your letter of August 29, 1984 in which you request a sixty day extension of the comment period on A Review of Benzene Health Hazards (Part B) by the Department of Health Services.

Unfortunately, our schedule for implementing AB 1807 does not allow us to postpone the submission of the benzene report to the Scientific Review Panel (SRP). We have committed to making the submission on September 14. The Panel will have 45 days (plus 15 extra days, if requested and granted) to review the report and return its written findings to the Air Resources Board. During that period, you may submit written comments on the report directly to the SRP or we can forward the comments for you.

I would like to note that we are not required to release Part B for public review before its submittal to the SRP. However, we did make it available to the public as soon as we received it in order to assist SRP review by maximizing the opportunity for public review and submittal of comments to the Panel for its consideration. A copy of your letter and this response will be included in the report to the Scientific Review Panel.

Thank you again for your comments. If you wish to discuss these comments more, please contact Barbara Fry at (916) 322-8276.

Sincerely,

Donald J. Ames for

William V. Loscutoff, Chief
Toxic Pollutants Branch
Stationary Source Division

Natural Resources Defense Council, Inc.

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NEW YORK, N.Y. 10168
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August 31, 1984

Mr. William V. Loscutoff, Chief
Toxic Pollutants Branch
Air Resources Board
P.O. Box 2815
Sacramento CA 95812

RE: Department of Health Services' Report on Benzene (Part B)

Dear Mr. Loscutoff:

I am writing in response to your request for comments on the Department of Health Services report, Health Effects of Benzene. I apologize for the lateness of our comments and hope that you will find them useful nonetheless.

As you know, NRDC has been an active critic of the federal Environmental Protection Agency's program to regulate airborne toxic contaminants. We are therefore very pleased to see California's program begin to move forward, as evidenced by publication of this report on the health effects of benzene. Generally speaking, we believe the report deserves high commendation. It is thorough, up to date, and scientifically sound. It is thoughtful in both analysis and presentation. The report's conclusions are all based on conservative assumptions and should brook little disagreement among the scientific community.

We are particularly impressed with the report's treatment of the related questions of thresholds and risk. We completely agree with the conclusion that there are no compelling arguments for a benzene threshold and that it is prudent under the circumstances to conclude that none exists. We also agree with the report's distinction between voluntary and involuntary risk. As the report points out, public tolerance of involuntary risks is much lower than for those incurred voluntarily. This important distinction must be kept in mind when considering emission standards for various sources.

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The report's discussion of risk would be benefited, however, by inclusion of a related point. This report considers only the risk from benzene, and its conclusions will be used to set a standard for control of benzene emissions. But we also know that similar risks are imposed by hundreds of other airborne toxic substances, and that the total risk from all these exposures is likely to be far greater than the risk from each of them individually. Indeed, the total risk may be greater than the cumulative sum of all the risks due to synergism, a possibility not explored by the report. While there is not currently much evidence to enable us to quantify either cumulative or synergistic risks, their likely existence argues for additional conservatism in setting emissions standards for individual pollutants.

The report's executive summary is a clear and concise collation of the report's most important findings. The summary stresses primarily the acute toxic health effects and cancer resulting from benzene exposure. To these we would add reference to reproductive effects, which are discussed in the body of the report. As the report suggests, these can also be significant and should be highlighted in the summary.

In conclusion, the Department of Health Services' report represents an important contribution to our understanding of the health effects of benzene. While NRDC believes it could be strengthened in some respects, we generally support its conclusions. We hope that the report -- which clearly demonstrates the need for concern about benzene emissions -- will be followed in short order by regulatory action.

If you have any questions about these comments, please do not hesitate to call me or my colleague, Lawrie Mott.

Sincerely,

Laura B King

Laura B. King
Senior Staff Scientist

cc: Assemblywoman Sally Tanner

OCAW
Oil, Chemical & Atomic Workers
International Union, AFL-CIO

International Offices:
255 Union Blvd., Lakewood, CO 80228
303-987-2229
Mail: P.O. Box 2812, Denver, CO 80201

EXPRESS MAIL

August 28, 1984

Mr. William V. Loscutoff, Chief
Toxic Pollutants Branch
Air Resources Board
P.O. Box 2815
Sacramento, CA 95812

Dear Mr. Loscutoff:

Thank you for the opportunity to comment on the Department of Health Services' report on Benzene (Part B). This report has been reviewed by the health and safety staff of the Oil, Chemical and Atomic Workers International Union. We find that this is a good study that appropriately considers the health risks to persons exposed to benzene, whether from the workplace or the environment.

We agree completely with the position of the Department of Health that there is no known safe threshold for benzene exposure so that it should be treated as if it had no threshold.

We were also glad to see the Department take a prudent position on benzene risks from atmospheric emissions. The Union would only recommend that the Department review the two most recent benzene studies which serve to further underscore its carcinogenicity. These are:

1) "Statistical Analysis of Hematology Data From the Chronic Test of Benzene." By Program Resources, Inc., P.O. Box 12794, Research Triangle Park, NC 27709, 5/31/84

2) NTP Technical Report on the Toxicology and Carcinogenesis Studies of Benzene, NIH Publication #84-2545, Draft 7/84

We also took the liberty to review Part A, "A Review of Benzene Uses, Emission and Public Exposure", prepared by the staff of the Air Resources Board.

We would agree with the Air Resources Board that "additional testing of benzene emissions from petroleum refineries and asphalt plants should be performed prior to considering control measure development for these sources".[1] We would urge that this testing be done without delay so that any necessary control measures can be required and instituted in a timely manner.

Thank you for submitting these two documents for review.

Sincerely,

Dan C. Edwards

Dan C. Edwards, Director
Health and Safety Department

SK/DCE/mb
cc: Robert Wages, V-P, OCAW
Jack Foley, Director, District #1
Thomas Lind, Int'l Representative
Robert Boudreau, Int'l Representative

[1] Since the two studies cited in the report offer only rough approximations of benzene emissions from refineries and asphalt plants, it is reasonable to want more precise measurements.

Western Oil and Gas Association
727 West Seventh Street, Los Angeles, California 90017
(213) 627-4866

September 10, 1984

William V. Loscutoff
Chief, Toxics Pollutant Branch
Air Resources Board
1102 Q Street
Sacramento, California 95812

Express Mail

Re: ARB Report on Benzene
Health Effects -- Part B

Dear Mr. Venturini:

The Western Oil and Gas Association ("WOGA") thanks you for providing an opportunity to submit written comments on the Department of Health Services' ("DHS") report, "Health Effects of Benzene - Part B," to be submitted to the Scientific Review Panel ("SRP") along with the report itself. The general comments that follow are intended to be constructive and apply not only to this report but to future health effects evaluations as well. We will submit more detailed comments on the benzene report at a later date.

Introduction

WOGA does not dispute that benzene must be listed as a toxic air contaminant. California law requires that substances identified as hazardous air pollutants pursuant to section 112 of the Clean Air Act must be identified by the Board as toxic air contaminants. (Health and Safety Code § 39655.)*/ The purpose of these comments is to assure that the best scientific data and analysis is used to estimate the risk to human health from benzene at ambient levels. In subsequent proceedings, these risk estimates will guide the Air Resources Board ("ARB") in deciding whether ambient benzene levels can be reduced in a manner that will result in improved health at an acceptable cost. Accordingly, it is important that the risk estimates be as accurate and realistic as possible.

While the DHS Part B report attempted to do this, it seriously overestimated the likely risk of exposure to benzene because it:

a. Did not critically evaluate the animal studies used;

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*/ All statutory references will be to the California Health and Safety Code, unless otherwise noted.

b. Mixed science and policy decisions in estimating risk and did not clearly identify when this mixing occurred;

c. Failed to present a range of risks which would show the uncertainties in the analysis, as required by law;

d. Based its risk estimates on a number of conservative assumptions which do not have a sound scientific basis;

e. Disregarded all data from human studies; and

f. Made no effort to relate the results of the risk assessment to observed effects in humans.

Each of these points are discussed in the sections that follow.

Lack of Critical Evaluation of Laboratory Data.

The report fails to critically review the animal studies on which the risk estimate is based. It appears that the risk estimate was based on the NTP Study results simply because these results showed effects from benzene at the lowest dose. The report does not evaluate the quality of the study or the appropriateness of using it as the sole basis for estimating the risk to humans posed by benzene. Accordingly, the risk estimates derived from this constricted data base are highly uncertain.

Lack of clear separation between scientific and policy decisions.

The Tanner bill (Health & Safety Code §§ 39650 et seq.) established the regulatory framework for the identification and regulation of toxic air contaminants. Separate and distinct duties and responsibilities were provided for both the DHS and the ARB.

The statute directs DHS to "evaluate the health effects of and prepare recommendations regarding substances . . . which may be or are emitted into the ambient air of California

which may be determined to be toxic air contaminants." (Section 39660(a).) It further directs that:

> "The evaluation shall assess the availability and quality of data on health effects, including potency, mode of action, and other relative biological factors, of the substance.
>
> "The evaluation shall also contain an estimate of the levels of exposure which may cause or contribute to adverse health effects and, in the case where there is no threshold of significant adverse health effects, the range of risk to humans resulting from current or anticipated exposure."
>
> (emphasis added, Section 39660(c).)

Thus, under this regime, the DHS's function is to objectively review the scientific data and to make "recommendations" to the Board as to whether a substance should be designated as a toxic air contaminant. (Section 39660(a)).

The ARB, in turn, has been given the authority to identify a substance as a toxic air contaminant following a public hearing (Section 39662(b)) and to decide if regulation is necessary. (Section 39665.) It should also be noted that the law grants discretion to the Board in its consideration of substances proposed for identification as toxic air contaminants. The statute states that:

> "In evaluating the nature of the adverse health effect and the range of risk to humans from exposure to a substance, the state board shall utilize scientific criteria which are protective of public health, consistent with current scientific data."
>
> (emphasis added, Section 39662(d).)

The important thing to note from these sections is that the policy decisions regarding whether to identify a substance as a toxic air contaminant and, if so, how stringently to regulate have been left to the discretion of the ARB. To assist the ARB in making these decisions, the statute directs DHS to evaluate the available data and present a range of risks on which the ARB can base its decision.

Unfortunately, the Part B report fails to distinguish between science and policy decisions and the risk assessment and risk management functions clearly delineated by the statute. This occurs because many policy decisions are incorporated into the review as scientific decisions. We refer to the fact that the most conservative assumptions concerning the most constricted data base were applied at every critical point. (We will discuss the conservative assumptions in more detail below.)

The choice of whether and to what extent to use conservative assumptions is in itself a policy decision of great significance to the risk estimate. Since the policy decisions made were not clearly identified as such, the ultimate decisionmaker -- in this case, the ARB -- is not informed when policy decisions have been made or of the magnitude of their impact on the risk estimates. Thus, the picture the ARB will receive from the Part B report is that only one scientifically credible risk number is possible when in fact several are credible.

Failure to Present a "Range of Risks"

The statute directs DHS to present a "range of risks" to humans from exposure to a given substance. (E.g. sections 39660(c) and 39662(d).) We do not believe that the risk estimates for benzene provided in the report satisfy this command.

The report could and should have presented a more realistic picture of the uncertainty involved in these estimates by using more than one model and by using more than one set of defensible assumptions. This would have produced the range of risk estimates required by the statute, rather than over-simplifying risk to a single number. It would also have provided a more realistic estimate of risk under a variety of scenarios and shown how sensitive risk estimates are to the assumptions applied to the data.

The Conservative Assumptions Used Overestimate Risk.

The comments below are not intended to be exhaustive but to briefly identify some of the questionable assumptions in the report.

1. Selection of an Extremely Rare Tumor

Although a number of benzene risk assessments have been made, WOGA is not aware of any that have relied upon the NTP benzene study and certainly none which based the whole estimate on preputial cancers in mice at the 100 mg/kg dose level. It appears that this study, this dose level and this cancer can only have been chosen because they yield the highest value of unit risk.

These choices should be questioned. Preputial tumors are rare and were observed only in mice. They have not been observed in rats or in animals exposed by gavage and inhalation in the 1983 Maltoni studies. Furthermore, there is no tissue in humans that corresponds to the preputial gland in mice, where the tumors were observed in the RTP study. For these reasons, there is no conclusive evidence that benzene produces nonhematopoietic or nonlymphatic tumors in humans.

2. Selection of the Most Sensitive Species in Which an Effect Occurred.

The report states that data should come from the most sensitive species available. (p. 85.) This conservative assumption may be illuminating but where human data show that humans may not be as sensitive a contrasting assumption and its consequences should also be presented. Relying solely upon the most conservative assumption results in an estimate biased in one direction.

3. Selection of the Most Sensitive Route of Exposure.

Basing risk estimates on exposure data from oral studies in animals tends to overestimate risk for humans since humans are exposed to benzene almost exclusively by inhalation. There are acknowledged differences in the distribution and excretion of benzene following different routes of exposure. An example of this difference is seen in the 1983 Maltoni animal studies which used the multistage model to project human equivalent cancer risk/ppb benzene for both oral and inhalation routes. Inhalation of benzene at doses similar to that given by gavage resulted in calculated risks that are three to four times lower than those calculated from the oral studies. For this reason, in attempting to estimate risks to humans breathing benzene it would be more appropriate to use animal

data derived from tests using inhalation as the route of exposure. The report does not discuss this point nor defend the approach taken.

4. The Interspecies Scaling Factor.

Surface area adjustment was used for interspecies scaling. (P. 72-73) Available empirical information suggests that mg/kg body weight per day is the best estimator. Alternate adjustment methods should have been evaluated and discussed for their impact on the calculated risk values.

5. Assumption of the Multipotential Carcinogenicity of Benzene.

The assumption is made, based on animal data, that benzene is a multi-potential carcinogen when only leukemia has been shown to occur in humans as a result of benzene exposure. This assumption cannot be justified. The report also refers to benzene as causing "leukemia" in animals. There is presently no accepted animal model for benzene-induced leukemia.

