Air Quality Criteria for Beryllium and Its Compounds (1966)

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AIR QUALITY CRITERIA FOR BERYLLIUM AND ITS COMPOUNDS

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AIR QUALITY CRITERIA FOR BERYLLIUM AND ITS COMPOUNDS

I. Purpose of Study

The enactment of Public Law 88-206, known as the Clean Air Act, delegates to the Secretary of Health, Education and Welfare, authority to compile and publish air quality criteria for air pollutants. In addition, Section 7 of this Act directs cooperation by other Federal agencies to control air pollution from their facilities.

The United States Air Force has placed great emphasis on the conditions of operations as a means of protecting military and civilian personnel from possible toxic effects from the release of propellants and other military chemicals into the atmosphere. However, the introduction of fuels containing beryllium in motor test-firings presents a potential health hazard to on-site personnel and to the general population in the vicinity of the facility. Up to the present time, test-firings have been carried out at various locations in the United States and atmospheric contamination from fuels containing beryllium has not been a major problem because of the small amounts of beryllium that have so far been used. With the development of larger motors, the hazards associated with propellants containing beryllium and the problem of site selection have become matters of concern to both the U. S. Air Force and the U. S. Public Health Service.

To assist the States and local governments in the control of air pollution, the U. S. Public Health Service requested the National Academy of Sciences-National Research Council, through its Advisory Center and Committee on Toxicology, to make a study of the toxicity and hazards of beryllium and its compounds and to make recommendations for the establishment of air quality criteria. In carrying out this assignment, the Committee invited a number of people knowledgeable on this subject, to discuss the epidemiological and medical aspects of beryllium toxicity, experimental studies, and

industrial control procedures. The knowledge gained from the discussions as well as from the published literature, forms the basis of the recommendations set forth in this report. The Committee gratefully acknowledges the valuable contributions made by those who presented their data and opinions.

II. Acute Chemical Pneumonitis

Exposure to excessive concentrations of certain beryllium compounds results in inflammatory reactions ranging from rhinitis to tracheitis, bronchitis and pneumonitis, depending upon the degree of exposure. For example, air concentrations of 1000 µg Be/m^3 or more produce acute effects in all exposed individuals whereas only a small percentage are affected at air concentrations of 100 µg Be/m^3 or less. There is usually spontaneous recovery from the acute effects after removal from the contaminated atmosphere, but in some cases, intensive therapy may be required.

The acute effects, which are dose-related, are produced by exposure to mists, fumes and/or dust of soluble beryllium compounds. The earlier reports of acute effects thought to have been produced by beryllium oxide are more likely to have been due to contamination of the oxide with soluble beryllium compounds. These acute effects have been commonly referred to as "acute beryllium disease" but it is doubtful if they are peculiar to exposure to beryllium compounds since similar effects are produced by other chemical irritants of the pulmonary tract. Most of the acute cases have not been productive of the chronic form of the disease. As far as can be determined, there are no cases of uninterrupted progression from acute chemical pneumonitis to chronic beryllium disease from a single exposure. Acute disease from non-occupational exposure has not, to our knowledge, been reported.

III. Chronic Beryllium Disease

A. Pathogenesis

The pathogenesis of chronic beryllium disease is still unknown. The fact that only a small percentage of the persons exposed develop the disease lends support to the hypothesis advanced by several investigators that there is an immunological abnormality associated with the disease, or that the susceptibility is in some way related to an inborn error of metabolism.

In chronic beryllium disease, the lung is the primary target organ and the lesions produced are characterized by a progressive granulomatous process occurring in the interstitial tissue and the alveolar walls. There is a latent period between exposure and the appearance of the disease which varies from months to as long as 23 years.

Among the factors associated with the chronic disease that have complicated the interpretation of the epidemiological studies are the following: The extremely small amounts of beryllium-containing materials alleged to have produced the disease; the well-documented fact that many persons have received severe exposures to beryllium-containing compounds without developing the disease; the latent period between exposure and symptoms; the occurrence of illness in only a small percentage of the exposed population; the similarity between chronic beryllium disease and other chronic diffuse pulmonary diseases; the uncertainty as to the identity of the physical-chemical properties of the beryllium compounds involved; and the lack of any quantitative data on the magnitude of the exposure and particle size.

