Review of the Carcinogen Assessment Group's Report on POPULATION RISK TO AMBIENT BENZENE EXPOSURE and the EPA External Review Draft on BENZENE HEALTH EFFECTS ASSESSMENT

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TABLE OF CONTENTS

SUMMARY.....i

I. INTRODUCTION.....1

II. THE CAG MATHEMATICAL MODEL.....4

III. ESTIMATE OF CURRENT AMBIENT BENZENE EXPOSURE (X_1).....5

A. Automobile Emissions.....7

B. Vicinity of Gasoline Service Stations.....8

C. Chemical Manufacturing Plants.....10

D. Comments.....10

IV. ESTIMATE OF OCCUPATIONAL BENZENE EXPOSURE (X_2).....11

A. Cohort Definition.....11

B. Environmental Measurements.....12

C. Latency.....15

D. Confounding Exposure.....15

E. Comments.....17

V. DISCUSSION.....17

VI. CONCLUSION.....20

REFERENCES.....22

SUMMARY

The Carcinogen Assessment Group's (CAG) Preliminary Report on Population Risk to Ambient Benzene Exposure is inappropriate and misleading as a basis for regulatory action because:

1. It is based on a nonthreshold mathematical model that is consistent with EPA administrative policy but is at variance with clinical, toxicological, and scientific experience.
2. It inappropriately extrapolates data from a 100 ppm range to 1/100,000th of that figure.
3. In the absence of obtainable data, it attempts to justify a guess of ambient benzene exposure by presenting calculations and estimates not documented in the scientific literature.
4. The calculations are based on a conversion of estimates from eight-hour TWA exposures that have been associated with disease to 24-hour lifetime time-weighted averages. The 24-hour lifetime TWA denies the existence of biological repair mechanisms and assumes a strict cumulative dose effect, a concept considered naive by a majority of the scientific community. Averaging over expected lifetime also ignores the long latency periods of cancers.

The Benzene Health Effects Asessment (BHEA) report reaches a conclusion which is at variance with data presented within

their report and ignores relevant information presented at the recent OSHA hearings on the health effects of occupational exposure to benzene. The BHEA report indicates (a) that benzene causes chromosomal aberrations, pancytopenia, and leukemia, and (b) that none of these show a dose-response relationship. Therefore, they conclude that their findings are relevant to concerns of benzene air concentration in the part per billion range.

Observations that counter their conclusions include:

1. Clinical experience over 50 years has shown the disappearance of aplastic anemia due to benzene with the reduction of benzene levels to below about 20 ppm.
2. Of the two human epidemiologic studies, one showed chromosomal aberrations associated with measurements of 125-532 ppm and the other may have shown effects in workers of a factory with 25-150 ppm exposure and showed no effect in workers of a factory with 12 ppm exposure.
3. All leukemia studies where human benzene exposure was measured and published found benzene air concentrations in the hundreds of ppm's. Detailed information brought out at the recent OSHA hearings showed that the cohort of workers reported in the Infante study were exposed to air concentrations measured at 100, 200, and 500 ppm in areas where the employees were known to work, contrary to the impression of the original report.

I. INTRODUCTION

A discussion of the health consequences of benzene exposure cannot be concerned solely with an analytical model that assumes no knowledge or experience with benzene toxicity. Simplifying assumptions lack value when they contradict evidence. The Preliminary Report on Population Risk to Ambient Benzene Exposure by the Carcinogen Assessment Group (CAG)[1/] assumes a no-threshold level on the basis of EPA policy that carcinogens have no threshold. However, the wealth of experience and laboratory findings indicates that with respect to benzene, the hematotoxic effects, chromosomal aberrations, and leukemia associations seem to disappear at air concentrations of about 10-25 ppm benzene.