6. Choice of Model.

The report states that the multistage model was used because "it at least is based on some of the theoretical concepts of carcinogenesis." (p. 79) However, there are a number of other extrapolation models which are based on other theoretical concepts of carcinogenesis and which adequately fit the experimental data, such as the Weibull or multi-hit models. Several of these models may be better predictors of observed data than the multistage model. The selection of one model over that of another is clearly a policy decision which should not be ascribed solely to scientific considerations and which should be adequately evaluated and explained.

7. The Assumption of a Zero Threshold.

While the report states that the data did not permit the establishment of a threshold for benzene at this time, it should still state its criteria for determining whether a threshold exists for future determinations.

8. Failure to Consider Human Data.

The most serious flaw in the risk estimation is the total disregard of data from human studies. Such data have been used by other governmental agencies which have assessed risk from benzene exposure. Human data can be used to set plausible upper limits for cancer incidence at different levels of exposure and can be used also as the basis for extrapolating cancer risk to the low dose region.

Human data from epidemiological studies was dismissed because of the uncertainty in the exposure level estimates. While this uncertainty is present, the report ignores the important fact that the exhibited biological effects in humans are certain even though the exposure levels which produced them may not be. In contrast, while exposure levels may be certain in animal studies, the comparable biological human effect is not. Yet, this reciprocal uncertainty in the animal data was not addressed.

We do not mean to suggest that animal data should not be used. Rather, it must be recognized that both kinds of data have their inherent uncertainties. Therefore, we urge that both human and animal data from valid studies be considered in the risk assessment and that significant uncertainties inherent in such data should be qualitatively and quantitatively evaluated.

In summary, the consistent application of the most conservative assumptions on each of the points discussed above resulted in an estimate of health risks from benzene that is based on inadequate and inappropriate data. In addition, the results of this risk assessment have no relevance to actual human data and should not be used as the basis for regulatory decisions.

No attempt has been made to compare the risk estimates to reality.

To evaluate whether the risk estimate mathematically derived from the animal data is in touch with reality, the estimated risk number should have been compared with numbers of observed incidences of benzene-related cancer and leukemias in the human population. If the risk estimate is extrapolated to ambient and/or past workplace exposure levels, we believe the predicted cancer and leukemia incidences will be significantly

higher than observed leukemia incidences. If so, reliance cannot be placed on the risk estimate at other exposure levels.

Conclusions and Recommendations.

Based upon our preliminary review, WOGA believes that the Part B report is seriously deficient and recommends that the report be revised as follows:

1. All available animal and human data should be critically evaluated and justification should be provided for the studies selected.

2. Policy decisions should be avoided if possible.

3. If policy decisions must be made, they should be clearly identified as such prior to any discussion of risk.

4. A range of risk estimates should be developed using various models, various human and animal studies and different assumptions. This will provide the ARB with the range of risk required by the statute.

5. Data from valid human studies should be used in addition to valid data from animal studies.

6. The criteria to be applied by DHS for determining thresholds for exposure to toxic air contaminants should be clearly specified.

7. Risk estimates should be characterized as theoretical estimates only and should be compared to observed human data to assess their statistical fit.

We thank you for the opportunity to submit these comments. If you have any questions, please contact Dr. Michael Cardin at (213) 977-6734.

Very truly yours,

Robert Harrison /NB

Robert N. Harrison
Assistant General Manager

APPENDIX C

HEALTH EFFECTS REQUEST TO DHS

State of California

Memorandum

To : Peter Bonk, Director
Department of Health Services
714 P Street
Sacramento, CA 95814

Date : March 30, 1984

Subject: Evaluation of Benzene

From : Air Resources Board

James D. Boyd
Executive Officer

I am writing to formally request that the Department evaluate the health effects of benzene as a candidate toxic air contaminant in accordance with Assembly Bill 1807 (Tanner). According to Health and Safety Code Sections 39660-62, your Department has ninety days to submit a written evaluation and recommendations on the health effects of benzene to the Air Resources Board.

Attached for your staff's consideration in evaluating benzene are: Attachment I - a list of references on benzene health effects which were identified in an ARB letter of public inquiry and received in response to the inquiry letter; Attachment II - a suggested list of topics that we believe should be included in your benzene evaluation and recommendations; and Attachment III - ambient benzene concentration data which should be used to estimate the range of risk to California residents as required in Health and Safety Code Section 39660(c).

My staff is available for consultation in conducting this health effects evaluation. We look forward to continuing to work closely with you and your staff in carrying out this legislative mandate. If you have any further questions regarding this matter, please contact me at 445-4383 or have your staff contact Peter D. Venturini, Chief of the Stationary Source Division at 445-0650.

Attachments

cc: G. Duffy
A. Kelter w/attachments
R. Koutra w/attachments
P. Venturini
Assemblywoman Tanner
C. Berryhill

Memorandum

To : James D. Boyd
Executive Officer
Air Resources Board
1102 Q Street
B-4

Date : July 25, 1984

Subject: Health Assessment of Benzene

From : Office of the Director
714 P Street, Room 1253
5-1248

Attached please find the health assessment of benzene prepared by staff of the Epidemiological Studies Section for the Air Resources Board in support of its efforts to determine if this substance should be listed as a toxic air contaminant. This final document includes clarifications requested by your staff on our June 29 draft version.

While AB1807 did not provide resources to carry out this additional activity during FY 1984, we put the highest priority on providing you this document by temporarily reassigning staff from other mandated activities. The Section chief, a staff physician, an epidemiologist, and a toxicologist have devoted a total of more than 1300 person hours (not including clerical time) to prepare this document.

Peter Rank
Director

Attachment

APPENDIX D

SAMPLING AND ANALYSIS METHODS FOR BENZENE

APPENDIX D. SAMPLING AND ANALYSIS METHODS FOR BENZENE

1. Sites

Benzene sampling by the ARB staff in the SCAB commenced in September 1983 (see Figure 1 for relative locations). El Monte, the first operational site, is 15 kilometers east of the Downtown Los Angeles (DOLA) North Main Street air monitoring station operated by the South Coast Air Quality Management District (SCAQMD). The DOLA site, already in use for criteria pollutant sampling, was the second site selected for benzene sampling. A third sampling site was established at the California State University Dominguez Hills facility in Carson, some 25 kilometers south of DOLA. A fourth sampling site was located at the SCAQMD Riverside station in Riverside, 125 kilometers east of DOLA. Table D-I summarizes the activities around the four monitoring sites.

2. Principle of the Method

2.1 Ambient air is sampled into a polyvinyl fluoride (Tedlar) film sample bag at a constant rate for a 24-hour time interval (9 a.m. to 9 a.m.) by means of an automatic sampler.

2.2 After sampling, the ambient air bag sample is returned to the laboratory and the contents are analyzed by gas chromatography (GC), using a photoionization detector (PID).

2.3 A portion of the air sample is transferred by a syringe to a cryogenic trap.

2.4 The integrated sample is introduced into the chromatrograph sample stream by means of a gas sampling valve.

2.5 The GC data system quantitates benzene by integrating the peak area and calculating the concentration from factors determined during calibration with standards.

3. Range and Sensitivity

3.1 The minimum measurable concentration of benzene has been determined to be 0.5 part per billion (ppb) using prescribed instrument conditions, 40 ml of sample, and a cryogenic trap.

3.2 The range of benzene measurement is 1.0 to 1000 ppb. The upper limit may be expanded by extending the calibration range or by diluting the sample.

4. Confirmation of Chemical Identity

4.1 Any organic compound present in the sample having a retention time similar to that of benzene under the operating conditions described in this method may interfere with the quantitation. Proof of chemical identity for benzene requires confirmation by other means.

4.2 Benzene is positively identified by means of a gas chromatograph/mass spectrometer.

5. Calibration, Precision, and Accuracy

5.1 The calibration procedure employs the principles set forth in the "Quality Assurance Handbook for Air Pollution Measurement Systems" (U.S. Environmental Protection Agency, 1976). It includes periodic checks, and calculations of the confidence interval based on precision.

5.2 Standard reference materials are used in the linearity check at concentrations which bracket the anticipated range of pollutant concentrations. The calibration data are fitted to a straight line, $Y = a + bX$, by the method of least squares. The calibration is acceptable if the F-ratio is less than the 95% rejection limit.

5.3 The 95% confidence intervals are obtained by multiplying the square root of variance by the appropriate value of 't' from a 't' table.

5.4 References:

Bennett, C. A. and Franklin, N. L., "Statistical Analysis in Chemistry and the Chemical Industry," p. 222-232, John Wiley & Sons, Inc., New York (1954).

Draper, N. R. and Smith, H., "Applied Regression Analysis," p. 30, John Wiley & Sons, Inc., New York (1966).

Purnell, H., "Gas Chromatography," pp. 301-302, John Wiley & Sons, Inc., New York (1962).

U. S. Environmental Protection Agency, "Quality Assurance Handbook for Air Pollution Measurement Systems, Volume I - Principles," Research Triangle Park, North Carolina 27711 (1976).

6. Advantages and Disadvantages of the Sampling Method

6.1 The air sampling equipment is easily set up and involves no liquids. The ambient concentrations of benzene are stable for at least 72 hours in the Tedlar sampling bags. Sampling bags are kept away from direct sunlight and are not exposed to temperatures greater than 90°F.

6.2 A representative integrated sample is readily obtained because the equipment samples at a constant rate.

6.3 The sample is easily and repeatedly introduced into the GC by means of a volumetric gas sampling valve or cryogenic trap.

6.4 The lower concentration limit of the analysis may be extended by concentrating the sample by freezing out a larger volume of the sample.

6.5 The polyvinyl fluoride (Tedlar) film sample bag is susceptible to leaks and permeation through the bag.

6.6 The sample is susceptible to contamination when it passes through the diaphragm pump.

6.7 Samples collected in Tedlar bags have a shorter shelf life than samples collected in other containers and sample medians such as stainless steel canisters or adsorbent tubes.

7. Apparatus

7.1 The sample system consists of a diaphragm pump, seven day timer, flow indicator, pressure regulator, flow controller, flow by-pass system and the sample bag (see Figure 2). The diaphragm pump (of steel and Teflon construction) draws ambient air through the sample system at approximately 5 liters per minute. Thirty-five ml per minute of this air stream is sampled, the remaining flow is by-passed and vented. The sample flows through a diaphragm pump, a solenoid valve, a pressure regulator (set for 2-3 psig to prevent any accidentally over-filled sample bag from bursting), a flow control needle valve, a flowmeter, and into the sample bag. A seven-day timer regulates the sampling period.

7.2 Tedlar bags, 2 mil thickness, 50 liter capacity, equipped with stainless steel quick disconnect fittings.

7.3 Rigid opaque containers for Tedlar bag samples to protect contents from sunlight.

7.4 A gas chromatograph equipped with a cryogenic inlet system and photoionization detector.

7.5 A freeze-out system consisting of a U-shaped stainless steel trap filled with stainless steel clippings.

7.6 A stainless steel column (6 ft. x 1/8 inch), packed with 10% N,N-bis(2 cyanoethyl) formamide on 100/120 mesh chromasorb PAW.

7.7 For a confirmation of benzene, an alternate column should be used such as a stainless steel GC column packed with 10% tricyanoethoxy propane (TCEP).

7.8 An analog recorder and a means to quantitate peak areas.

7.9 A 100 ml ground glass syringe or other suitable device to transfer air samples from the Tedlar bag to the GC sample inlet.

7.10 Assorted gas cylinder regulator, flow meters, thermometers, and a barometer.

8. Reagents

8.1 All reagents are of chromatographic grade.

8.2 Benzene NBS standard, 9.74 $\pm$ .10 ppm in ultra pure air. The date of gas cylinder preparation, certified benzene concentration, and recommended shelf life are affixed to the cylinder.

8.3 Helium, 99.995%

9. Procedure

9.1 Preparation of bags.

9.1.1 Bags are constructed from 2 mil Tedlar sheeting (27 inches x 27 inches).

9.1.2 The seams are heat sealed to form an approximate 50 liter envelope.

9.1.3 Swagelock SS-QC4-D-400VT stainless steel quick disconnect fittings are attached with a stainless steel adapter and buna O-ring, Cajon SS-4-TA-OR-ST.

9.1.4 All newly fabricated bags are leak and contamination tested. This involves three pressurization and evacuation cycles using zero air. After a final pressurization to a drum-head tightness, the bags are stored for 24 hours to test for leakage. If the bags do not remain taut, they are repaired or discarded. If the bags remain taut, the contents of the bags are analyzed for benzene by GC. The contents of the bag must not exceed the benzene content of the zero air by a value greater than 2 ppb. If this criteria is met, the bags are evacuated for field use. If the bags exceed the benzene level, the pressurization/evacuation and analysis cycle procedure is repeated.

9.1.5 Due to extensive handling, most bags are not suitable for recycling. Bags suitable for recycling are analyzed with a flame ionization detector, evacuated, refilled with zero air and evacuated for field use.

9.2 Preparation of sampling device for ambient sampling.

9.2.1 The sample bag is attached to the sampler via the stainless steel quick disconnect.

9.2.2 The sample pump is turned on and the flow adjusted with a metering valve to 35 ml/min as determined on the rotameter.

9.2.3 The timer is set to start the sampler at 9 a.m. of the scheduled sampling day and set for a 24 hour duration.

9.2.4 A label is attached to the sample bag noting the bag number, sampling day, starting sample flow, sampling location, and project log number.

9.2.5 After sampling is completed, the sampler is turned on manually and the final sample flow noted on the bag label. The sampler is turned off and the sample bag removed via the stainless steel quick disconnect.

9.3 The sample bags are transported to the laboratory in a rigid opaque container.

9.4 The bag samples received at the laboratory are logged in, placed in storage, and analysis initiated.

9.5 Analysis of samples (freeze-out method)

9.5.1 Freeze-out/Injection:

9.5.1.1 Immerse the sample loops in liquid nitrogen and allow the temperature to stabilize (approximately 5 minutes).

9.5.1.2 After flushing the syringe with about 40 ml of the sample, withdraw 40 ml from the sample bag with a syringe.

9.5.1.3 Transfer the sample into the trap.

9.5.1.4 Back fill the syringe with 40 ml of helium and flush the 40 ml through the trap; then flush helium through the trap for 2 minutes.