From the data presented to the Committee, as well as from published reports, we believe that the chronic form of the disease is produced by exposure to certain insoluble beryllium compounds. This is supported by the circumstances surrounding

the so-called "neighborhood cases," the experiences in the beryllium lamp industry where the oxides were present in the phosphor, and from experimental data. The few cases of chronic disease alleged to be associated with exposure solely to soluble beryllium compounds could have been due to hydrolysis in the tissues to insoluble compounds such as beryllium hydroxide or oxide, or to an unknown exposure to some active beryllium compound, although there are no data to support these speculations.

The Committee also gained the impression that repeated short exposures to high concentrations are important in the development of the disease in susceptible individuals. Analyses of lung tissues at autopsy have shown the content of beryllium to range from micrograms to milligrams per gram of tissue. There was no correlation between the amount of beryllium in the lung and the existence of the chronic disease. The pattern of occurrence of the chronic disease among occupationally exposed workers in beryllium-producing plants does not show an increase in risk with increased duration of exposure. On the other hand, there is now persuasive evidence that the risk of developing chronic beryllium disease increases with the intensity of the exposure.

B. Differential Diagnosis

The differential diagnosis of chronic beryllium disease from other chronic diffuse pulmonary diseases, particularly sarcoidosis, has been a subject of controversy. Although the diagnosis may be difficult at times, there is no doubt that certain insoluble beryllium compounds produce a diffuse pulmonary granulomatosis in susceptible individuals. In most cases a differential diagnosis can be made, especially if there has been a history of beryllium exposure. Although there has been some question concerning the possible relation of beryllium compounds to the development of sarcoidosis, worldwide epidemiological studies show that chronic beryllium disease and sarcoidosis are separate and distinct entities.

C. Incidence of Chronic Disease

The Beryllium Registry now shows over 400 cases of chronic beryllium disease from industrial and approximately 60 cases from non-industrial exposure but the total exposed population is unknown. In one fluorescent lamp plant the incidence of the chronic disease was 10-15 per cent due largely to uncontrolled exposures to the high content of beryllium oxide in the phosphor, whereas in other plants under more rigid controls, the incidence has been less than one per cent. A study in the Reading, Pennsylvania area has revealed 30 non-occupational cases from a population of 120,000, which is 0.025 per cent or one in every 4,000.

The use of 2.0 μg Be/m^3 as a guide in controlling atmospheric contamination has to date resulted in no cases of chronic disease among industrial workers. Likewise, 0.01 μg Be/m^3 has to date resulted in no cases of chronic disease among non-industrial workers. In some plants there have been exposures to concentrations well above the 2.0 μg Be/m^3 for prolonged periods without the occurrence of the disease. Many of the neighborhood cases can be attributed to repeated peak exposures to dust from laundering of work clothes. The analysis of dust clouds from simulated laundering conditions has given values as high as 500-1000 μg Be/m^3.

The epidemiological studies on the incidence of chronic beryllium disease reported by various investigators, have for the most part been incomplete. There are no data on particle size, the concentration and duration of exposure, or on the chemical and physical nature of the compounds reported to have produced the disease. However, from the evidence presented, the Committee believes that exposures to low ambient air concentrations of beryllium compounds are less important in the production of the chronic disease than repeated brief exposures to high concentrations.

It has been stated that the incidence of chronic beryllium disease is higher among females than males in both occupational and non-occupational populations. While the data indicate that this alleged increase in susceptibility may be due to the physiological stress of pregnancy, the unique form of exposure to high concentrations of beryllium from laundering work garments may also have masked the true incidence of the disease among the two sexes.

