

# Benzene — Attempts to establish a lower exposure standard in the United States

## A review

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ZENZ, C. Benzene—Attempts to establish a lower exposure standard in the United States: A review. *Scand. j. work environ. & health* 4 (1978) 103—113. Production, usage and potential occupational exposure to benzene are described in this review, as are selected, relevant reports presenting evidence implicating benzene as a causative factor in leukemia, particularly acute myelogenous leukemia, pancytopenia (including aplastic anemia) and chromosomal aberrations. A chronologic account of events in the 1970s in the United States, largely based on epidemiologic evidence collected and prepared by the National Institute for Occupational Safety and Health, caused the regulatory agency, the Department of Labor, through its Occupational Safety and Health Administration to declare benzene a human leukemogen and carcinogen and to publish an emergency temporary standard of 1 ppm in May, 1977, but this standard has not been legalized.

**Key words:** aplastic anemia, benzene, chromosomal aberrations, leukemias, occupational uses, United States regulations and standards, worker exposures.

Enormous quantities of benzene are produced and used in workplaces throughout the world, with production in the United States estimated to be approximately five billion kilograms, in 1976. According to the National Institute for Occupational Safety and Health (NIOSH), nearly 750,000 American workers may be at risk of exposure to benzene. It is the intent of this review to provide some perspective into the often lengthy and complicated methods for workplace standard setting in the United States. These activities may involve extensive interactions among the Occupational Safety and Health Administration (OSHA) of the U.S. Department of Labor,

the National Institute for Occupational Safety and Health (NIOSH), state agencies, labor and consumer groups, the Environmental Protection Agency (EPA), industry, and trade associations. Events in the 1970s are heavily influenced by these organizations and changing attitudes of the public, in addition to reported and available scientific data. In the United States, there has been much controversy and debate with occupational health exposure "standards," particularly with respect to benzene, long recognized as highly toxic, affecting the hematopoietic system with chronic exposure. There is abundant literature demonstrating a cause-and-effect relationship between benzene exposure and blood abnormalities in man for over 75 years, and expanding evidence now links certain leukemias and benzene exposure.

It is not the intent in this review to discuss the acute manifestations of benzene

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toxicity, which are well known, but to highlight the major, more recent reports of chronic exposures, most commonly encountered in occupational settings where benzene may be used more openly, perhaps with poorly controlled conditions, in contrast to the larger firms with their closed production — refinery/transport systems.

## OCCUPATIONAL BACKGROUND — INDUSTRIES, PROCESSES AND USES

Originally, benzene was produced primarily as a by-product of the coking process in steel mills; but today, this process accounts for only 6 % of total U.S. production. During World War I, benzene production was greatly stimulated by the demand for toluene for explosives with heavy production continued for the synthesis of various intermediate compounds, such as cyclohexane, phenol, styrene, and making certain detergents and pesticides. The two major industries producing benzene are the petrochemical and petroleum refining industries, converting certain lower octane hydrocarbons into the higher octane aromatic hydrocarbons by catalytic reformation. These two industries produce more than 94 % of the total U.S. production of benzene, with nearly 80 % of this production used to produce toluene. Benzene may be a component or a contaminant in toluene, gasoline, petroleum, naphthas, and other hydrocarbon derivatives.

The vast production suggests potential widespread worker contact. Benzene possesses excellent solvent and other properties, as a clear, colorless liquid, with a pleasant, nonirritating odor, a high evaporation rate [always an important factor in workplace assessments of exposure (benzene = 2.8; ether = 1.0)], a vapor density of 2.7 (air = 1), and a boiling point of 80.1°C (760 mm Hg).

Benzene is commonly found in paint and varnish removers (> 50 %) and in "model cements" (glues) and many adhesives and in some oil-based paints. Other industries, in the past, widely using benzene were the printing, rotogravure and lithographic, and rubber fabricating, but now most have substituted other solvents such as toluene and xylene. Many rubber products require

direct worker contact and/or along with machines that fabricate certain products such as tires, belting, footwear, hosing, tubing, fuel cells and outer garments which may be termed as partially "hand made," using adhesives or cements by layering, wrapping, forming, "stitching" sheets of rubber or rubber-coated "cloth" (natural or synthetic) or metallic, into "plys" or other finished forms, often heat-cured (to speed production) for eventual consumer use. The early history of the rubber industry indicated that some of the most common solvents in cements were aromatic hydrocarbons, benzene found to be the most suitable.