Forty years of clinical experience with benzene hematotoxicity in the USA have shown that by reducing occupational exposure from several hundred ppm to about 10 ppm the clinical entities of benzene-induced aplastic anemia, pancytopenia, and monopenias have been almost eliminated. Those cases still being identified frequently show some high exposure under unusual circumstances.

In the USA the permissible levels have regularly been lowered over the past forty years to a point now where the only clusters of cases being reported originated prior to the present controls. A similar pattern for limiting benzene exposure is now evolving elsewhere, in Italy and Turkey for example, with similar results.

Data presented in the Benzene Health Effects Assessment (BHEA)[2/] document substantiate these judgments. I. M. Chang (p. 79) has demonstrated that hematologic toxicity was observed in workers exposed only to benzene concentrations above 20 ppm. Vigliani et al. (p. 81) found that benzene exposure for his observed group ranged from 25 to 1500 ppm. Hutchings et al. (p. 72) showed little hematologic difference between 800 controls and 87 Australian air force workers exposed to concentrations generally of 10-35 ppm with excursions well over 100 ppm.

Much has been made of the oberservations of chromosomal breaks. Nevertheless, while Tough et al. (p. 27) found significant increases in unstable aberrations in workers exposed to 25-110 ppm benzene versus sex-matched unexposed workers, they were unable to demonstrate similar increases in workers at another plant exposed to approximately 12 ppm. Subsequently they explained their initial finding as suggestive of an age effect. Working with a group of workers exposed to 129-532 ppm, Forni et al. (p. 28), showed an excess of stable and unstable chromosome aberrations.

Leukemia researchers have indicated that the association between benzene and leukemia disappears below 100 ppm. Aksoy's group of shoeworkers were exposed to levels of 210-650 ppm (p. 98) and worked in environments that he described as "not good; their shops usually are small, not hygienic, and poorly ventilated." In 1969, the solvent was changed from 100 per

cent benzene to one containing one to seven per cent benzene. By 1976, the number of cases had dropped to zero, although mild exposures were still occurring. Vigliani reported his cases in workers exposed to 200-500 ppm (p. 102).

Even the study, "Leukemia Among Workers Exposed to Benzene" by Infante, et al.,[3/] of the Pliofilm workers indicates a dose-threshold effect. Five of the seven leukemia cases occurred in workers during the early 1940's, when the recommended safe concentration was 100 ppm and environmental quality control was inadequate to assure adherence even to this level. The other two cases developed in workers hired during the years when the recommended safe level of exposure was reduced to 50 ppm in 1947 and 35 ppm in 1948.

The University of North Carolina group has carefully studied the 1964-73 mortality experience of the retired and active employees of the Akron plant and was unable to identify leukemia as the cause of death of any Pliofilm worker. Likewise, Dr. Marvin Sakol, the local hematologist who diagnosed the Akron cases and has had a special interest in them for the past 20 years, has found no further case of leukemia in a Pliofilm worker.[4/] (The 20-year period has been sufficient to observe cancer incidence, for those cases Infante identified at the lower estimated dosage of 35 ppm had a mean latency of 5-6 years, which is consistent with Aksoy's observation of case dropoff 4-7 years after high exposure had ceased.) Introduction of environmental controls seems to have taken care of the problem of benzene-associated leukemia in Turkey, Italy and the U.S. (Ohio and elsewhere).

II. THE CAG MATHEMATICAL MODEL

The CAG report has developed an equation based on a non-threshold linear model to estimate the number of cases of leukemia that might be caused by current ambient benzene air concentrations. They have applied the data from the Infante report and the report, Human Exposures to Atmospheric Benzene by Mara and Lee of Stanford Research Institute (M-L report),[5/] on an estimate of current ambient benzene air concentration, assuming both the validity and applicability of these reports to the question under consideration.