9.5.1.5 Stop the helium flushing. Remove the 1/4 inch U-trap from liquid nitrogen (LN_2).

9.5.1.6 Isolate the cryogenic trap by using an "isolation valve" which allows the carrier gas to by-pass the trap.

9.5.1.7 Replace the LN_2 Dewar with a Dewar containing hot water at about 80°C on the trap.

9.5.1.8 Allow all the ice to melt from the trap.

9.5.1.9 Using the valve, introduce the sample into the carrier gas stream.

9.5.2 Measurement of area: The area of the sample peak is measured by any suitable integration device.

9.5.3 GC conditions for benzene

Helium gas flow: 20 ml/min

Heating bath temperature for cryogenic trap: 80°C

Column temperature: ambient

Detector temperature: 150°C

10. Calibration and Standards

10.1 Gas mixture standard: 9.74 $\pm$ .10 ppm benzene in ultra pure air in a pressurized cylinder for which the gas composition has been certified by NBS. The date of gas cylinder preparation, certified

benzene concentration, and recommended maximum shelf life must have been affixed to the cylinder before shipment from NBS. The gas mixture standard shall be used to prepare a chromatograph calibration curve by dilution of the standard.

10.2 Standard of lower concentrations are prepared in the range of one-thousandth of the NBS value to coincide with ambient concentrations. At least two sets of standards with not less than three independent analyses are performed to create multipoint calibrations and to perform zero-span checks.

10.4 Calibration

10.4.1 Determination of benzene retention time. Establish chromatograph conditions identical with those in Section 9.5.3 above. Determine proper attenuator position. Flush the sampling loop with zero helium and activate the sample valve. Record the injection time, the sample loop temperature, the column temperature, the carrier gas flow rate, the chart speed and the attenuator setting. Record peaks and detector responses that occur in the absence of benzene. Maintain conditions, with the equipment plumbing arranged identically to Section 9.5.3 and flush the sample loop for 30 seconds at the rate of 100 ml/min with one of the benzene calibration mixtures and activate the sample valve. Record the injection time. Select the peak that corresponds to benzene. Measure the distance on the chart from the injection time to the time at which the peak maximum occurs. This quantity, divided by the chart

speed, is defined as the benzene peak retention time. Since it is quite likely that there will be other organics present in the sample, it is very important that positive identification of the benzene peak be made.

10.4.2 Preparation of chromatograph calibration curve. Make a gas chromatographic measurement of each standard gas mixture using conditions identical with those listed in Section 9.5.3. Flush the sampling loop for 30 seconds at the rate of 100 ml/min with one of the standard gas mixtures and activate the sample valve. Record C, the concentration of benzene injected, the attenuator setting, chart speed, peak area, sample loop temperature, column temperature, carrier gas flow rate, and retention time. Record the laboratory atmospheric pressure. Calculate A, the peak area multiplied by the attenuator setting. Repeat until two consecutive injection areas are within 5 percent, then plot the average of those two values vs. C. When the other standard gas mixtures have been similarly analyzed and plotted, draw a straight line through the points. Perform calibration daily, or before and after each set of bag samples, whichever is more frequent.

11. Quality Assurance

11.1 Bag material tests were performed to determine suitability of Tedlar used to construct sample bags.

11.1.1 A bag material stability test was performed to determine if benzene was generated within the bag material. A test bag was filled with nitrogen gas from a liquid nitrogen source and the contents analyzed initially and after 72 hours. The benzene level remained below the quantitation level of 1 ppb and below the noise level (0.1 ppb).

11.1.2 A permeability test was performed to determine whether any changes in ambient benzene concentrations would occur in the bag from the time that sampling started until the sample was placed in the gas chromatograph.

Five Tedlar bags were filled with 10 ppb benzene in zero air and the contents of the bags were analyzed at various intervals. The results were:

	Time, Hours (Approximately) Benzene Concentration (ppb)				
Bag #	1	7	25	52	72 (3 days)
HS 51	9.9	9.9	9.7	9.5	9.5
HS 52	9.7	9.8	9.7	9.9	9.8
HS 53	9.6	9.6	9.6	9.7	10.0
HS 54	9.5	9.6	9.5	9.5	9.9
HS 55	9.6	-	10.0	9.9	10.3

11.1.3 Bag Record

A log of each bag is kept to ensure that at no time is an ambient bag used to sample high concentrations of benzene (> 100 ppb) or any other hydrocarbons. The log contains date of fabrication, leak testing, sampling, sampling site/date, bag identification, and bag destruction date.

11.1.4 Bag Contamination

If a bag is found to have sampled source level concentrations (> 100 ppb) of hydrocarbons, the bag is destroyed and associated hardware is decontaminated.

11.2 Each sampler is tested for contamination before field use by pumping gas from a chamber containing zero air until a sample bag is collected. The contents of the bag are analyzed for benzene contamination. If the benzene level remains within 1 ppb of the original zero air analysis the sampler system is then deemed ready for field use. If the system fails this test, it is disassembled, decontaminated, reassembled, and retested. This check is repeated every six months for each sampler system or more frequently if anomolies occur.

11.3 Analysis Audit

Immediately after the preparation of the calibration curve and prior to the sample analyses, an analysis audit is performed by injecting an audit gas sample from a mixing chamber into the GC. The analysis should be within 5 percent of the benzene audit concentration.

12. Calculations

12.1 The hydrocarbon concentrations, in ppb, are calculated by a data system using the external standard method.

$$\text{Concentration}_i = \text{Area}_i \times \text{Calibration Factor}$$

Where in: Area_i = integrated benzene peak area

12.2 The calibration factor (CF) is calculated during calibration by the equation:

$$CF = \frac{\text{Conc}}{\text{Area}}$$

The replicate calibrations are averaged and the arithmetic mean is stored as the CF to be used in subsequent analyses.

12.3 Concentrations may be converted from ppb to ug/m^3 by means of the following formula:

$$ug/m^3 = \frac{(P)(MW)(ppb)(10^3)}{(82.07)(T)}$$

Wherein: P = pressure in atmospheres

MW = molecular weight of benzene

82.07 = gas constant in $(cm)^3(atm)/degK$ mole

T = absolute temperature, (°K)

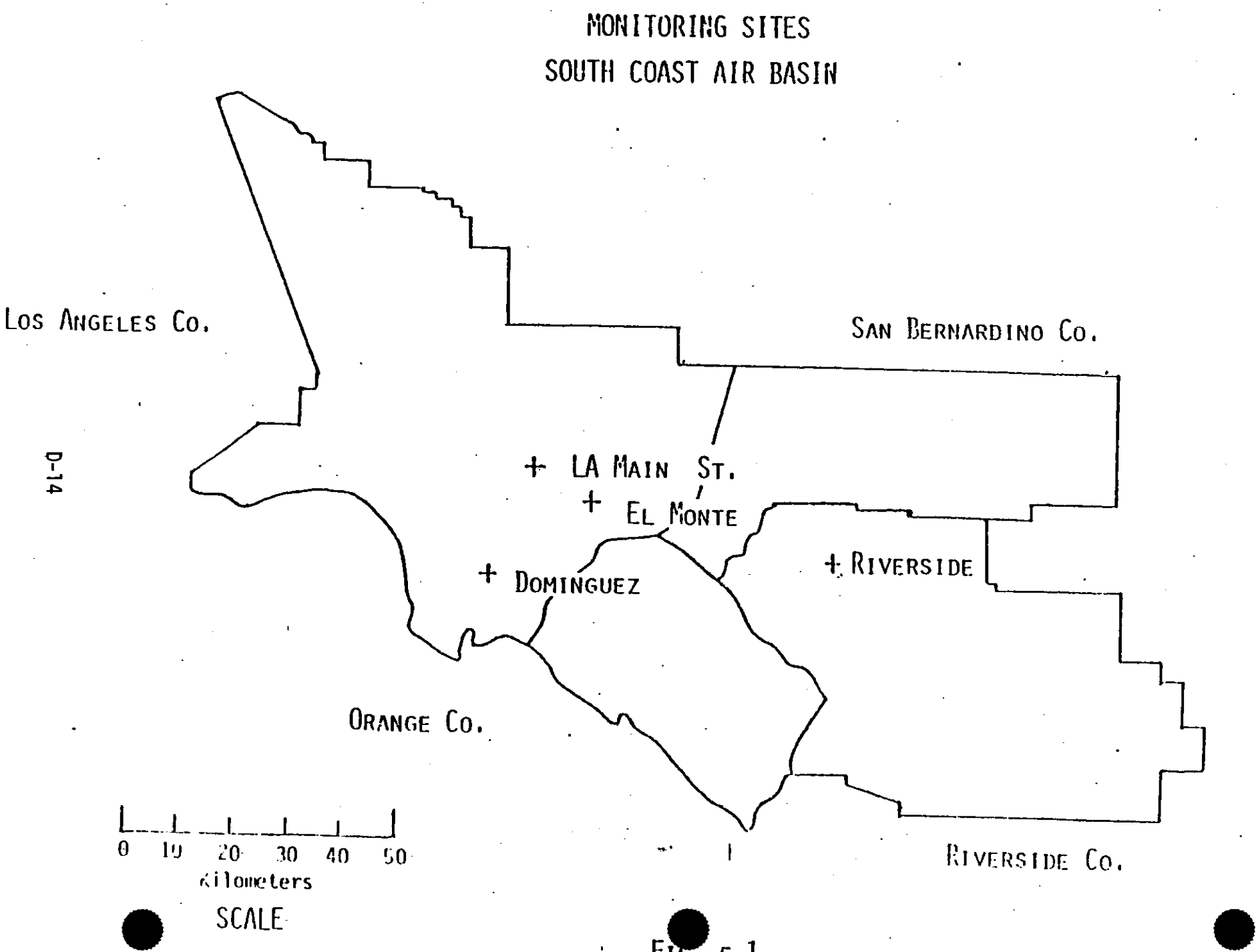
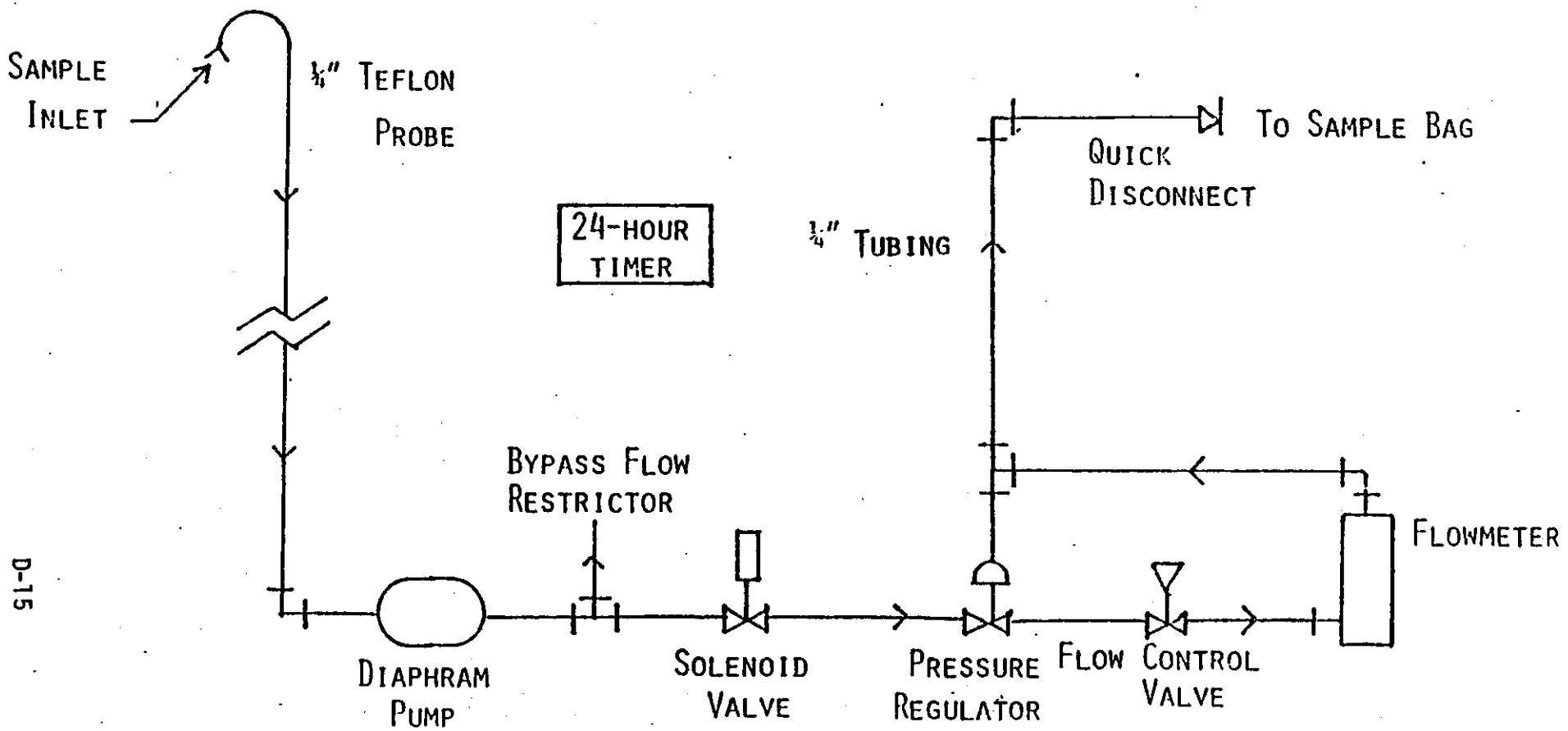

MONITORING SITES
SOUTH COAST AIR BASIN
LOS ANGELES CO.
SAN BERNARDINO CO.
LA MAIN ST.
EL MONTE
DOMINGUEZ
RIVERSIDE
ORANGE CO.
RIVERSIDE CO.
0 10 20 30 40 50
Kilometers
SCALE

FIGURE 1



TYPICAL BAG SAMPLER FLOW SYSTEM

FIGURE 2

Table D-1

Description of ARB/HSLD Toxic Compound Monitoring Sites

Surrounding Activities	Downtown Los Angeles L.A. Dept. of Water and Power 1630 N. Main Street Los Angeles, CA[1]	Dominquez Hills CA State University Dominguez Hills 1000 E. Victoria St. Carson, CA[2]	El Monte ARB/Haagen-Smit Laboratory 9528 Telstar Ave. El Monte, CA[3]	Riverside 7002 Magnolia Avenue Riverside, CA[4]
Residential	West: Two-story apartment units, elementary school	North: Student housing, trailer park South: single family units	North: Low density residences South & West: Low density single family units	North: Low density single family units, convalescent home, several schools Southwest & West: Mixture of single and multiple family units, several schools South & East: Low density single family units
Traffic	Continuous gasoline and diesel powered light and heavy duty vehicles along North Main Street	Light-duty residential traffic	Freeway North of the monitor. On Telstar - gasoline and diesel vehicles with passenger cars dominant. Greatest volumes during commuting hours.	Heavy traffic along Arlington and Magnolia Avenues. Mainly light and medium duty gasoline and diesel-powered vehicles
Small Commercial/ Office use		Strip commercial	Business park area, commercial, light industrial, and office use	Office and strip commercial uses along Arlington and Magnolia Aves.
Light Industrial	North: Carnation processing plant, rubber products company, brass manufacturing and wholesaling. East: Milk processing, winery, railway transportation, concrete company, commercial trucking and shipping, paint company South: Railway transportation, trucking and shipping operations			
Heavy Industrial		North: Oil well pumping South: Oil refining and storage activities, chemical manufacturing East: Oil well pumping		
Agriculture		North and East: Commercial nursery crops		

1/ Monitor in a 2nd story window of 2 1/2 story building. Annual predominant wind direction: southwest.
2/ Monitor in a van southeast of campus. Annual predominant wind direction: west.
3/ Monitor in a trailer in the southwest parking lot. Annual predominant wind direction: south.
4/ Monitor in a one-story building on the southeast side of the Arlington-Magnolia intersection. Annual predominant wind direction: west.