Ordinarily, cements in the rubber industry are used or applied in open systems, and, if the solvent is not captured by a local exhaust system, it vaporizes into the work area. The cementing solvents may be hand-applied by cloth or brush, sprayed, mechanically applied by coated rolls, or mechanically dipped, while some sealing or cementing operations require only the application of a rubber solvent. In most applications, local exhaust ventilation and solvent recovery systems are seldom used, often observed in factories with unsatisfactory hygienic conditions. Although solvents other than pure benzene are and have been used in rubber cements in the industry, benzene is still unexpectedly present in many solvent mixtures.

Also, large quantities are used in chemical laboratories as a solvent or extractant, and as a reactant in numerous chemical processes such as in making pharmaceuticals. In the United States, benzene has found increasing use in automotive fuels for unleaded gasolines, ranging from 0.3 to 2.0 % content by volume, with European gasolines revealing ranges of benzene from 5 to 16 % (44, 45). Retail automotive service stations present another potential area of concern for risk to a large occupational group, the more than 190,000 service stations in the U.S. ("self-service" becoming more common), an aspect now under the surveillance of the Environmental Protection Agency.

The absorption, metabolism and excretion of benzene has been brought up to date and clearly described by Lauwerys (31) in a review on biological criteria for selected toxic chemicals.

## REPORTS LEADING TO CHANGING STANDARDS FOR BENZENE

No other occupational exposure air limits have shown so many downward revisions as benzene; since 1946, there have been four on the first published list by the threshold limit value (TLV) committee; in 1946 the recommended TLV for benzene was 100 ppm; in 1947, the TLV was reduced to 50 ppm; and, in 1948, to 25 ppm (table 1). The TLVs were directed primarily at substances which caused some physiological responses such as acute symptoms and signs, i.e., irritation of eyes, nose, throat or respiratory system; skin reactions, etc. The TLVs were not established on the basis of carcinogenic, mutagenic or teratogenic properties, nor the likelihood of synergistic effects of concomitant exposures to several substances.

In 1974, NIOSH submitted its criteria document concerning occupational exposure to benzene to the Secretary of Labor. This document stated that "the possibility that benzene can induce leukemia cannot be dismissed" (39), recommending retention of a permissible exposure limit of 10 ppm and ceiling concentrations of 25 ppm, measured over a 10-min period, but this recommendation was not based on benzene's potential leukemogenic hazards. In April 1976 the United Rubber, Cork, Linoleum and Plastic Workers of America petitioned the Secretary of Labor, urging that an emergency temporary standard regulating occupational exposure to benzene be issued, but the request was denied.

### "UPDATE" CRITERIA DOCUMENT FOR BENZENE

In August 1976 NIOSH published an "Update Criteria and Recommendations for a Revised Benzene Standard" (41). This document acknowledged a cause-and-effect relationship between benzene and observed blood abnormalities, especially aplastic anemia. In October 1976 NIOSH recommended a priority publication of occupational health standards to the Occupational Safety and Health Administration which emphasized concern to accelerate rule making processes, particularly for sub-

Table 1. U.S.A. recommended benzene concentrations in workplaces — a chronologic summary.

| Year      | Concentration (ppm) <sup>a</sup> |
|-----------|----------------------------------|
| 1946      | 100 MAC                          |
| 1947      | 50 8h, TWA                       |
| 1948      | 25 8h, TWA                       |
| 1963      | 25 ceiling                       |
| 1970      | 10 TWA                           |
| 1974 (16) | 10 TWA; Ceiling 25               |
| 1976 (52) | 1                                |

<sup>a</sup> MAC = maximum allowable concentration; TWA = time-weighted average.

stances presenting new evidence for carcinogenic effects on humans, with benzene heading the list (22). This communication reiterated:

that since the 1974 criteria were issued, seven epidemiological studies had been reported, along with case reports of benzene-related blood dyscrasias and chromosomal aberrations, and that NIOSH considered the recently accumulated evidence from clinical as well as from epidemiologic data to be conclusive at that time that benzene is leukemogenic because it produces progressive, malignant disease of the blood-forming organs, strongly recommended that OSHA publish an emergency standard for benzene without delay, recommending that the exposure level be kept as low as possible (1 ppm in air).