A formal derivation of the CAG's equation indicated many of the unspecified assumptions, but the essential equation derived is:

$$N \propto X_1/X_2 \quad \text{or} \quad N = Q\, X_1/X_2$$

where N is the number of deaths from leukemia, maximally estimated to be attributed annually unusually to current ambient benzene air concentrations on the basis of the numerous assumptions in the model and the data, Q is a constant partially derived from the data of the Infante report and equal approximately to 150, X_1 is the assumed mean current level of ambient benzene air concentrations in parts per billion, and X_2 is the assumed significant level of benzene exposure in parts per million to which the Infante data is related.

The interpretation of the estimated value of N is dependent upon an understanding of the assumption leading to the values of X_1 and X_2 that are used in the equation. In the

development of these numbers in the CAG report, the assumptions used have generally been those that would maximize the estimate of N. The estimate of the ambient benzene concentration (X_1) is derived from the M-L report and dependent upon the numerous assumptions therein. The estimation of the average occupational exposure (X_2) is developed from data reported in the Infante study and is a calculated value derived solely from an interpretation of the circumstances of that study and of the analytic model considered. Q, above, is itself a constant partially derived from the data of the Infante report.

III. ESIMATE OF CURRENT AMBIENT BENZENE EXPOSURE (X_1)

X_1, the estimate of the current ambient benzene exposure, is derived from the M-L report. Table 2 in the CAG report (adapted from Table I-1 in the M-L report) summarizes the number of people estimated to be exposed to various levels of ambient benzene from various sources. As presented, it serves as a basis for demonstrating how much each source and estimate is calculated to contribute to their estimation of the mean ambient benzene air concentration of 1.03 ppb. Our Table 1 which follows has been developed from it to more clearly demonstrate each group's contribution to the estimated total sum of person-ppb and thus to the mean ambient benzene air concentration.

Mara-Lee have assessed the contribution of a number of factors that make up the ambient benzene exposure. Our Table 1 (page 5) shows that the major contribution (45%) is from urban

TABLE 1

SUMMARY OF PERSON-PPB BENZENE EXPOSURES
BY SOURCE AND CONCENTRATION

(IN THOUSANDS)

CONCENTRATION	TOTAL PERSON-PPB (IN THOUSANDS)	URBAN EXPOSURE	GAS STA. VICINITY	CHEMICAL MFG.	COKE OVENS	PET. REF.	GAS STA. SELF-SERVICE	SOLVENT OPERATION
0.042	1,554						1,554.	
0.50	92,648.5	34,168.5	43,500	3,748.5	7,863	3,264.5		104.
1.50	116,869.5	68,029.5	46,500	1,455	781.5	96		7.5
3.00	1,527			1,359	150	12		6.
7.0	4,522			4,508	14			
30.0	9,570			9,570				
	226,615.	102,198.	90,000.	20,640.5	8,808.5	3,372.5	1,554.	117.5
% CONTRIBUTION TO EXPOSURE	100%	45%	40%	9%	4%	1.5%	0.7%	.05%

$$X = \frac{226{,}615. \times 1000}{220 \times 10^{6*}} = 1.03 \text{ PPB}$$

* TOTAL U.S. POPULATION

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exposures, the second important contribution (40%) is in the vicinity of gasoline service stations, and the third contributor (9%) is from chemical manufacturing plants. Mara-Lee have assumed that the urban exposures are due to automobile emissions.

A. Automobile Emissions

The calculation of ambient urban benzene in exposures (X_a) is attributed to auto emissions and is based on EPA in-house memoranda and their self-derived constants, applied to the Gifford-Hanna model for urban air pollution dispersion.[6/] It (X_a) is based on 4 given constants whose validity and applicability have to be assumed and upon 4 variables specific for each city.