APPENDIX E

AMBIENT MONITORING DATA AND METHODS OF AIR QUALITY MODELING

I. INTRODUCTION

This appendix presents estimates of the annual average* ambient concentrations of benzene in the South Coast Air Basin (SCAB). The estimates apply to areas not immediately around large point sources of benzene. Estimating the locally high concentrations near sources requires different data and modeling techniques than those described here. The sources are mostly not in residential areas. Because residential population data were used to estimate the populace's exposure to benzene, neglecting such locally high concentrations does not introduce serious error.

The general methodology employed is:

1. Establish a relationship between ambient carbon monoxide (CO) measurements and ambient benzene measurements at the ARB's four monitoring stations for toxic air pollutants.

2. Apply the relationship to annual average CO measurements at the numerous CO monitors around the basin to calculate the probable benzene concentrations at those monitors.

3. Calculate the average of the annual means over the basin, both as a simple geographic average and a population-weighted average.

For step 3, population data developed by the Southern California Association of Governments for 1979 were used. Those data are tabulated according to a 5 km by 5 km grid (see Figure 1 at the end of the appendix) that is often used in air quality modeling for the SCAB. The estimates of annual average benzene concentrations are presented for those grid cells

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* "Annual average" denotes the mean of all available 24-hour data during one year.

through interpolation of the results derived for the CO monitoring locations in step 2.

Also, this appendix presents estimates of the number of people exposed as a function of concentration.

II. AMBIENT BENZENE MEASUREMENTS

ARB's Haagen-Smit Laboratory (HSL) has been monitoring benzene at four locations in the SCAB. At the time of the modeling, benzene data were available beginning September 12, 1983 through December 29, 1983. All samples are collected over a 24-hour period, beginning at 0900 PST of the listed date and ending at 0900 PST the following day. The data reported for each site are shown in Table 1. HSL estimates the accuracy of the reported values as $\pm$10 percent of actual values.

Samples are collected 5 days per week at the El Monte site and about once every 5 days at the Downtown Los Angeles, Riverside, and Dominguez sites. None of the four sites is known to be influenced by nearby large sources of benzene. Among the 117 samples collected in 1983, the benzene concentrations range from 1.3 ppb at Dominguez in September to 16 ppb at El Monte in December. The average for all samples during the sampling period in 1983 (approximately the 4th quarter) is 5.7 ppb.

III. CO AS A SURROGATE FOR BENZENE

The ambient measurements of benzene in Table 1 are inadequate to reliably define the spatial and temporal distributions of benzene concentrations throughout the SCAB. Fourth quarter data are generally not representative of annual averages for any pollutant and would probably over-estimate annual averages of benzene.

Table 1

Haagen-Smit Laboratory
Ambient Benzene Concentrations

Benzene Concentrations, ppb

Date	El Monte	Downtown Los Angeles	Dominguez	Riverside
9-12-83	-*	-	-	3.0
9-13-83	2.6	3.7	-	-
9-14-83	2.5	-	-	3.4
9-15-83	2.5	-	1.3	-
9-18-83	3.2	-	-	-
9-19-83	4.2	-	-	-
9-20-83	3.7	3.3	-	2.3
9-21-83	2.7	-	-	-
9-22-83	2.7	-	-	-
9-25-83	1.5	8.1	-	-
9-26-83	2.7	-	-	2.4
9-27-83	2.0	-	2.3	-
9-28-83	1.2	-	-	-
9-29-83	2.8	2.7	-	-
10- 2-83	3.2	-	-	2.7
10- 3-83	4.4	-	5.1	-
10- 4-83	2.7	-	-	-
10- 5-83	4.4	5.3	-	-
10- 6-83	5.1	-	-	3.3
10-10-83	5.9	-	5.0	-
10-11-83	8.2	11.0	-	-
10-12-83	7.1	-	-	4.7
10-13-83	4.3	-	4.4	-
10-16-83	3.8	-	-	-
10-17-83	6.7	8.5	-	-
10-18-83	7.4	-	-	-
10-19-83	10 0	-	4.5	-
10-20-83	6.8	-	-	-
10-23-83	5.3	6.7	-	-
10-24-83	7.4	-	-	1.9

* A dash (-) indicates that no sample was obtained.

Table 1 (cont'd)

Haagen-Smit Laboratory
Ambient Benzene Concentrations

Benzene Concentrations, ppb

Date	El Monte	Downtown Los Angeles	Dominguez	Riverside
10-25-83	9.5	-	10.0	-
10-26-83	8.7	-	-	-
10-27-83	6.8	7.6	-	-
10-31-83	6.3	-	4.3	-
10- 1-83	5.0	-	-	-
11- 2-83	6.9	6.7	-	-
11- 3-83	9.9	-	-	9.1
11- 6-83	5.2	-	4.4	-
11- 7-83	6.7	-	-	-
11- 8-83	6.8	5.2	6.3	-
11- 9-83	7.6	-	-	5.9
11-13-83	3.6	-	3.9	-
11-14-83	6.1	6.6	-	-
11-15-83	10.0	-	-	7.7
11-16-83	7.1	-	6.3	-
11-17-83	3.7	-	-	-
11-20-83	2.5	2.1	-	-
11-21-83	5.4	-	-	4.6
11-22-83	9.6	-	-	-
11-24-83	3.5	-	-	-
11-27-83	4.7	-	-	7.7
11-28-83	9.8	-	10.0	-
11-29-83	7.7	-	-	-
11-30-83	2.5	3.4	-	-
12- 1-83	9.0	-	-	5.1
12- 4-83	4.0	-	6.0	-
12- 5-83	6.6	-	-	-
12- 6-83	9.6	9.4	-	-
12- 7-83	13.0	-	-	7.9
12- 8-83	16.0	-	-	-
12-11-83	4.5	-	-	-
12-12-83	7.8	6.6	-	-
12-13-83	10.0	-	-	9.4
12-14-83	15.0	-	-	-
12-15-83	13.0	-	-	-

Table 1 (cont'd)

Haagen-Smit Laboratory
Ambient Benzene Concentrations

Benzene Concentrations, ppb

Date	El Monte	Downtown Los Angeles	Dominguez	Riverside
12-26-83	1.4	-	-	1.9
12-27-83	2.8	-	-	-
12-28-83	4.1	1.2	-	-
12-29-83	5.0	-	-	4.7
*1- 2-84	6.9	-	-	-
1- 3-84	9.9	9.6	-	-
1- 4-84	10.0	-	-	6.5
1- 9-84	8.4	8.9	-	-
1-10-84	12.0	-	-	7.7
1-11-84	9.8	-	-	-
1-12-84	5.8	-	-	-
1-16-84	-	-	-	7.4
1-17-84	8.4	-	-	-
1-18-84	8.2	-	-	-
1-19-84	9.6	10.0	-	-
1-22-84	5.4	-	-	4.8
1-23-84	8.2	-	9.5	-
1-24-84	14.0	-	-	-
1-25-84	10.0	11.0	-	-
1-26-84	1.8	-	-	1.2
1-29-84	5.8	-	7.0	-
1-30-84	9.2	-	-	-
1-31-84	4.7	5.7	-	-
2- 1-84	1.9	-	-	-
2- 2-84	6.3	-	-	-
2- 5-84	7.3	-	-	-
2- 6-84	10.0	12.0	-	-
2- 7-84	11.0	-	-	8.2
2- 8-84	7.0	-	5.6	-
2- 9-84	2.4	-	-	-
2-13-84	5.2	-	-	5.0
2-14-84	7.5	-	-	-
2-15-84	8.4	-	-	-
2-16-84	-	5.6	-	-

* Data from 1-2-84 and later were not used in the modeling work.

Table 1 (cont'd)

Haagen-Smit Laboratory
Ambient Benzene Concentrations

Benzene Concentrations, ppb

Date	El Monte	Downtown Los Angeles	Dominguez	Riverside
2-20-84	6.1	-	9.4	-
2-21-84	6.1	-	-	5.3
2-22-84	5.6	7.4	-	-
2-23-84	6.9	-	-	5.2
2-26-84	-	-	6.2	-
2-27-84	4.2	-	-	-
2-28-84	6.5	4.4	-	-
2-29-84	5.3	-	-	5.2
3- 1-84	6.6	-	8.3	-
3- 4-84	5.2	-	-	-
3- 5-84	5.7	-	-	-
3- 6-84	7.1	-	-	4.8
3- 7-84	7.8	-	-	-
3- 8-84	4.5	-	-	-
3-11-84	4.9	6.6	-	-
3-12-84	3.0	-	-	3.9
3-13-84	2.3	-	1.6	-
3-14-84	2.8	-	-	-
3-15-84	2.9	4.2	-	-
3-18-84	5.1	-	-	1.7
3-19-84	-	-	5.5	-
3-20-84	5.9	-	-	-
3-21-84	2.4	3.8	-	-
3-22-84	6.0	-	-	4.3
3-25-84	1.9	-	2.3	-
3-26-84	2.8	-	-	-
3-27-84	2.6	3.6	-	-
3-28-84	4.8	-	-	3.9
3-29-84	2.3	-	3.3	-

Since the major portions of both benzene and CO emissions are from motor vehicle exhaust, CO may be a reasonable surrogate for benzene. Also, since both CO and benzene are relatively inert with regard to atmospheric chemistry, one can hypothesize that their ambient concentration ratio will not be significantly affected as the pollutants are dispersed. These comparisons suggest that CO is a good surrogate for benzene. If the hypothesis is valid, a statistically significant correlation should exist between ambient benzene and CO.

CO was actually measured at only the downtown LA and Riverside sites. CO values were interpolated to the other two benzene monitoring locations from the surrounding CO stations. An inverse distance-squared interpolation routine developed by McRae[1/] and modified for this application was used to estimate 24 hour CO concentrations at El Monte and Dominguez for the same dates as the benzene measurements. Major mountain ranges were regarded as barriers that prevent interpolations to grid cells from stations across the mountain range.

Using all 117 pairs of benzene and CO observations (or interpolated CO numbers), the four-station data were analyzed for statistical correlation with a SAS linear regression program.[2/] The resulting Pearson correlation coefficient is 0.82 which is significant at the 0.01 percent level.* The standard error of the benzene estimate is 1.27 ppb. These results are encouraging, especially given the fact that most of the CO concentrations were interpolated. The regression derived from the SAS program is:

$$\text{benzene (ppb)} = 0.51 + 1.875 \times \text{CO (ppm)}$$

---

* There is one chance in 10,000 that the populations do not correlate but still yield a calculated correlation coefficient of .82.

The 24-hour CO and benzene concentrations for each station were also analyzed to determine statistical correlation using multiple linear regression with the additional variable dT, defined as (Tmax-Tmin)/Tmin where Tmax = the daily maximum temperature in degress Kelvin and Tmin = the daily minimum temperature in degrees Kelvin. The term was included as a reasonable surrogate for venting of benzene from storage tanks during daily solar heating. As shown in Table 2, dT was significant only at the downtown Los Angeles site. This term dT was not used in the overall equation and is not reflected in the results of this study.

The correlations between benzene and CO at both the Dominguez and the Riverside sites are high, .93 and .89 respectively. Since the CO at Riverside was measured and the CO at Dominguez was interpolated, the results are encouraging. These results are somewhat offset by the results at DOLA, where a correlation of only .59 was found. However, since the overall correlation coefficient was 0.82, the methodology employed here should give reasonable results.

Table 2

Regression Results

Independent Variables in Regression	Correlation Coefficient vs. Benzene				
	Dominguez	Riverside	El Monte	DOLA	All Stations
CO	.93	.89	.73	.59	.82
CO and dT	.94	.89	.75	.67	--

IV. ANNUAL AVERAGE AMBIENT BENZENE CONCENTRATION ESTIMATES

Annual average benzene concentrations were estimated at each CO monitor using the linear regression equation on page E-7 and annual average CO concentrations from 1981 and 1982. (CO data for the full 1983 calendar year were not released when the work was done and thus are not considered in this report.) Since 31 stations measure CO on a continuous basis in the SCAB, there is a high degree of spatial resolution for the calculated benzene values. Table 3 shows the 31 continuous CO monitoring sites in or near the SCAB. It also shows the measured annual CO concentrations and the benzene concentrations calculated with the regression equation. The highest annual average benzene concentrations were modeled in Burbank, Lennox, and Lynwood, where they are estimated to be about 7 ppb. The annual average benzene concentrations at the air monitoring stations shown in Table 3 were interpolated to the grid square centers of Figure 1 using the McRae inverse distance-squared interpolation routine.[1/] The resulting gridded annual average ambient benzene concentrations are shown graphically in Figures 2 and 3.