Although some investigators have observed only acute forms of benzene-associated leukemias (4, 6, 52, 53), recent connection with chronic leukemias have been described (36, 37, 56) in workers who had potential exposure to benzene. Reports prior to 1974 of chronic myelocytic or lymphocytic leukemia (25, 26, 32, 47) and erythroleukemia (13, 17, 23, 42, 43) are not as numerous as the observations of acute myelocytic or lymphocytic types (3, 15, 16, 25, 26). Because of the rarity of erythroleukemia, Vigliani and Forni (53) regard as significant the three cases which they observed. Because case records accumulated by one investigative group (53) of patients with acute or subacute leukemia have become so numerous in the past two decades, many cases formerly diagnosed as acute pancytopenia are now considered to be examples of acute leukemia.

In 1974, McMichael et al. (36) reported on the first phase of a study of a population at risk comprised of active and retired employees of a major tire manufacturing plant in Akron, Ohio, consisting of a cohort of 6,678 male rubber workers who were followed for nine years (1964 through 1972), along with data on 1,783 deaths. Comparison with the 1968 U.S. national mortality data yielded a standardized mortality ratio (SMR) of 99 from all causes of death for the full cohort and of 93 for the active employment subcohort in the age range of 40 to 64. Among other findings of cause-specific deaths, the highest SMRs were for deaths from causes related to the hematopoietic and lymphatic systems. The SMR showed an excess mortality of approximately 2 to 2.5 and was higher for the "active" age range (40—64) than for the full age range (40—84). For leukemia deaths in the 40 to 64 age range, the SMR was 315 — approximately a threefold excess. It was recognized that, because no distinction was made in this evaluation between different groups of workers having different work experiences, a "dilution effect" could occur. A second phase of the study (35, 37) compared different groups of rubber workers. McMichael et al. (36) stated that, from this initial study alone, it should not be assumed that the observed cause-specific mortality excesses were attributable to work-environment exposure within the rubber industry. Such excesses could have been a spurious association such as a "selected" population in which all persons living in Akron might have been exposed to some specific unknown factor. Similar findings from five other plants in widely differing parts of the U.S., however, make this explanation unlikely, in the opinion of the authors. Pending completion of the second phase of the study, the authors stated that they could only suspect, rather than conclude with confidence, that working in certain jobs within the rubber industry entails an increased risk of dying from these specific causes.

In the follow-up of the same cohort (36), McMichael et al. (37) in 1975 extended the epidemiologic study to indicate an association between leukemia and jobs entailing exposure to solvents among which benzene

was once the solvent of choice. After noting that leukemias in general demonstrated a threefold excess in mortality in the 40 to 64 age range, and with further subclassification of the International Classification of Diseases categories to identify specific leukemia, a sevenfold excess of deaths from lymphatic leukemia in the 40 to 64 age range was observed. Six of eight deaths were from chronic lymphatic leukemia. Myeloid leukemia was the next highest category in this age range, showing a twofold excess. At smaller plants not located in Akron, but in Ohio, a complete study was not performed for reasons of cost and time; nevertheless, a proportional mortality analysis demonstrated a 45 % excess of leukemia (37). The question of whether the observed mortality excesses were associated with specific job categories within the rubber industry was then investigated. Nineteen of 70 occupational titles were associated with solvent exposure and were grouped as "heavy," "medium," and "light" solvent exposure. A discriminant function analysis based on time spent in various work groups and independent of the previously observed mortality excess revealed a statistically significant positive association between solvent exposure and lymphatic leukemia. One job title within the three solvent exposure groups, tire repair, showed a sixfold difference between cases and controls in a comparative test of relative risk of lymphatic leukemia. (It was pointed out that tire repair involves considerable swabbing of tires with solvent, and, at some time in the past, the solvent predominantly used was benzene.) Finally, it was of interest to the authors (37) that it was lymphatic rather than myeloid leukemia that appeared to be associated with solvent-exposure jobs.