The constants are:

K_1 = 225 per meter^2 -- an empirical factor derived from several unidentified studies

K_2 = 0.22 grams benzene emitted per mile driven

K_3 = 0.148 grams benzene evaporated per trip

K_4 = 3.3 trips per vehicle per day

The variables for each city are:

VMT = number of vehicular miles travelled annually by locally registered vehicles

N = number of locally registered vehicles

A = area of city in meters^2

U = mean annual wind speed through the morning mixing layer

The finally derived equation is:

$$X_a = 3\text{1}2.5\ K_1\ (31.69 \times 10^{-9}\ K_2\ VMT \div 11.22 \times 10^{-6}\ K_3K_4N)\ AU$$

Although the validity of the formula itself has not been demonstrated, it does simplify to a workable equation of

$$X_a = VMT/UA$$

The morning wind speed has been used in the formula (according to M-L, p. 80) rather than the faster afternoon winds, in order to estimate higher concentrations. It should be noted that the mean ambient concentration is calculated without any measurements of ambient benzene concentration.

Nonetheless, this formula has been used to estimate that residents of Chicago, Detroit, Los Angeles, New York, and Philadelphia are exposed to 1.1 - 2.0 ppb benzene and that the residents of Houston and all other Standardized Metropolitan Statistical Areas (SMSA's) with populations greater than 500,000 are exposed to 0.1 - 1.0 ppb benzene from automobiles.

In essence, the estimates of ambient benzene exposure due to auto and gas fumes are highly theoretical constructs with no direct measurements to sustain them. Vast assumptions are being made that predict non-existent data at the limits of detection with current measurement technology.

B. Vicinity of Gasoline Service Stations

The estimation of ambient benzene exposure for people dwelling in the vicinity of gas stations is based on their conclusion (M-L, p. 47) that "individuals resident within 300 m (meters) of a service station may be exposed to annual average

concentrations of 1.0 ppb or more, whereas those residing beyond 300 m are expected to be exposed to less than 1.0 ppb on an annual average basis." The assumption from this conclusion is that urban dwellers who live within 300 meters of a service station are exposed to 1-2 ppb benzene (1.5 ppb average) and arbitrarily that all other city dwellers are exposed to .1 to 1 ppb (0.5 ppb average).

The M-L data are based on the following evidence: (a) monitoring data at one location in one study (Battelle, 1977b), which states that benzene concentrations are below 1 ppb within 300 meters of a service station and (b) the Youngblood 1977d model, which indicates (Table V-7, M-L report) average annual benzene concentration estimates of 1 ppb 50 meters from gasoline stations dispensing 0.7% benzene gasoline and operating around the clock and 150 meters from similar stations selling 3.0% benzene gasoline. However, most automobile gasoline is 0.9% - 1.5% benzene (Table V-2, M-L). The calculations presented are inconsistent with the Youngblood estimates.

Based on this model a radius of less than 100 meters might be a more appropriate estimate of the distance at which the air concentration is estimated to be 1 ppb. Furthermore, no evidence is presented to indicate that people living farther from the stations receive any detectable exposure from this source. Recalculations based on these modifications of the model would reduce the benzene exposure attributable to gas station vicinities by about 95%, to a contribution of only 5.2×10^6 ppb-person years to the M-L model.

C. Chemical Manufacturing Plants

The third major contribution to the mean ambient benzene air concentration is the chemical manufacturing source. This estimation has also been based upon the use of the Youngblood dispersion model. Those most knowledgeable about the chemical industry[7/] have commented that the estimated exposures are off by at least two orders of magnitude. Mara-Lee, in estimating the benzene exposure among sources (Table 1-2, M-L report), estimated that persons exposed to levels greater than 10 ppb were exposed to an annual average of 15 ppb. The CAG without explanation has doubled this to 30 ppb, which has a net affect of raising the M-L estimate of benzene exposure from chemical manufacture by 30%. Were that tabulation returned to the M-L estimate, the mean ambient benzene concentration would have been calculated as 1.008 ppb, not 1.03 ppb.