Risk assessment calculations require annual average benzene concentration estimates for the populated areas. Both residential and employment populations have been gridded for 1979 by the Southern California Association of Governments for use in transportation modeling studies. Total population in the modeling region is 9,792,000. Total employment is 4,961,000. Population plots are shown in Figures 4 and 5. In general, the most densely populated areas also have high employment and high benzene concentrations.

Table 3

Measured Annual CO and Calculated Benzene at
Air Quality Monitoring Stations

Station	Annual CO (ppm) 1981	Annual CO (ppm) 1982	Annual Benzene (ppb) 1981	Annual Benzene (ppb) 1982
7000060 Azusa	1.72	1.18	3.74	2.72
7000069 Burbank	3.51	3.29	7.09	6.68
7000591 Glendora-Laurel	0.87	0.81	2.14	2.03
7000076 Lennox	3.47	3.42	7.02	6.92
7000087 LA No. Main	2.54	2.49	5.27	5.18
7000084 Lynwood	3.25	2.97	6.60	6.08
7000072 No. Long Beach	1.59	1.93	3.49	4.13
7000083 Pasadena-Walnut	2.60	2.82	5.39	5.80
7000088 Pasadena-Wilson	-	2.07	-	4.39
7000085 Pico Rivera	1.96	2.08	4.19	4.41
7000075 Pomona	2.33	1.79	4.88	2.30
7000074 Reseda	3.00	2.80	6.14	5.76
7000084 West Los Angeles	2.45	2.80	2.34	5.76
7000080 Whittier	2.30	2.08	4.82	4.41
3000176 Anaheim	2.06	1.27	4.37	2.89
3000192 Costa Mesa	1.65	1.65	3.60	3.60
3000186 El Toro	0.46	0.99	0.97	2.37
3000177 La Habra	1.48	1.97	3.29	4.20

Table 3 (Cont'd)

Measured Annual CO and Calculated Benzene at

Air Quality Monitoring Stations

Station	Annual CO (ppm) 1981	Annual CO (ppm) 1982	Annual Benzene (ppb) 1981	Annual Benzene (ppb) 1982
3300146 Riverside-Magnolia	2.17	2.36	4.58	4.94
3300144 Riverside-Rubidoux	1.09	1.18	2.55	2.72
3300137 Palm Springs	0.89	0.83	2.39	2.07
3600197 Fontana-Arrow	1.32	1.07	2.99	2.52
3600176 Fontana-Foothill	1.10	0.56	2.57	1.56
3600192 Redlands	1.10	0.88	2.57	2.16
3600194 San Bernardino E3R	1.48	1.04	3.29	2.46
3600175 Upland - ARB	1.84	1.55	3.96	3.42
3600157 San Bernardino	2.01	-	4.28	-
5600413 Simi Valley	-	0.91	-	2.22
5600420 Ventura-Figuero	-	0.69	-	1.80
4200363 Goleta	-	0.86	-	2.12
4200355 Santa Barbara	1.32	1.48	2.99	3.29

The data are available on magnetic tape or paper on request to the ARB's Technical Services Division.

Both population and cumulative population exposures to benzene are plotted in Figures 6 through 9. These were constructed from Figures 2, 3, and 4. Figures 8 and 9 indicate that 80 to 90 percent of the population is exposed to annual average concentrations above 4 ppb benzene. Table 4 shows population-weighted averages and the grid (geographic) average benzene concentrations using both 1981 and 1982 CO data. Table 4 also shows the annual average among the four benzene stations estimated by multiplying the average of all actual benzene measurements at the four stations, 5.7 ppb, by the ratio of basinwide annual CO to fourth quarter CO from both 1981 and 1982.

Table 4

Annual Benzene Concentration Averages
(ppb)

	1981	1982
For SCAB, by regression equation[a]		
population-weighted average	4.8	4.6
grid average	4.0	3.7
For benzene stations, by CO ratio[b]	4.0	3.9

a Values apply to the indicated year.

b Values apply to 1983, calculated using CO data from the indicated year.

The population-weighted benzene apparently exceeds the geographical average by about 20 percent. The four monitoring stations apparently reflect the average concentration across the basin, although annual average concentrations are considerably higher at some locations.

IV. LIMITATIONS TO ANALYSIS

Several important assumptions were made to estimate annual benzene concentrations in the SCAB. These impose limitations on the use of the data. The most important limitations are summarized below:

1. All available CO data have been used in this study. The spatial representativeness of each station is unknown. Some of the CO monitoring probes are closer to local sources than others. Lennox is designated as a microscale* station; the other stations with high calculated benzene concentrations, Burbank and Lynwood, are not. It is uncertain how this difference in spatial representation between stations affects the results.

2. Indoor benzene concentrations may not be directly related to ambient concentrations. This study makes no attempt to examine indoor exposure.

3. Benzene concentrations may be high on roadways. No attempt has been made in this study to estimate near-road exposures to benzene.

4. This study does not include benzene exposures in the workplace.

5. Stationary sources of benzene are not explicitly included in this report. They are considered indirectly through their contribution to benzene measured at the four monitoring stations. It is possible that areas near large sources (like refineries) may have higher concentrations than those estimated here.

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* Directly affected by specific sources

V. OTHER AMBIENT BENZENE DATA

The EPA data base compiled by SRI, International[3/] contains data from ambient monitoring for benzene at several places in California. The data are all from short-term studies and mostly samples of less than 24 hours duration. Table 5 synopsizes these data. They were not used in the foregoing analyses.

Table 5

Various Short-Term Benzene Monitoring Data

	Year	Month	Sample Duration (hrs.)	Samples	Mean (ppb)
Azusa	1975	Aug-Sep	3*	44	4.3
Dominguez	1976	May	1	1	10.7
El Monte	1975	Jul-Sep	3*	104	5.1
Long Beach	1975	Jun-Jul	3*	39	2.8
Los Angeles	1979	Apr	24	9	6.0
Oakland	1979	Jul	24	8	1.5
Riverside	1980	Jul	24	11	3.8
Torrance	1976	May	1	1	4.3
Upland	1975	Jun-Aug	3*	46	5.3

* The samples were all within the 2 a.m. to 3 p.m. period.

VI. BENZENE CONCENTRATIONS NEAR SOURCES

The major sources to which the public is often exposed are busy roadways and filling stations. Following are the available data on ambient benzene concentrations near such sources. Except for the modeling of concentrations near a freeway and near a busy intersection, all the data are absolute (total) concentrations.

Fentiman[4] et al monitored benzene concentrations at six to eight sites around each of two lone filling stations and a four-station intersection. Sampling times ranged from 8 to 19 hours and covered all times of the day. One or two samples were collected at each site. The highest average benzene concentration (between 100 and 1300 feet of the pumps) at any site was 1.9 ppb. Downwind samples were not significantly higher in benzene than were up or crosswind samples. Because the stations were not equipped with vapor recovery, the data over-estimate benzene concentrations for similar situations in urban California.

Fentiman[4] also measured ambient benzene in 25-hour samples six to ten feet on both sides of a busy street (1600 vehicles/hr, avg). The average measurement upwind of the road was 7.1 ppb; the average downwind was 3.0 ppb. Benzene did not correlate well with traffic density.

NIOSH[5] cites two British studies in which employees at filling stations and bulk loading plants wore personal benzene monitoring devices (sampling the wearer's ambient air). Results from the filling stations ranged from 0.2 to 3.2 ppm. The stations were vending gasolines containing 2.8 to 5.8 volume percent benzene (3.3 to 6.9 weight percent), whereas a typical value in California is 1.7 weight percent.[6] Also, the stations did not

have vapor recovery equipment, which is designed to capture 95 percent of hydrocarbon vapors in urban California.* Therefore, the results of similar tests in California should be about 2 percent of the British results (assuming that California gasolines are as volatile as British gasoline, which may not be true), or 4 to 65 ppb.

In a study in the U.S.,[8] the air was sampled near the mouths of people dispensing gasoline at self-service stations without vapor recovery. The mean result was 1,210 ppb. This result corrected for vapor recovery is 60 ppb.

The ARB staff has modeled** benzene concentrations near a busy roadway. For a high traffic density on a large freeway (20,000 vehicles per hour) and at worst-case meteorology (F stability and 1 meter/second wind), the calculated roadside concentration is 50 ppb above background, decreasing to 19 ppb at 50 meters and to 7 ppb at 150 meters.

The ARB staff has modeled*** benzene concentrations downwind of the intersection of Wilshire Boulevard and Veterans Avenue in the South Coast Air Basin. The modeling is based on typical weekday traffic density (100,000 vehicles per day on Wilshire and 20,000 vehicles per day on Veterans), and hourly meteorological data from Los Angeles International Airport. At a distance of 80 feet from the intersection (four sites), the maximum hourly benzene concentration varied from 9.7 to 17 ppb above background. The maximum annual average benzene concentration varied from 0.5 to 1.4 ppb above background.

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* Stations with vapor recovery dispense 88 percent of all gasoline in California.

** CALINE 3 line source dispersion model; 20,000 gasoline vehicles per hour; average benzene emission rate per vehicle .0992 gm/mile (4.2 percent benzene in exhaust hydrocarbon)

*** EPA's ISCST model for area sources; 20 m.p.h.; composite benzene emission factor of .1041 gm/mile (4.1 percent benzene in catalyst exhaust, 4.2 percent benzene in non-catalyst exhaust, 2.3 percent benzene in diesel exhaust).

REFERENCES FOR APPENDIX E.

1. McRae, Goodin, Seinfeld, Mathematical Modeling of Photochemical Air Pollution, Environmental Quality Laboratory, California Institute of Technology, Pasadena, California, April 1982.

2. SAS Institute Incorporated, SAS User's Guide: Statistics 1982 Edition, Box 8000, North Carolina.

3. Brodzinsky, R. and Singh, H. B., Volatile Organic Chemicals in the Atmosphere - An Assessment of Available Data, SRI International, April 1983, EPA 600/3-83-027a.

4. Fentiman, A.F. et al.; Environmental Monitoring - Benzene, Battelle Columbus Laboratories, PB 295-641, 1979.

5. U. S. Department of Health, Education and Welfare (NIOSH); Occupational Exposure to Benzene, 1974.

6. Air Resources Board, Haagen-Smit Laboratory, 1980 Hydrocarbon Composition of Gasolines in Los Angeles, HS-10-LHC, 1980.

7. Air Resources Board, Technical Services Division; "EDB Exposure Near A Freeway," memo from Donald McNerny to William Loscutoff, October 15, 1984. (Memo reports modelling of EDB; results were linearly adjusted by the emissions rate of benzene [in grams per mile per vehicle] relative to the emission rate of EDB.)

8. U.S. EPA; Evaluation of Air Pollution Regulatory Strategies for Gasoline Marketing, EPA-450/3-84-012a, p. 6-14, July 1984.