A third study by McMichael et al. (35) in 1976 involving the same cohort of rubber workers previously reported (36, 37), indicated that mortality from lymphatic leukemia was also very strongly associated with working in the synthetic plants, a place where NIOSH has been unable to identify benzene-related exposures. The synthetic plant is essentially a chemical plant making synthetic rubber as styrene-butadiene and neoprene products. An unexpected association of lymphatic

leukemia with the janitoring-trucking occupational title group was explained by speculating that the transfer of workers to this group occurred for medical reasons, especially where conditions were not rapidly fatal and for which active employment could be maintained while in apparent disease remission or stabilization. Andjelkovic et al. (11), studying the same cohort as McMichael et al. (35, 36, 37), distinguished between active worker mortality experience and retired worker mortality experience, particularly in workers who retired before age 65. Results were essentially the same as previously reported (35, 36, 37) with findings of excess mortality for both active and retired workers from neoplasms of the lymphatic and hematopoietic tissues. In addition, the expectation was confirmed that workers who retired prior to the normal retirement age of 65 would have a less favorable mortality experience than active workers of the same age range; however, the magnitude of the excess, an SMR of 202 as compared with 61 for the active workers, was unexpected.

In 1976, Monson and Nakano (38) reported another mortality study in a cohort of 13,571 white male rubber workers, again in Akron, Ohio. From the records of 5,079 deceased employees, excess deaths from leukemia occurred most often among workers in the tire (18 observed/11.7 expected) and in the processing (10/4.2) divisions. Excesses were also seen among workers in the chemical division (2/0.7), in elevator areas and cleaning (3/0.4), in shops (7/6.6), and in industrial products (9/7.0). Benzene was reported to have been used extensively in that industry; while pure benzene was no longer used as a solvent, it was stated to be a contaminant in many of the solvents still used (38).

In a mortality study of 20,163 petroleum-refinery workers carried out in 17 refineries (9), mortality from lymphomas was reported to be greater than expected, though not statistically significant, in three categorized exposure groups listed as high exposure (laboratory, maintenance, and salvage-recovery jobs), low exposure (plant security, utility, purchasing, and motor transport jobs), and medium exposure (all other jobs). An unknown number of workers may have had exposure to ben-

zene. In an epidemiologic survey of leukemia reported by Thorpe (48) in workers in a variety of petroleum and petrochemical operations, a number of problems of data collection were experienced. The incidence of leukemia was not considered to be abnormal compared to that of the general population in the counties concerned, emphasizing the need for improvement in the recording and storage of biologic observations, job histories, occupational exposures, and demographic data, but this report did not state how many workers had benzene exposure.

Animal experiments designed to investigate the carcinogenic action of benzene have failed to give reliable information on its capacity to produce an increased incidence of leukemias (55). Lignac (33) in 1932 claimed to have produced six cases of leukemia and two cases of lymphosarcoma in a strain of white mice given 0.001 ml benzene in olive oil once a week by subcutaneous injection for up to 11 months. Attempts to repeat these observations yielded equivocal results (10, 27, 30). A high tumor incidence often manifested as leukemias in untreated mice has been found to be caused by certain virus strains. It has been considered that leukemias described in the earlier experiments in mice after benzene treatment have, in large part, developed spontaneously or by virus infection, rather than being caused by benzene.

The literature is plentiful with medical case reports of leukemia directly associated with occupational exposure to benzene. These leukemias have occurred throughout the industrial world, most frequently as a result of using benzene in solvent applications. In France, Goguel et al. (26) in 1967 described 50 instances of leukemia, of which six had already been reported, in the Paris region from 1950 to 1965; 44 new cases included 13 chronic myelocytic leukemias, 8 chronic lymphocytic leukemia, and 23 acute leukemias with frequent disturbances of the erythrocytes and their precursors noted. Girard and Revol (25) added four observations of acute myeloid leukemia and nine cases of chronic lymphocytic leukemia in 1970. In the Soviet Union, Tarieff et al. (47) found six acute and ten chronic cases of leukemia among what were described as printers, primers, apparatus men, and chemists. In papers published

mostly through the 1970s, Aksoy and co-workers (1, 2, 3, 4, 5, 6, 7, 8) in Turkey have identified more than 50 patients with aplastic anemia and 34 cases of leukemia, all in workers having chronic exposure to benzene. These included one case of erythrocytic leukemia, three cases having a possible genetic predisposition, and one case of chronic myelocytic leukemia. In addition, a suggested relationship between Hodgkin's disease and chronic benzene exposure was reported. In Italy 34 fatal cases of benzene-associated aplastic anemia and leukemia have been observed (53). Vigliani (52) presented data from the Institute of Occupational Health of Pavia, Italy, showing that of 16 deaths occurring from 1960 and 1974 among 142 workers identified with chronic benzene poisoning, 3 died of aplastic anemia and 13 died of leukemia, and "there is, therefore, ample reason to believe that acute leukemias developing concurrently with cases of anemia, or as a terminal stage of an aplastic anemia in workers exposed to benzene, are really cases of occupational cancer." The observation of at least 20 cases of acute erythro-leukemia in the literature is considered to be significant because of the rarity of the disease (53). Vigliani and Saita (54), in 1964, calculated that, for workers heavily exposed to benzene in the cities of Milan and Pavia, the risk of acute leukemia was at least 20 times that of the general adult population. Cases of benzene-associated leukemia have also been reported in Spain (43) and Scandinavia (42).