D. Comments

In summary the M-L report as presented in the CAG report is an analytic hypothesis in need of testing with real data. Prior to being accepted as basis for rule-making, appropriate studies should be performed to determine both the validity of the estimates of ambient benzene exposure and the source of these exposures. Further, consideration should be given to the determination of the appropriate methods of control for any sources that may be found to contribute excessively to ambient exposures, if these are determined to be a health hazard.

IV. ESTIMATE OF OCCUPATIONAL BENZENE EXPOSURE (X_2)

The estimation of the average occupational exposure is a calculation based on an interpretation of the circumstances described in the Infante study. Since the description of the cohort and its exposure circumstances is limited in both the BHEA report and the CAG report, we will review problems with the 2 reports as they relate to the Infante study and the Infante report itself.

A. Cohort Definition

The BHEA describes the Infante cohort (p. 113) as "white male workers exposed to benzene in manufacture of a rubber product" and "employed at any time during the period 1940 through 1949." Evidence presented at the OSHA hearings by the authors of the original study demonstrate that this description is incomplete. The Infante study reports the pooled data of two cohorts of some of the workers exposed to benzene in the manufacture of Pliofilm in two different plants in the 1940's. At one plant, St. Mary's, the approximately 400 workers employed on the dry side of the Pliofilm process were excluded from the study. At the other plant, Akron, employees exposed to benzene in the pliofilm department who terminated employment in 1944 or earlier were silently excluded from the study while those employed at the same time but who continued to work past 1944 (after which complete personnel records are available) remained a part of the cohort. Had they been excluded, 3 of the 5 cases of leukemia identified at the plant would not be part of the study. The net effect of these exclusions is to include those

with high or long-term exposures and eliminate those with lower dose or shorter duration exposure.

B. Environmental Measurements

The BHEA report is imprecise both as to the dates industrial hygiene measurements were taken and in which plant they were taken. As a result, one is given an erroneous impression of the benzene exposure.

The earliest report is from the St. Mary's plant late in 1946.[8/] At that time an investigation was conducted by the Industrial Commission of Ohio to assess the efficacy of "a new exhaust system recently installed for the elimination of benzol hazards in the Pliofilm Department." The investigator reported that as a result of the new equipment, "the characteristic odor of benzol could no longer be detected" and added: "concentrations had been reduced to a safe level and in most instances ranged from 0 to 10 or 15 ppm." Further, he provided a clue as to the degree of care that had been given to benzene exposures when he said, "If sufficient care is used to keep lids on containers and to prevent overflow of containers and other forms of spillage, it is believed that the concentration can be kept at safe levels at all times." In commenting on the newly installed exhaust system he said, "it is very efficient and if properly operated will provide a safe atmosphere for the employees in this department." He indicated in his report that he considered a safe concentration as 100 ppm.

It is not unreasonable to assume that the company invested in the new equipment at least in part because benzene levels were frequently and significantly greater than 100 ppm.

The Akron plant was evaluated by the Ohio Division of Safety and Hygiene in April 1948.[9/] Measurements were taken throughout the plant. A reading of 120 ppm was recorded at the front of the dryer, where employees could reasonably be expected to be working. A measure of 500 ppm of benzene was reported at the top of a tank, a place where, the report notes, "one or more employees would spend approximately one hour per day."

In the mid-1950's, a review was made in Plant C of the Akron Plant of the benzene air concentrations in 16 of the areas where the Pliofilm employees worked. Although the recommended maximum level at the time was 35 ppm, 12 of the 16 areas had levels measured as high as 100 ppm. Eleven of the areas had means approaching or exceeding the legal limit (2 at 34 ppm, 9 at greater than 35 ppm). Of the 414 specimens collected in the review, one-third were measured at no greater than 35 ppm.