IV. Experimental Studies

Acute pneumonitis, closely resembling the acute disease seen among beryllium industrial workers, has been observed in a variety of laboratory animals exposed to beryllium compounds for short periods. Likewise, pulmonary lesions resembling those found in humans suffering from chronic pulmonary disease, have been produced in animals following the intratracheal administration of high doses of beryllium oxide. Although the pulmonary granulomas produced experimentally in animals may not be morphologically the same as those found in humans with the chronic disease, the Committee believes that the response of animal lung to various beryllium compounds is relevant in assessing the hazards associated with the handling of these compounds.

A. "High-fired" versus "Low-fired" Beryllium Oxide

It has been demonstrated by several investigators that a definite relationship exists between the chemical and physical properties of beryllium oxide produced by calcining at different temperatures and its toxicity in animals. In 1949, it was observed that beryllium oxide calcined at 1350° C was virtually non-toxic when administered by inhalation to dogs, guinea pigs, rabbits, and rats, whereas material calcined at 1100° C and 400° C caused a progressive increase in mortality with decreasing calcining temperature.

Granulomatous lesions have been produced in the lungs of rats and rabbits following the intratracheal administration of beryllium oxide calcined at low temperatures (c. a. 500° C). The lesions appeared as early as three weeks. Beryllium was found in the lung, liver, kidney, spleen, bone, and lymph nodes. Beryllium oxide produced by calcining at high temperature (c. a. 1600° C) failed to produce any granulomas six months after intratracheal administration and there was a marked reduction in the translocation of beryllium from the lungs to other organs. Parallel studies with material prepared at intermediate temperatures have shown an intermediate capacity to produce pulmonary lesions.

These differences in toxicity closely parallel changes in the chemical and physical properties of the beryllium oxide. As the calcining temperature is increased, the degree of crystallinity, average crystalline size, refractive index, and density increase while the surface area markedly decreases.

B. Rocket Exhaust Products

Recent studies on rocket exhaust products indicate that the beryllium is almost entirely in the form of beryllium oxide with only a small percentage of beryllium metal and soluble beryllium compounds. With respect to particle size, crystallinity, and density, the physical-chemical properties of the beryllium oxide produced from the motor test-firings are strikingly similar to the oxide formed by calcining at 1600° C.

Preliminary studies in animals indicate that the physiological effects from the intratracheal administration of rocket exhaust products from operational firings are similar to those from "high-fired" beryllium oxide. The products from inefficient firings produce severe lung injury typical of "low-fired" beryllium oxide and soluble beryllium compounds.

C. Carcinogenesis

While certain beryllium salts and oxides have been productive of osteogenic sarcomas in rabbits following intravenous administration and primary lung tumors in rats and monkeys following inhalation, there is no evidence that community or industrial exposure to beryllium compounds is associated with an increase in the incidence of cancer in humans.

V. Analytical Procedures

The methods now in use for the analysis of beryllium in the atmosphere are accurate, sensitive, and reliable if carried out by trained and experienced personnel. However, none of these methods permits identification of the particular form of beryllium beyond a gross separation of soluble from insoluble compounds. Quantitative studies of atmospheric concentrations of beryllium in various locations of the United States where beryllium is not being produced, show values ranging from 0.00002 to 0.003 μg Be/m^3. In areas where beryllium enters the atmosphere from stack emission, ore deposits, or in the fly-ash from burning of coal, the concentrations may range from 0.003 to 0.07 μg Be/m^3. In developing air quality criteria, practical procedures are needed which will include: (1) the separation of insoluble and soluble beryllium compounds; (2) identification of the insoluble forms of beryllium, i.e. beryllium oxide, hydroxide, and silicates; (3) a differentiation of the "high-fired" and "low-fired" beryllium oxide, and (4) a description of particle size.

There are several research efforts directed toward the physical-chemical characterization of beryllium compounds which show promise of providing useful analytical procedures: (1) x-ray diffraction studies reveal that with increasing temperature, the crystallite size of the beryllium oxide increases. Also, with increasing temperature, the density and refractive index increase whereas the surface area decreases; (2) solubility studies have

shown that "low-fired" beryllium oxide is much more soluble in blood serum and hydrochloric acid than "high-fired" beryllium oxide, although both are essentially insoluble in water, and (3) surface adsorption of certain dyes has been reported to differentiate between "high- and low-fired" beryllium oxide.