Figure 1
SOUTH COAST AIR BASIN MODELING GRID

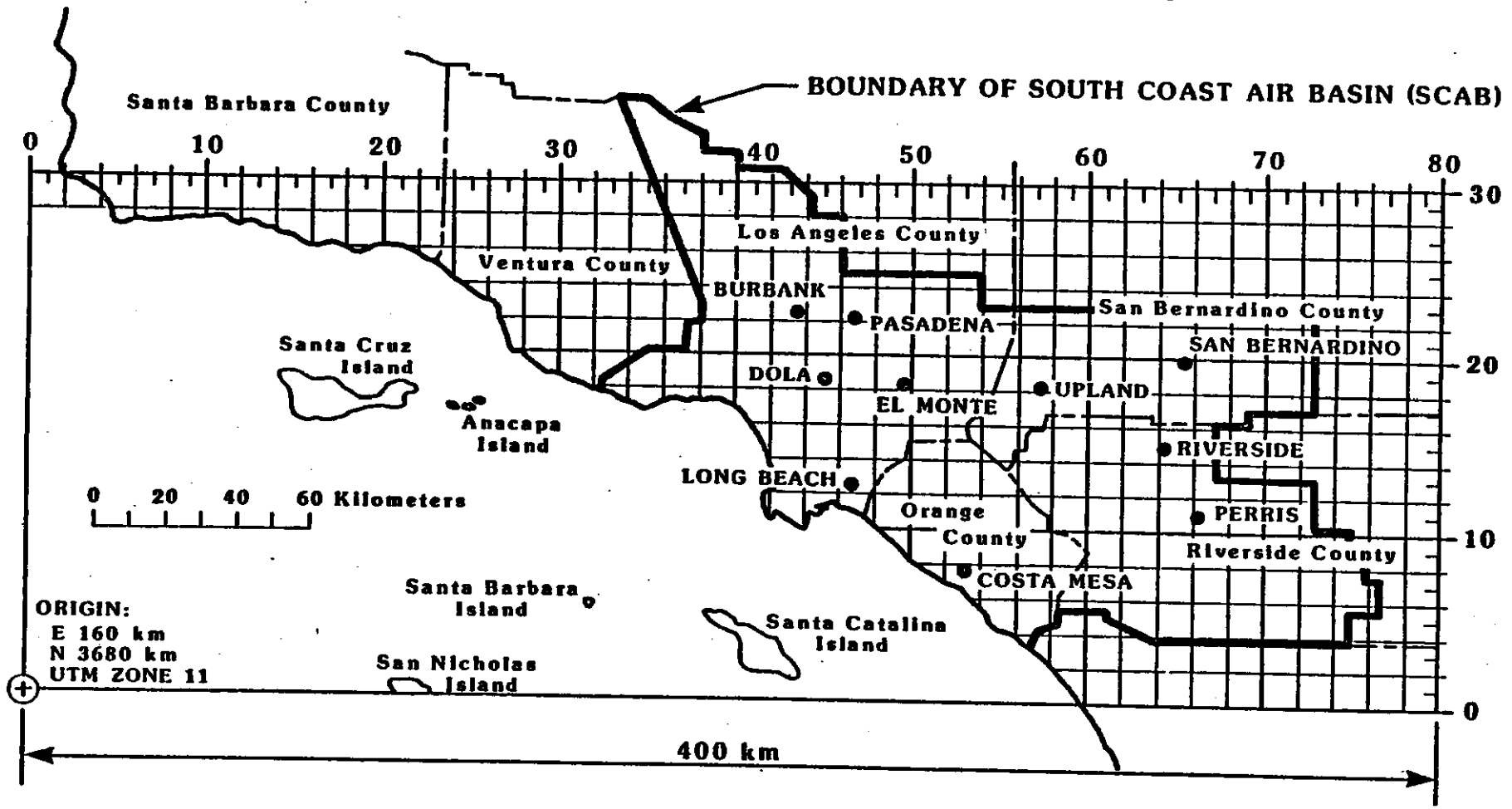


FIGURE 2

SOCAB 1981 Total Benzene in 5 KM Cells

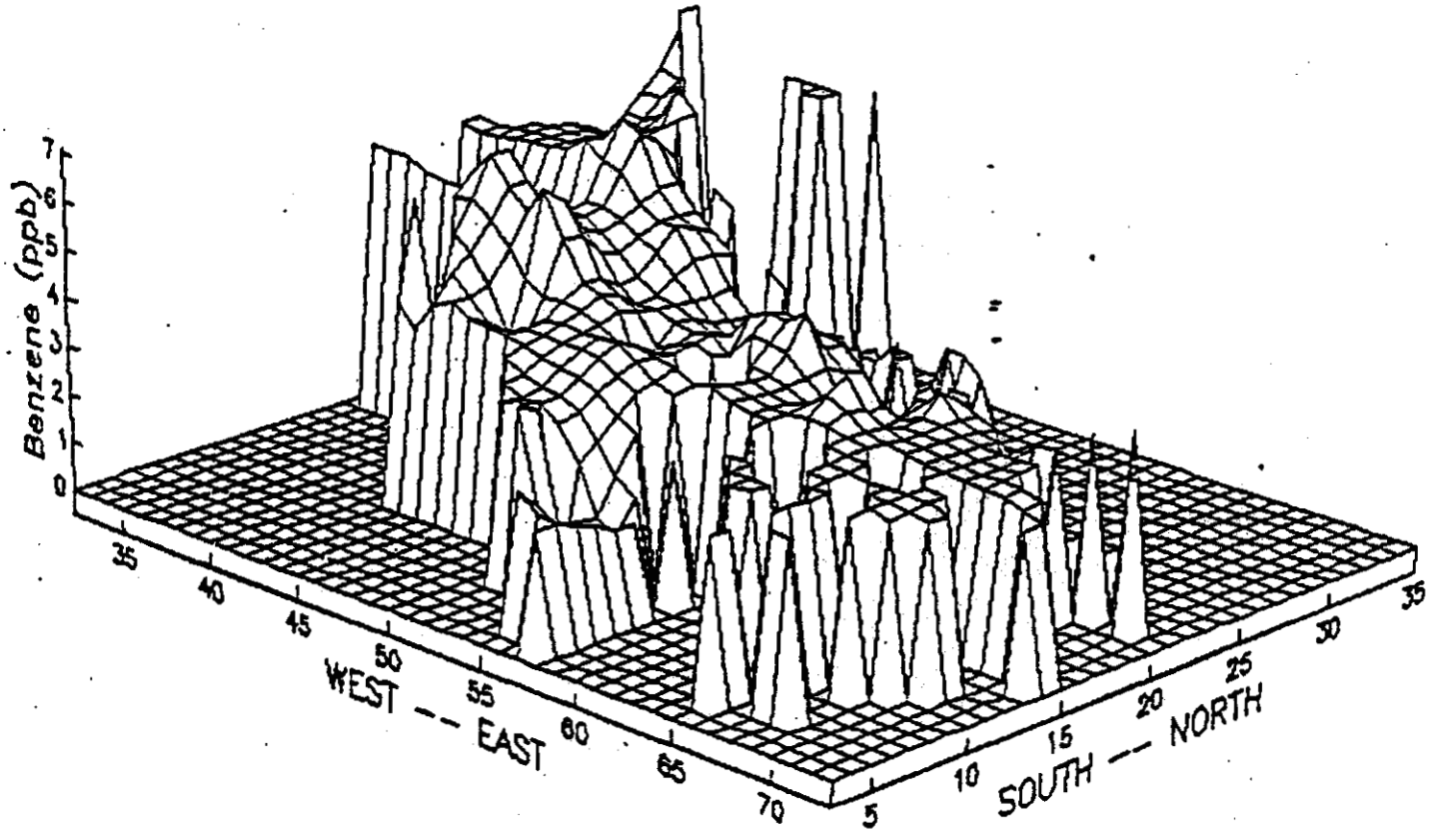


FIGURE 3

SOCAB 1982 Total Benzene in 5 KM Cells

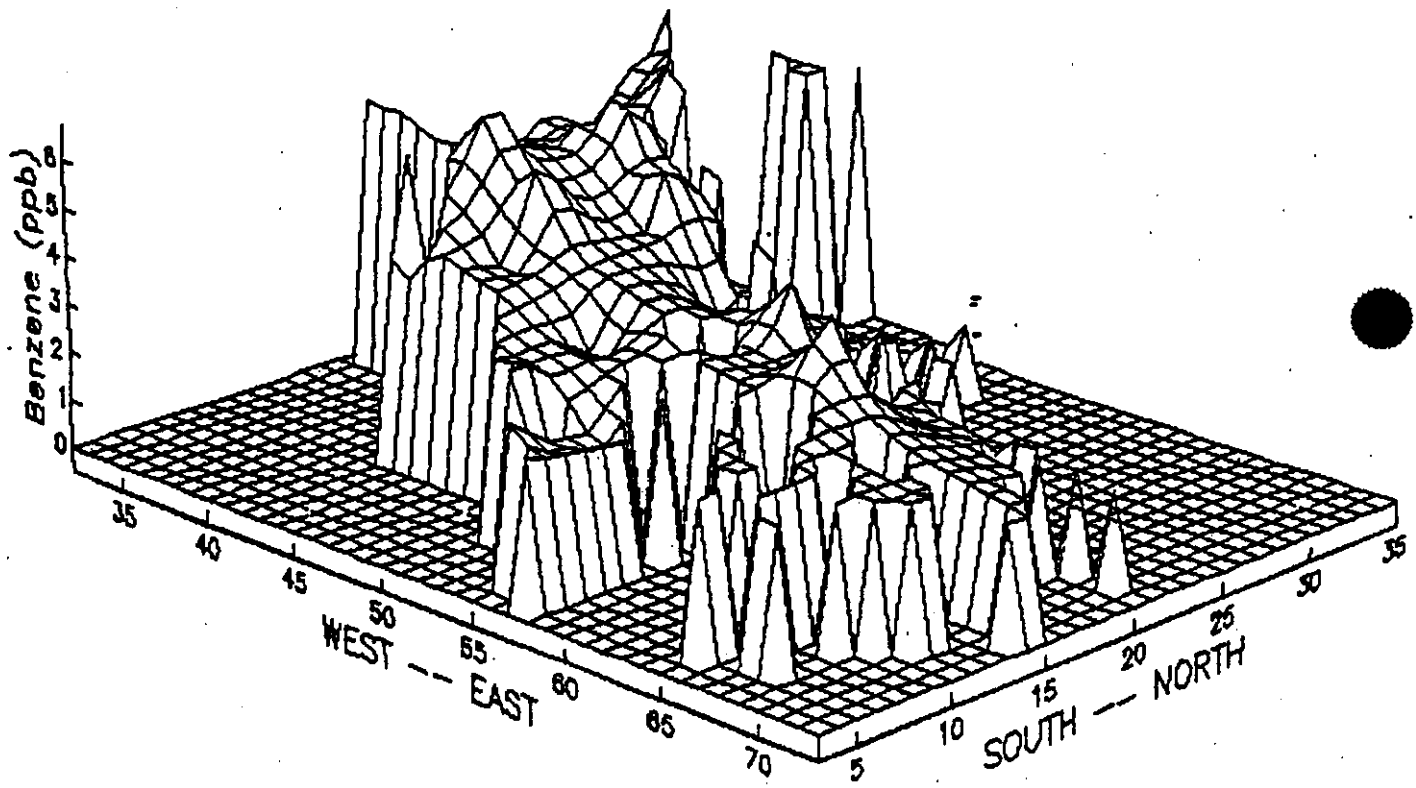


FIGURE 4

SOCAB Population 5 KM Grid Cells

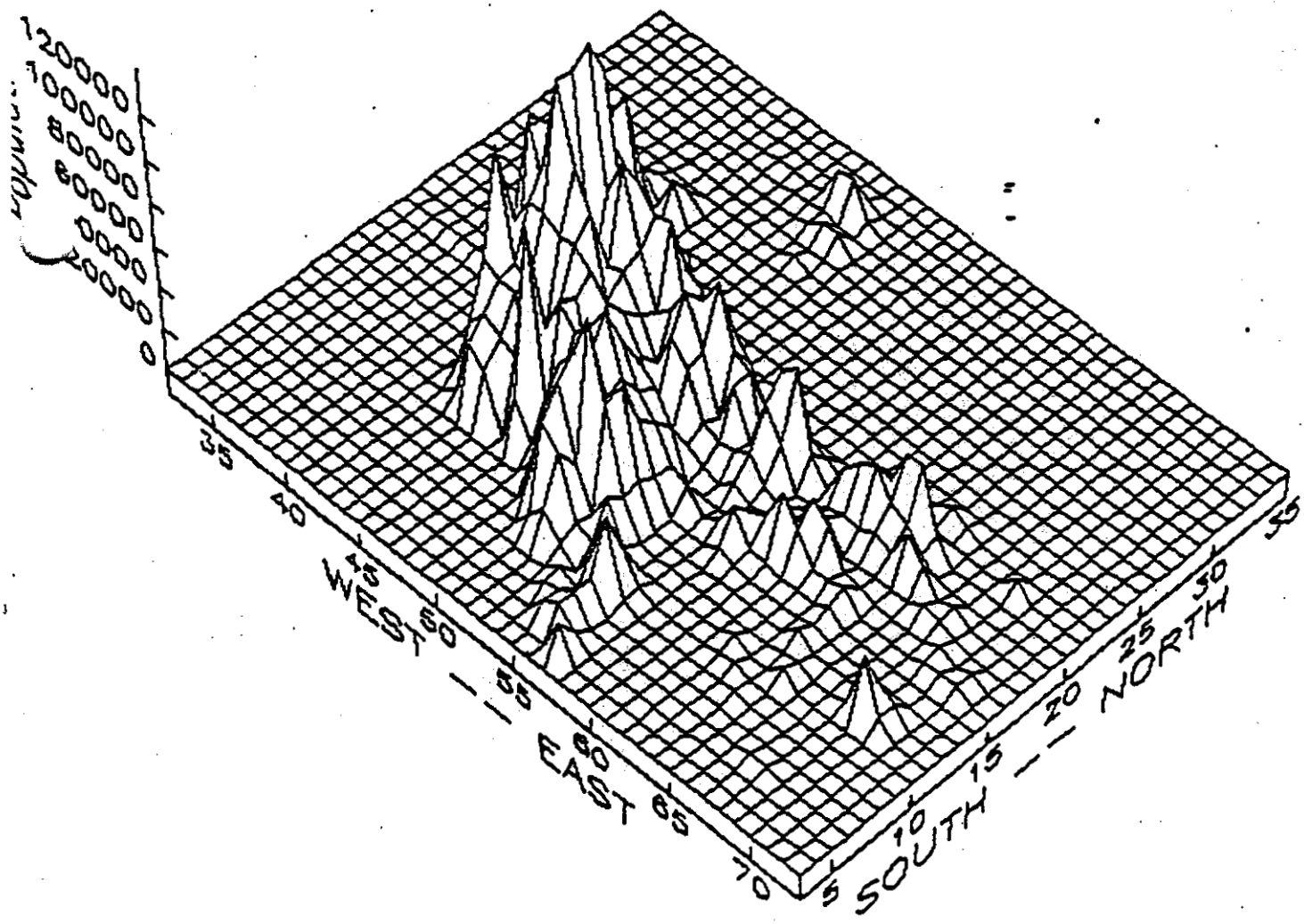


FIGURE 5

SOCAB Total Employment 5 KM Cells

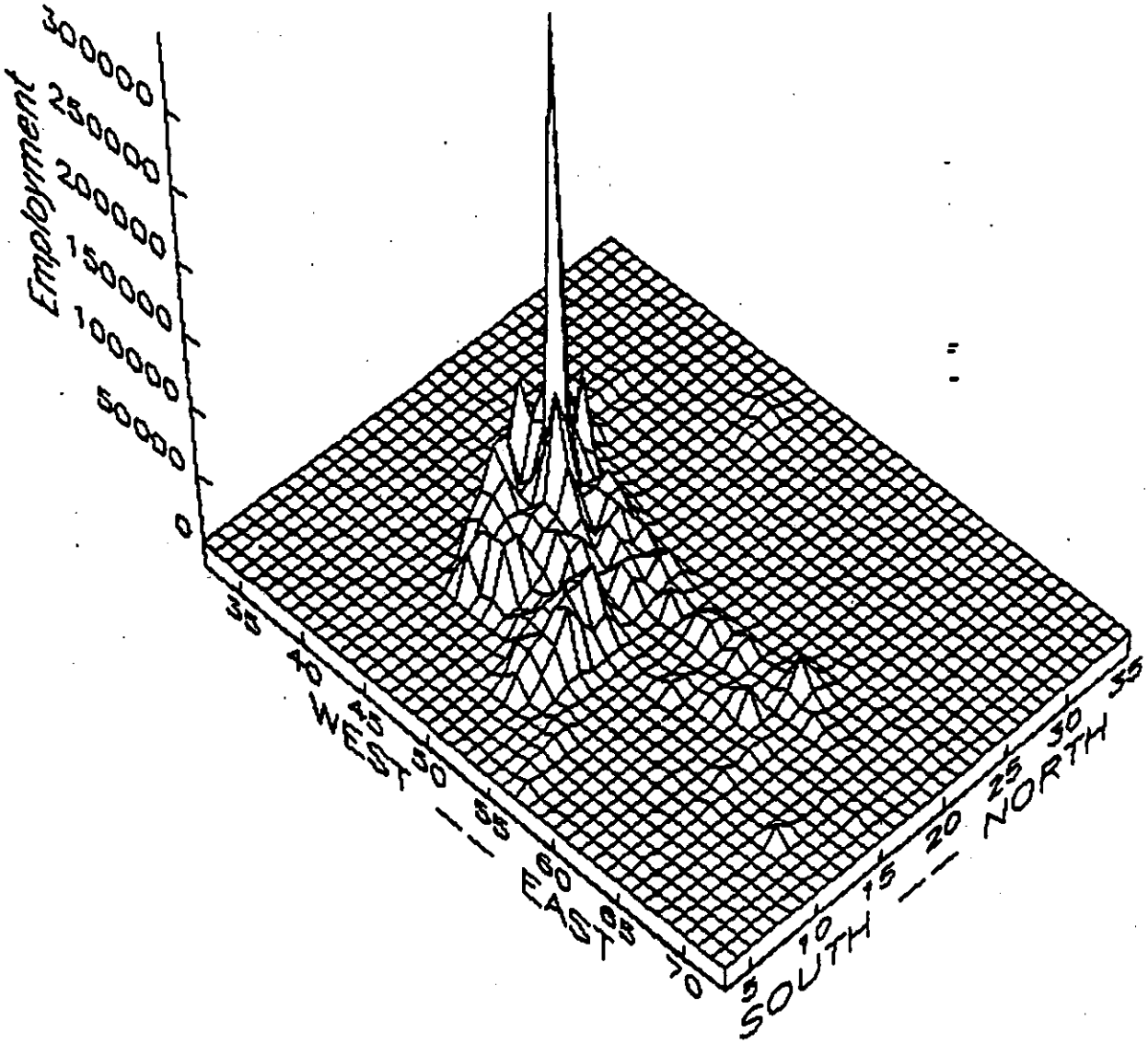


FIGURE 6

1981 BENZENE EXPOSURE FOR SOCAB

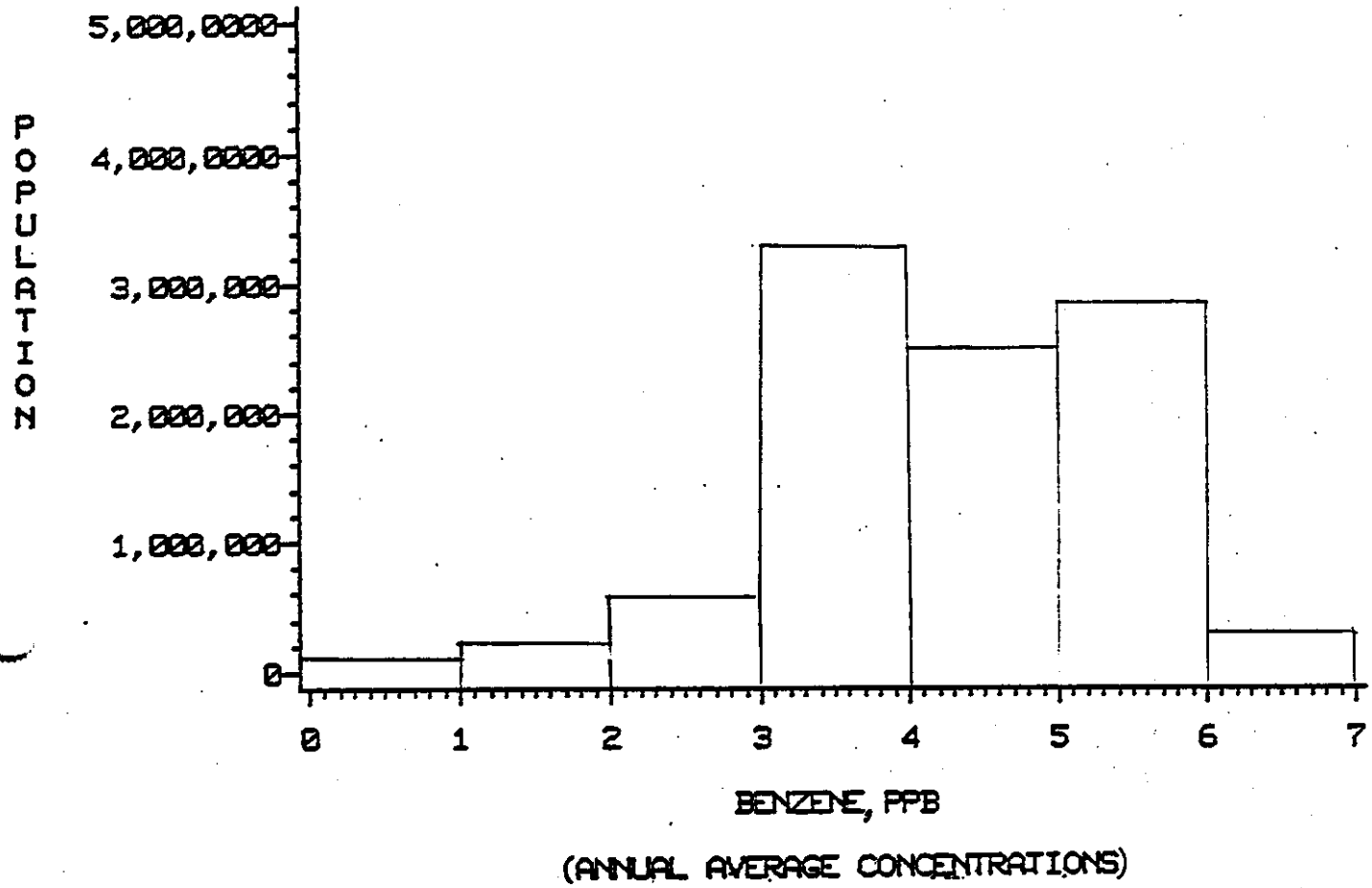
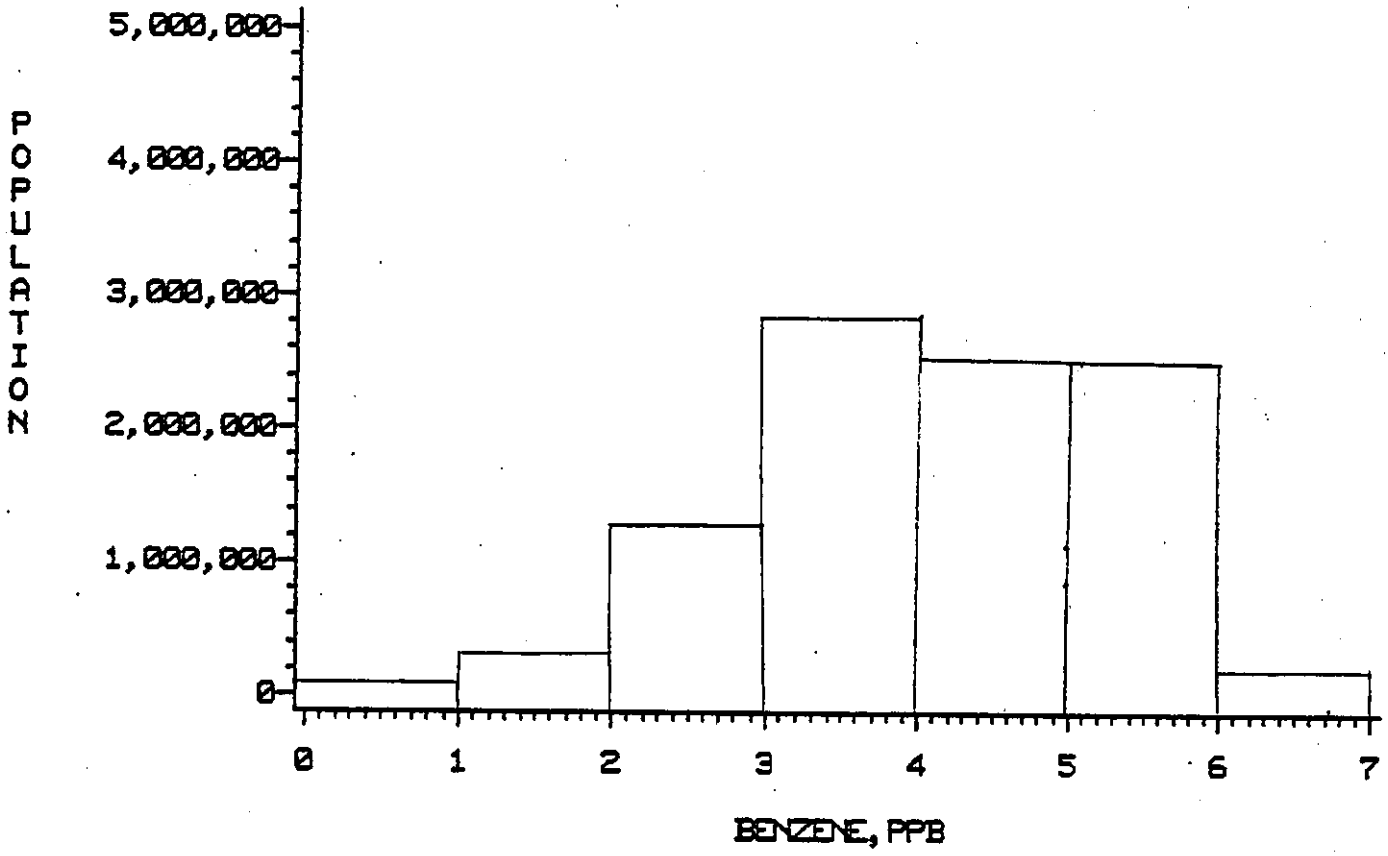


FIGURE 7

1982 BENZENE EXPOSURE FOR SOCAB



ANNUAL AVERAGE CONCENTRATIONS

Part B Summary

Part B of the benzene report to the Scientific Review Panel is the Department of Health Services' (Department) health effects evaluation of benzene. The Department has examined and evaluated the available scientific evidence with regard to three issues:

1. Is there sufficient evidence that benzene meets the definition of a "toxic air contaminant" under Health and Safety Code Section 39655?

2. Is there sufficient evidence to identify a threshold exposure level for benzene below which no significant adverse effects would be expected?

3. If no threshold exposure level can be identified, what is the range of risk to humans due to current or anticipated exposures to benzene?

The Department finds there is sufficient evidence that benzene meets the definition of a toxic air contaminant. In particular, they are in agreement with the International Agency for Research on Cancer (IARC) that there is sufficient evidence to consider benzene a human carcinogen. The Department does not find there is sufficient positive evidence to identify a threshold level for the carcinogenic effects of benzene in humans. Neither does the Department find that there is sufficient evidence to definitively prove that no threshold exists. Therefore, as a matter of science policy and consistent with the positions of the EPA and IARC, they recommend that benzene should be treated as a substance without a threshold for carcinogenesis. Based upon the available evidence they recommend the use of those quantitative dose-response curves for benzene's carcinogenic effect which are bounded above by the animal test data and below by the human epidemiologic data. The upper bound curve is based upon the upper 95 percent confidence limit for the multistage model using the most sensitive site in mice, the preputial gland, which yields a value of $170 \times 10^{-6}/1$ ppb benzene. The lower bound curve is based upon extrapolations of human epidemiologic data carried out by the Carcinogen Assessment Group of EPA, and yields a value of about $22 \times 10^{-6}/1$ ppb benzene.