On January 17, 1956,[10/] another study was made of the St. Mary's plant by Ohio officials. In drawing together their findings, investigators said, "local exhaust ventilation controls were considered of excellent design." (emphasis ours) However, that statement apparently was interpreted differently by the authors of the BHEA, who said the Ohio inspectors found that "the exhaust ventilation was excellent." The inspection report also noted benzene concentrations of up to 35 ppm at the work stations where hydrochloric acid was added to the rubber and at the neutralizer work stations. The report indicated that worker exposure did occur in areas where the maximum allowable

concentration was exceeded. Respirators were available, and though mandatory at these places, there is question of their use.

The BHEA also discusses the results of 112 surveys conducted at the St Mary's plant between 1963 and 1974. The surveys were taken, the authors note, to determine "the benzene exposure levels of the 7 individuals who developed leukemia." However, the BHEA authors were apparently unaware that the 7 individuals who developed leukemia had all died before 1962, thus, these surveys (1963-74) are not directly relevant to the leukemia cases of the Infante report.

When compared to exposures two decades earlier, these more recent measurements should be considered as representing the lowest of worker exposures. A total of 43% of the 112 surveys showed measurements greater than the acceptable threshold limit value (TLV) at that time. Within this figure 25% showed means greater than the TLV acceptable at the time they were taken. */

These measurements, although inadequate and infrequent compared to what one wishes might be available, definitely indicate that the exposures even as late as the 1960's and 1970's exceeded the TLV at this time. For example, in 1974 measurements of up to 203 ppm were recorded in a storage area and in a strippers' area.

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*/ The data from 1972 appear to be quite atypical of that from the other years. If these data are excluded from the analysis, then 38% of the areas had measurements greater than the TLV at the time, including 24.5% in which the means were greater than the TLV at that time.

The results also are reinforced by data obtained from another survey by the University of North Carolina in 1973 and 1974. The survey team identified exposures of between 200 and 250 ppm or greater in areas where workers spent up to 30 minutes at a time and where respirators were not worn even though they were required. Additionally, they report levels of up to 20 ppm (twice the then current TLV) in the "dry" areas that had been excluded from the Infante report as no-exposure areas.

C. Latency

The assumption inherent in the Infante report is that the leukemia observed is due to benzene exposure. But this assumption can be challenged on a number of grounds. If the leukemia is due to benzene and is dose related, then those with higher doses should have shorter latencies. However, the group hired during the period when 100 ppm was considered safe had a mean latency of 17 years, while those hired during the period when 35 ppm was considered safe had a mean latency of 5 to 6 years. The five cases at the Akron plant had a mean duration of exposure of 11 years; the two St. Mary's cases had exposures of 1 month and 6 months. (See our Table 2.)

D. Confounding Exposure

Furthermore, exposures to other substances are strongly suggested. Unlike the Akron workers who worked on many production lines in the plant other than Pliofilm, the St. Mary's group worked essentially only in the Pliofilm Department. Also, additional inquiry has revealed significant exposures to

TABLE 2

LEUKEMIA CASES IN COHORT OF INFANTE REPORT
ON BENZENE AND LEUKEMIA IN PLIOFILM WORKERS

CASE	PLANT	LEUKEMIA TYPE	YEAR OF INITIAL EXPOSURE	STANDARD AT TIME OF INITIAL EXP.	YEAR OF DEATH	AGE AT DEATH	EXPOSURE DURATION
1. GH	AKRON	ACUTE MYELOCYTIC	1940	> 100	1961	62	10½ YEARS
2. AJ	AKRON	ACUTE GRANULOCYTIC	1942	100	1961	57	18 YEARS
3. GN	AKRON	ACUTE MONOCYTIC	1942	100	1957	57	6 YEARS
4. RF	AKRON	ACUTE MYELOCYTIC	1945	100	1958	60	12 YEARS
5. GF	AKRON	ACUTE MYELOGENOUS	1949	35	1970	67	8½ YEARS
6. GS	ST. MARY'S	MONOCYTIC	1941	100	1958	36	6 MONTHS
7. CL	ST. MARY'S	CHRONIC MYELOCYTIC	1948	35	1950	29	1 MONTH

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foundries, pesticides, cattle, paint remover, wood working, military service in Hiroshima after the hydrogen bomb was dropped, and medical histories that include lymphatic disease, allergy to chemical drugs and heavy sulfa drug usage. All these exposures have been considered to be leukemogenic and carcinogenic.