The consistent observations of chromosomal aberrations associated with benzene exposure continue to be reported (21, 46, 56). The implications of the chromosome findings with respect to benzene leukemia are still not clear, but the possibility of a chromosomal instability acting as a stimulus for a latent leukemogenic virus has been speculated upon (53).

The recently reported isolation of a complete human RNA tumor virus (Type C) associated with acute myelocytic leukemia (18, 24, 34) raises again the possibility that a chemical carcinogen activates a latent leukemogenic virus in accord with the generalized suggestion of Todaro and Huebner (49). The demonstration of a relation between exposure to benzene, the appearance of a virus in exposed human

beings, and the occurrence of acute leukemia in these people would strongly support such an hypothesis.

In a 1973 review of industrial carcinogens, Eckardt (20) stated that:

The accumulation in the literature of cases of leukemia following benzene exposures leads to the inevitable conclusion that benzene is a leukemogenic agent, particularly in cases that have displayed a panmyelopathy. Although this had long been suspected, the data reported in the literature was not sufficiently convincing to establish the leukemogenic nature of benzene. However, the more recent observations seem to establish this association beyond a doubt. More recent observations of chromosome change in workers exposed to benzene lend further weight to the leukemogenic nature of benzene. In any event, in our operations, we are proceeding as if benzene were a leukemogenic agent, eliminating exposures where-ever possible and reducing them to the lowest possible level where complete elimination cannot be accomplished.

It is apparent from the literature that so-called benzene leukemia continues to be reported. The inadequacies in correlating exposure-effect relationships were discussed by NIOSH in 1974 (40) and in studies subsequent to 1974 which would aid in evaluating the consequences of exposure to various airborne concentrations of benzene have not been found in the literature. Case records of patients with acute or sub-acute leukemia have become so numerous that, according to Vigliani and Forni (53), they exceed those of acute pancytopenia, a fact which has led to the belief that many cases previously considered as pancytopenia may, in fact, have been examples of hemocytoblastic leukopenic and aleukemia (52). Since the substitution of benzene with toluene in the rotogravure industry in Italy in 1964, no new cases of aplastic anemia or of leukemia due to toluene exposure have been seen among workers hired since 1964; however, the latency period may be too short to provide an adequate final assessment. Furthermore, workers have not shown the chromosome aberrations frequently seen in workers exposed to benzene (52). The statement by Gerarde (19) that benzene is unique among hydrocarbons in its myelotoxic potency seems as valid today as in

1960 when it was made. During preparation of the benzene "update" document, the Industry-Wide Studies Branch, Division of Surveillance, Hazard Evaluations and Field Studies, NIOSH's Cincinnati, Ohio, offices were conducting a wide-scale epidemiologic study with a team headed by Infante (28), reporting on their extensive investigation of mortality patterns in workers occupationally exposed to benzene in the production of natural rubber film (rubber hydrochloride, long marketed under the tradename, "Pliofilm"), at two localities in Ohio. Their follow-up was only 75 % completed in June 1977. Their preliminary findings demonstrated a five-fold excessive risk of total leukemia and a tenfold excess of myeloid and monocytic leukemias combined. In this retrospective cohort study, all white men who had had direct exposure to benzene at any time between January 1, 1940, to December 31, 1949, were studied. The departments and jobs in the Pliofilm operation which involved direct exposure to benzene were determined by a survey by NIOSH personnel which included a review of the Pliofilm process, engineering controls, and air sampling data with the rubber company personnel assisting in these determinations. Job classifications involving benzene exposure were determined without knowledge of the workers' vital status.