1981 BENZENE EXPOSURE FOR SOCAB

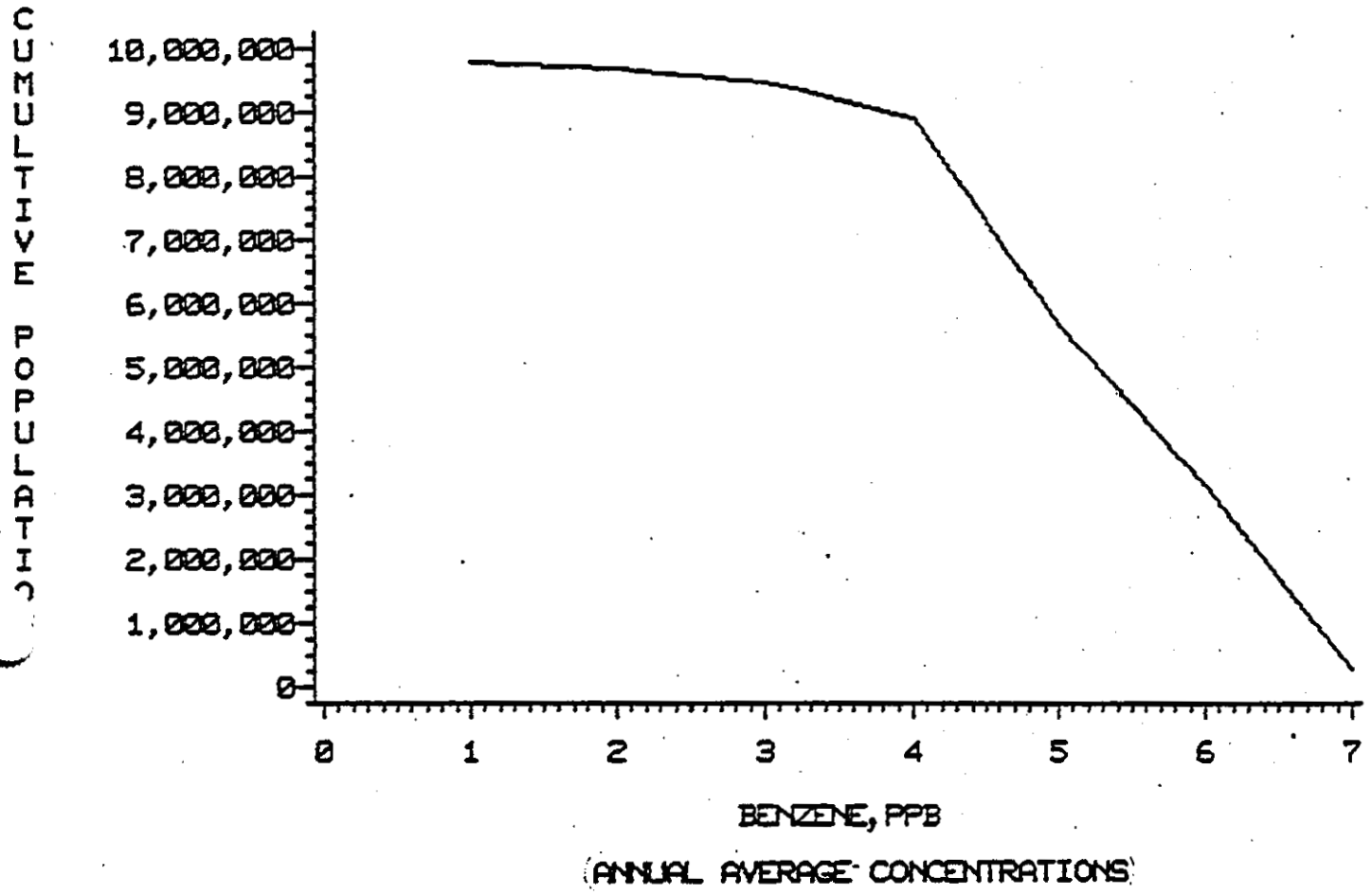
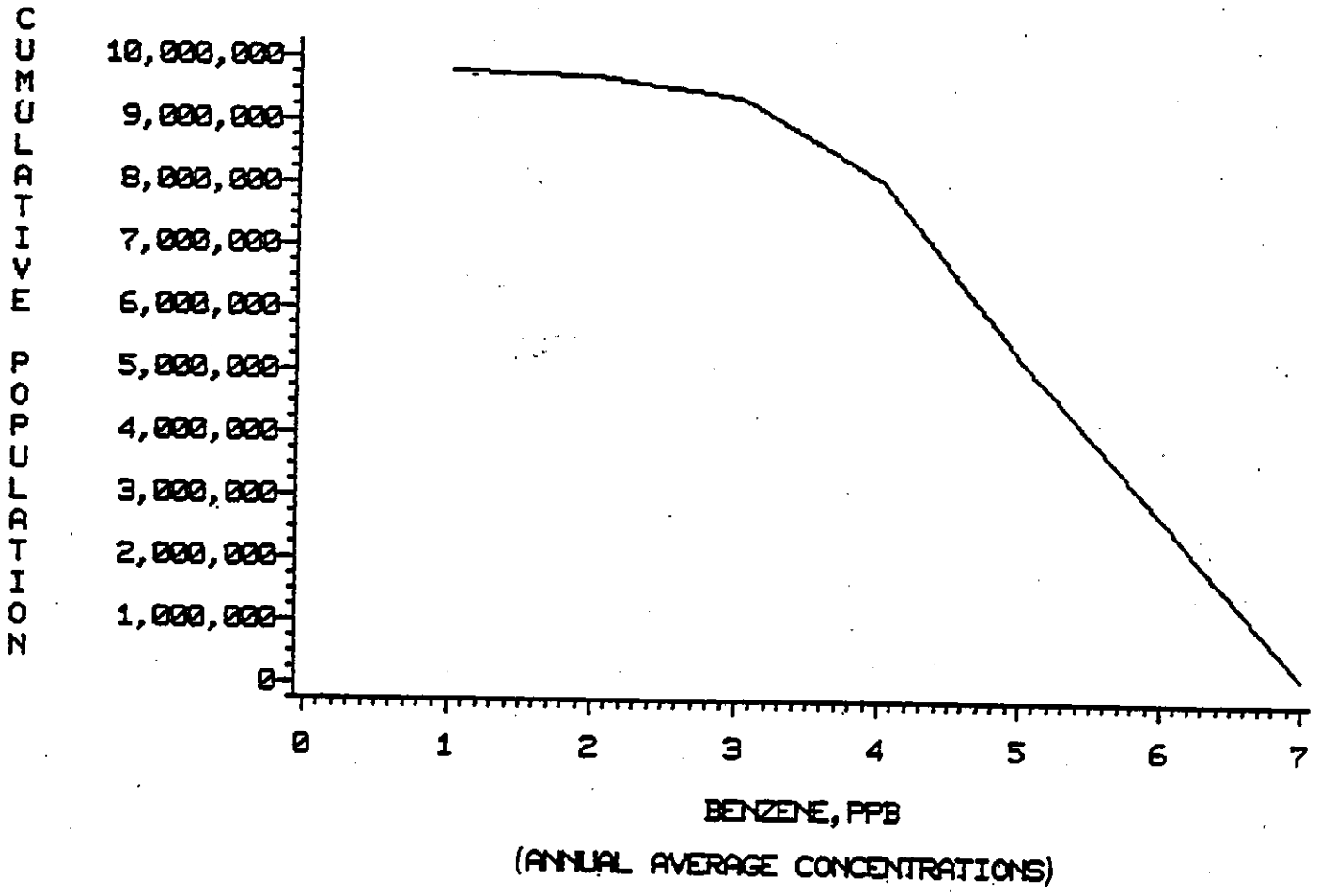


FIGURE 9

1982 BENZENE EXPOSURE FOR SOCAB



Memorandum

To : Science Review Panel

Date : November 14, 1984

Subject: Part B Health Effects of Benzene

From : Epidemiological Studies Section
2151 Berkeley Way, Room 515
Berkeley
8/571-2669

Enclosed is the Benzene Document, revised according to comments which we have received from you and the public. The executive summary, chapter one and chapter six dealing with risk assessment have been completely redone emphasizing the epidemiology-based risk assessment but in the context of the animal risk assessment. The results from several different models are presented. Our assumptions and the rationale for them are more explicitly stated as you requested. While the executive summary and chapter six does contain intact material from the earlier draft there has been so much reorganization that we elected not to clutter the margins with detailed descriptions of previous locations. Please treat chapter one and these two sections as if they were completely new. Chapters III, IV, VII, and the appendices are unchanged. In response to comments a number of fairly minor changes have been made for clarification in chapters II and V and to certain sentences in chapter VI. We discovered that our word processor does not allow a deleted phrase to be lined through. This means we were not able to follow the convention upon which we had originally agreed.

Instead:

| If a totally new sentence or paragraph has been added, you will find a vertical line in the left margin, similar to the one next to this sentence here.

| *If existing material has been reworded a marginal vertical line with* an an asterick will apear, (as in the left margin of this sentence
* | here) and you may refer to the enclosed "change sheet" which references the November and July pagination and gives the previous wording with <u>additions</u> underlined and deletions type in *italics*,

If a sentence or paragraph has been completely deleted, you will see an asterick in the left margin (as we have done here). If you wish to
* see what was deleted check the "change sheet" which will contain the deleted sentence or paragraph in *italics* next to the November document's page number.

We believe that the earlier convention would have produced a terribly confusing document given all the changes which have been made. Perhaps an even better system then this can be developed.

Raymond Neutra, M.D., Dr.P.H.

Charles Gardipee, M.D., M.P.H.

Part B Health Effects of Benzene

(Summary of Changes)

Pages

November Revision	July Draft	Comments
pp 1-5	not paged	Executive summary, rewritten Delete previous summary
pp 7	pp 1-9	Chapter 1, rewritten; delete previous Chapter 1
p 9-10	p 10	Add p 10, 4, 2. Gene Mutations or DNA Damage in Bacteria *and Fungi*.
p 10-11	p 11	Change p 10, line 21, The absolute number of revertants, however, increased by less than a factor of two and there was no linear

		dose-response relationship demonstrated. Change p 11, line 1, *This reflects* This non- linearity may, in part, be due to toxicity of benzene oxide *at the doses tested* to bacteria.
p 11	p 11	delete ¶ beginning with, "*Cotruvo et al tested benzene ....*"
p 11	p 12	delete, *2.2 DNA Damage*, delete line beginning with, "*Numerous studies have shown....*"
p 11	p 12	¶ 3 delete sentence beginning with for example, Lebowitz....
		delete 3.2 DNA Damage and ensuing ¶ beginning with Numerous studies have shown...

p 12	-	Add, 4. Chromosomal Effects in Animals 4.1 Sister Chromatid Exchanges (SCEs)
p 13	p 14	Delete, 4. Chromosomal Effects in animals Add, 4.2 Micronuclei
p 14	p 15	Last ¶ p 15, reworded on p 14 first ¶ Animals were sacrificed 24 hours after the end of exposure and analysis was carried out on 250 metaphases per animal. There were significant increases in the percentage of cells with abnormalities *(including or excluding gaps)* for animals exposed to 100 and 1000 ppm benzene. The categories of chromosomal damage examined were: chromosome or chromatid gaps, chromatid breaks, chromosome breaks or fragments minutes and

		interchanges. There were elevated levels of chromosomal abnormalities (group mean percentage of cells with abnormalities) in rats exposed to 1 and 10 ppm, but these levels were not statistically significant. A positive dose-response relationship for most categories of abnormalities is was exhibited at benzene concentrations from 1 to 1000 ppm in this study.
p 14		add ¶2
p 15	p 16	delete ¶1, p 16, delete ¶ 2, p 16 add ¶ 1,15 add ¶ 2, p 15, ¶ 3, p 15.
p 16	p 17	Delete all of p 17, add all of p 16.
p 17	p 18	Delete ¶ 1 and 2, ¶ 18.

p 18	p 20	Delete ¶ 2, p 20, delete ¶ 4, p 20.
p 19	p 21	Add to ¶ 3, p 18 <u>Benzene induces SCEs in mice in vivo and in human cells in culture.</u>
p 18	p 21	Change ¶ 3, p 18. Benzene causes chromosomal aberrations <u>(chromosome and chromatid breaks, marker chromosomes (for example, dicentrics)</u> in animals and humans: *Studies in animals indicate that a single exposure at relatively high concentration can be as effective as multiple exposures at these high concentrations for producing chromosomal damage.*
p 29	p 31	Add ¶ 1.
p 32-33		Add p 30-31. and ¶ 1 p 32

p 32	p 31	Delete, *four major methods are in current use for identification of potential human carcinogens. These are described below.*
		Add, 1.2 Methods of Identification change, change 1.12.1
		1.12.2
p 33	p 32-33	1.12.3
		1.12.4 Case Studies
		1.12.5 Epidemiological Studies Human
p 34	p 33	Delete, 2. Animal Bioassays *in General* p 34 add reference end of ¶ 1 (NTP, 1984)
p 40	p 39	Delete ¶ 1, p 39, add ¶ 1, p 40 change ¶ 2, line 7-9, Cause-specific standardized mortality ratio (SMR) analyses were conducted comparing the workers' experience to that of the

		general (male and female) US population.
p 41	p 42	Delete ¶ 2 and ¶ 3 p 42. add p 1, p 41 which concludes on p 47.
p 41	p 43	Delete 3 ¶'s, on page 43.
p 47-49	p 45	add pages 48-50 delete ¶ 1, p 45,
p 50	p 45	Change, 2.2.2 Thresholds
p 51	p 47	Delete ¶ 1, p 47, moved to ¶ 2 p 53
p 51	p 48	Delete ¶ 2 p 48 first sentence, *Despite this....*
p 52	p 48	change first sentence ¶ 1, Several kinetic models *that* which produce a threshold in the dose-response curve *has* have been developed.

p 53	p 49	Change first sentence ¶ 1, *These* Variable threshold models would produce....
p 53	p 47	¶ 2, p 54 was ¶ 1 p 47.
p 56	p 52	change, 3. 2.3 Dose-Response Assessment based on Human Studies.
		Delete ¶ 2, 3, 4 p 52 add 1 2, p 56, 2.3.1 Available Data
p 57	p 53	Add, 2.3.2 EPA Dose-Response Assessment Model add ensueing 1 and p 59 and 60 delete 1 1, p 53.
p 60	p 57	Figure VI-1 changed.
p 61	p 84	Figure VI-2 changed.

p 62	p 53	Change, *3.2* 2.3.3 Review of Critiques of the *1977* CAG Dose-Response Assessment
p 62	p 54	Change line 2, p 63. *The relative risk parameter is estimated by taking the ratio of the observed leukemia deaths to the expected number of deaths.* In addition to the critcisms noted above for the Aksoy and Ott studies, the use of the entire U.S. population to calculate the back-ground rate of leukemia was questioned in the Rinsky evaluation.
p 62	p 54 & 55	change line 3, p 64, Another criticism focuses on estimating the slope parameter from *the average of three different diseases.* all types of leukemia rather than non-lymphatic leukemias. *For the Infante study, calculations for the*

slope were based on all leukemic deaths while the Ott study used only myelogenous leukemia, and the slope derived from Aksoy's data was based on all non-lymphatic leukemias.

p 63 p 55

Delete lines 7-12, p 55, ¶ 1,

On the other hand, the estimate of the exposure period in the Aksoy study may be under estimated since the workers in this study tended to work at home and thus they were likely to be exposed to benzene fumes even after they closed their shop for the day. In this case the slope estimated by CAG would be higher than actual.

p 63 p 55

Change line 15-16, ¶ 1,

		This is particularly true in the case of the Infante study were it is argued that CAG's use of the prevailing recommended occupational limit Here it is argued that exposure level used for the assessment substantially.....
p 64-82		new material to ¶4 p 82.
	p 56	delete entire page
p 82	p 58	add, 3.3 Dose-Response Assessment Based on Animal Data change, *4*. 3.3.1 Long-term Animal Bioassays available for Dose-Response Assessment change, *4.1* a) Historical Experimental Data.
p 84	p 58	change *4.2* b) Recent Bioassay Studies.

		delete 4.2.1 p 58
p 90	p 64	delete 4.2.2
p 95	p 65	change, 4.3 3.3.2 Discussion of Bioassay Results
p 95	p 69	change, Both Maltoni studies are interim results of lifetime bioassays.
p 99-108		add, new material in text
p 107		add table VI-6.
	p 78-87	delete textual material