E. Comments

In summary, the Infante study is an inappropriate basis for any regulatory procedure because (a) the cohorts are neither appropriately described nor appropriately chosen, (b) the exposure data indicated levels far in excess of those Infante et al. indicated in their report and (c) alternative etiologic risks that might contribute to the leukemia incidence have not been investigated or dealt with. Although the diagnoses of the leukemia cases in the Infante study are not in question, there is considerable doubt concerning the epidemiologic interpretations built upon them.

Contrary to the impression given by the Infante report, available data indicate that exposures very frequently exceeded the recommended levels.

V. DISCUSSION

If we assume the Infante data, including the interpretation of exposure levels, is valid, then the determination of the number of cases attributable to benzene is still dependent upon the use made of the exposure level determination.

Prior experience in the USA and abroad has shown leukemia to be associated with benzene only at levels of 100 ppm or greater. The Infante report also identifies a cluster of cases with such exposure. A threshold model of benzene health risk based on these observations would conclude that there is no risk associated with the low ambient benzene concentrations measured in parts per billion. A non-threshold, linear model of benzene risk would conclude that the risk is very, very low--maximally, about one death per year.

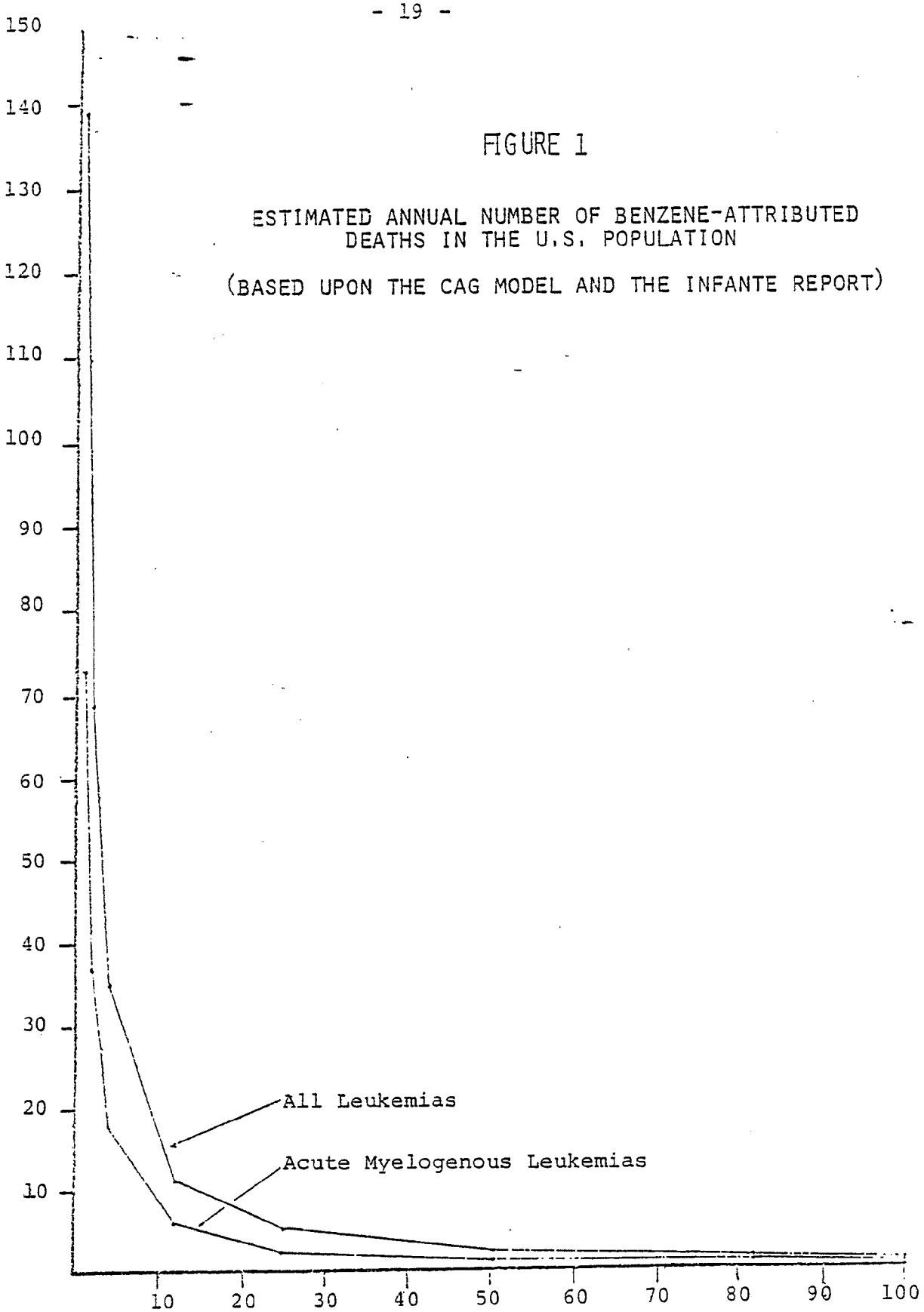
To magnify the risk from current ambient levels, the occupational exposure data has to be transformed to an expression that indicates that the observed effect is associated with a less than apparent exposure. One such transformation is the use of the life-time time weighted average exposure. Figure 1 demonstrates the effect of such transformations. The estimated number of leukemia deaths annually attributable to ambient benzene is dependent on the exact transformation performed on the occupational exposure data. If transformed from a 100 ppm exposure to a 1 ppm exposure, the estimated risk is increased by two orders of magnitude. The legitimacy of the transformation is open to question.