Follow-up of all study-cohort members was attempted for the time period from first employment to June 30, 1975. Up to April 1977 vital status had been determined for approximately 75 % of the 748 cohort members. The remaining 25 % were assumed to be alive to avoid overestimating the true risk of lymphatic and hemopoietic malignancies associated with benzene exposure. Causes of death were determined from death certificates and were coded according to the International Classification of Diseases in effect at the time of death; these codes were then converted to I.C.D. seventh revision numbers. A modified life-table technique was used to generate person-years at risk of dying according to five-year age group and five-year calendar periods.

Person-years of observation and causes of death were determined for the period January 1, 1950, to June 30, 1975. Person-years of observation and deaths occurring

before January 1, 1950, were excluded from analysis since vital statistics of lymphatic and hemopoietic malignancies were not published before that date.

Two populations were chosen as control groups for generating the numbers of expected deaths in the study population. The first group consisted of the U.S. white male general population standardized for age and time period over which the study cohort lived. The second group consisted of 1,447 white men who had been employed in Ohio at a fibrous-glass construction products factory between January 1, 1940, and December 31, 1949, and who had achieved five or more years of employment by June 1, 1972 (which was the cut-off date for vital status ascertainment in the fibrous-glass control population) (12).

One hundred and forty observed deaths from all causes were noted among benzene-exposed workers compared with 187.6 expected deaths. This deficit reflects in part the incomplete follow-up of the study population. There was a significant excess of deaths from malignancy of the lymphatic and hemopoietic systems (I.C.D. 200—205) compared to that expected on the basis of death rates of U.S. white males. This is due almost entirely to an excess of leukemia deaths (I.C.D. 204). To date, seven leukemia deaths have been observed, compared with an expected 1.38 ( $p$  0.02) based on rates for U.S. white males and an expected 1.48 ( $p$  0.02) based on rates for fibrous-glass workers. Even more striking was the observation that all seven leukemia deaths were from either the myeloid or monocytic types. The period between initial exposure and death ranged from 2 to 21 years. These observations, indicating a specific type of leukemia, are consistent with the data of Vigliani (54), which showed a predominance of acute myelogenous leukemia among workers exposed to benzene in the rotogravure and shoe manufacturing industries in Italy. Since data for specific types of leukemia mortality in the U.S. are not readily available for the study period, incidences of myeloid, monocytic, and total leukemia from the Connecticut Tumor Registry (14) for the period 1960 to 1962 were applied to the age-distribution of the benzene-exposed cohort to generate the specific proportion of total leukemia cases which

would be of the myelomonocytic types. Of the total expected number of incidence cases of leukemia, 50.37 % were calculated to be of the myeloid and monocytic types. This proportion was applied to the total number of expected leukemia deaths in the study cohort which had been previously generated on the basis of rates for the U.S. white male population. The results indicated an expected 0.6967 ( $0.5037 \times 1.3831 = 0.6967$ ) deaths from myeloid and monocytic leukemia, compared with seven observed, and a standardized mortality-ratio of 1,004. Thus, Pliofilm workers exposed to benzene have an estimated tenfold risk of dying from myeloid and monocytic leukemia.

Since publication of this report, a follow-up letter by Infante et al. to *Lancet* (29) stated:

In our previous report, we indicated that individuals lost to follow-up were treated in the statistical analyses as being alive until the end of the study period, resulting in an under estimation of the true leukemia risk. This assumption was not based necessarily on our expectations of finding additional leukemia cases but rather, on the inevitable reduction in person-years observation when vital status of these individuals is determined. The reduction in person-years results in a reduction of expected leukemia deaths and thus, an increased risk of leukemia mortality. Our original report based on analyses up to April 12, 1977, indicated an SMR of total leukemia of 506. Without identification of an additional case, follow-up to July 22nd, now indicated an SMR of 560 (7 observed versus 1.25 expected). Thus, the SMR is continuing to increase even in the absence of any newly identified leukemia deaths among those individuals previously classified as lost to follow-up or decrease in the cause of death unknown. The cohort was selected for the study prior to our knowledge of any case of leukemia occurring among Pliofilm production workers of either locality. This fact is clearly documented by evidence submitted at hearing (clarified in this review). Subsequently, a newspaper in locality A became aware of our study and initiated an investigation of its own resulting in the identification of leukemia cases among benzene-exposed workers, some of whom were former Pliofilm workers. In June, 1977, during routine ascertainment pathology reports for the leukemia cases, a hematologist in locality A informed us of several previously identified cases of leukemia among workers of that location.

## THE EMERGENCY TEMPORARY STANDARD

An emergency temporary standard ("EST") may be issued when the Secretary of Labor (or the Assistant Secretary of Labor for the Occupational Safety and Health Administration) determines that (a) employees are exposed to grave danger from exposure to substances or agents determined to be toxic or physically harmful or from new hazards; (b) such an emergency standard is necessary to protect employees from such danger. Upon publication of such a standard, the Secretary must set in motion the procedures for promulgation of a permanent standard, which must be issued within six months of publication.

Based largely on recent epidemiologic evidence, the Assistant Secretary of Labor issued an emergency standard for benzene on April 29, 1977, calling for a reduction of worker-exposure concentration from 10 ppm to 1 ppm. On May 10, 1977, a petition was filed by 19 oil companies, asking the court to declare the standard invalid, declaring that the standard would "seriously affect the employment of thousands of workers and the availability of gasoline and refined products to the nation's consumers." The companies, in their legal brief, also argued that the Occupational Safety and Health Administration "cited no evidence for the need of the standard because monitoring of benzene at refineries has uncovered no health problems." At this time, the trade association for the retailers of gasoline were concerned whether or not OSHA would ask that gasoline service stations be compelled to comply with the 1 ppm emergency standard, faced with the possible additional cost of installing recovery devices, estimated by trade sources as being nearly four billion dollars (57), despite the fact that U.S. commercial fuels for autos will not contain more than 1 % benzene. As it is estimated that there are over 190,000 service stations in the U.S., not to mention gasoline shipping terminals and storage tank areas, considerable uncertainty was compounded because refiners had hoped to substitute greater levels of benzene in unleaded gas as a substitute for other controversial additives as octane boosters.

However, the emergency temporary standard (51) was published May 27, 1977, by law requiring a formal hearing within 60 days, and these hearings were held in Washington, D.C., on August 9th and 10th before a federal judge. The emergency temporary standard with its subsequent amendments, exempted storage, transportation, distribution, dispensing or sale of gasoline as a fuel, subsequent to the discharge of gasoline from bulk terminals as well as exposure to liquids containing benzene in amounts of 1% or less by volume, with such controls falling under the jurisdiction of the Environmental Protection Agency.

During the hearings in August 1977 at the Department of Labor, many experts provided testimony relating to the emergency standard and a few pertinent portions are noted here. A document of Italian origin was submitted which was translated by the Congressional Research Service of the Library of Congress (50). The lengthy, translated text "Law No. 245, March 5, 1963," outlined the "Limitation of the use of benzol and its homologues in working activities," severely restricted the use of benzene by "all employees, whether state, public, including those carrying on artisan activities and those who work at home on a contract basis," prohibiting use of "solvents containing benzene in dry cleaning, degreasing and cleaning in general;" "in the waterproofing of fabrics, in the manufacture and mending of raincoats, in the manufacture and repair of footwear, the use of products such as glues, adhesives, cements dissolves in solvents containing benzol is prohibited; in the work of painting, decorating, varnishing and of coating in general, as well as the work of paint removing and pickling, the use of benzol is prohibited; the use of inks in which the thinning of dispersant substances contain benzol is prohibited;" at the same time prescribing rigid limitations with respect to the use of toluene and xylene as well, plus certain severe penalties for noncompliance.

NIOSH considers the accumulated evidence from clinical as well as from epidemiologic data to be sufficiently substantial at this time to consider benzene as leukemogenic and because it causes progressive, malignant disease of the blood-form-

ing organs, and recommending for regulatory purposes, benzene be considered carcinogenic in man. In view of these conclusions and since it is not possible at this time to establish an exposure level at which benzene may be regarded to be without danger, NIOSH urged that exposure to benzene be kept as low as possible and use of benzene as a solvent or diluent in open operations should be prohibited. Furthermore, product substitution should be a paramount consideration and wherever benzene is identified or its presence suspected, it should be replaced with less harmful substitutes wherever feasible. NIOSH recommends that occupational exposure be controlled so that no worker will be exposed to benzene in excess of 1 ppm (3.2 mg/m<sup>3</sup>) in air as determined by an air sample collected at 1 l/min for 2 h (41).

For the present, the OSHA emergency temporary standard has been withheld because of legal actions, and the prior standard for benzene (10 ppm) remains in effect.

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