Administrative policy, rather than scientific judgment can determine the use made of the data. If administrative policy stipulates a no-threshold, anything-can-cause-cancer approach, then conversion to a liftime time weighted average (TWA) will

FIGURE 1

ESTIMATED ANNUAL NUMBER OF BENZENE-ATTRIBUTED DEATHS IN THE U.S. POPULATION

(BASED UPON THE CAG MODEL AND THE INFANTE REPORT)



multiply the potential risk to up to 77 cases a year. Even so, only 6.8% of the exposure (15,619/16,615 thousand person-ppb), and thus only 6.8% of the cases are being attributed to exposures greater than 2 ppb benzene.

Thus, if the assumptions in all four reports (Infante, BHEA, M-L, and CAG) are accepted, establishing an environmental ambient benzene air concentration of 2 ppb would maximally reduce the cancer mortality by 5 cases per year, or 1/3,000th of the current national leukemia mortality rate.

As an attempt to validate the overall effect of their assumptions, the CAG report has applied to the Ott study the risk estimates derived from the Infante study and, because their predicted number of cases did not significantly differ from Ott's observed number, have concluded that their estimates are not grossly in error. The Ott study found one leukemia death in a population of benzene-exposed workers in which 0.9 cases could be expected. Ott would have had to find four cases in order to conclude that there was an excess risk, possibly attributable to benzene. The CAG model is thus so broad that it predicts a risk where none has been demonstrated.

VI. CONCLUSION

Our understanding of the biology of benzene toxicity and of the epidemiology of benzene-related leukemia is that there is no benzene-related leukemia induced below about 10-20 ppm, that under current conditions of ambient benzene air concentrations benzene is not carcinogenic, and that the CAG's

calculations are factitious. There is no need to establish an ambient benzene air concentration standard, because current ambient benzene air concentrations are neither a leukemogenic nor a hematotoxic hazard.

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