The observation that various beryllium oxides cause significantly different pulmonary responses makes the development of analytical techniques of particular importance in any further toxicological studies, monitoring programs, and epidemiological surveys.

VI. Proposed Air Quality Criteria

A. Continuous Exposure

From the evidence presented to the Committee, it is quite clear that the level of 0.01 μg Be/m^3 currently used as a guide for protecting the neighborhood population from undue exposure to beryllium materials in the effluent from industrial plants has been effective in controlling chronic beryllium disease. While it has been suggested that this level may be overly conservative, there are several compelling factors that favor the current level; the industrial plant emission consists of beryllium materials whose chemical composition, physical properties and toxicological effects are unknown; the industrial effluent is continuous without regard to local meteorological conditions and the associated distribution of beryllium materials in the neighborhood; and many of the industrial plants are located in close proximity to heavily populated areas. A significant increase in the present neighborhood level (0.01 μg Be/m^3) would depend upon the availability of more information on the identity and biological activity of the industrial effluent.

In view of the foregoing considerations, and in keeping with the Clean Air Act, the Committee finds no basis for changing the current level of 0.01 μg Be/m^3 averaged over 30 days for

communities exposed continuously to all forms of beryllium carried into the atmosphere from industrial effluents.

B. Intermittent Exposure

Beryllium entering the atmosphere from motor test-firing introduces a number of factors quite different from industrial plant effluents: the frequency of test-firing can be controlled, the exposures would be intermittent and of short duration, the test-firing would be made only under optimal micrometeorological conditions with an extensive monitoring control system, and a large proportion of the beryllium in the exhaust is "high-fired" beryllium oxide. It is evident that under these conditions, the time-weighted average for non-occupational populations in industrial areas is not applicable to military operations and the level of 0.01 μg Be/m^3 is unnecessarily restrictive. The Committee believes that the general population in the vicinity of a test facility can tolerate without undue risk, peak concentrations which are significantly greater than the present levels for continuous exposure to industrial effluents. Peak concentration is meant to imply a concentration-time relationship within relatively short periods of time.

Therefore, (1) for soluble beryllium compounds a maximum exposure of 75 μg-min Be/m^3 may be tolerated within the limits of 10-60 minutes, accumulated during any two consecutive weeks. This is equivalent to 2.5 μg Be/m^3 for 30 minutes and is based on the fact that the industrial level of 25 μg Be/m^3 for 30 minutes has proven to be safe; (2) for beryllium oxides occurring in rocket exhaust products, a maximum of 1500 μg-min Be/m^3 may be tolerated within the limits of 10-60 minutes accumulated during any two consecutive weeks. This is equivalent to 50 μg Be/m^3 for 30 minutes and is based on the consideration that beryllium in the rocket exhaust has been shown to be predominantly crystalline beryllium oxide possessing chemical and physical properties closely resembling those of "high-fired" beryllium oxide.

VII. Conclusions

As a result of the Committee's deliberations, certain facts have emerged which heretofore have not been fully recognized. It is now quite evident that all beryllium compounds are not equally toxic. Soluble beryllium compounds are productive of acute chemical pneumonitis while certain insoluble forms cause chronic beryllium disease. Exposures to low ambient air concentrations of beryllium are less hazardous than brief exposures to high concentrations. The experimental animal studies with beryllium oxides prepared by calcining at different temperatures have provided convincing evidence that "high-fired" beryllium oxide is less toxic than "low-fired" beryllium oxide. Although there has been some doubt concerning the differential diagnosis of chronic beryllium disease, the Committee believes that a positive diagnosis can now be made in most cases.

VIII. Recommendations

A. Research

Recognizing that certain inadequacies exist in our knowledge concerning the pathogenesis and epidemiology of chronic beryllium disease, the Committee feels that further research should be directed toward providing information in the following areas:

1. A carefully-planned retrospective epidemiological study of occupationally and non-occupationally exposed persons should be made in the neighborhood of an industrial plant as well as prospective epidemiological studies in the vicinity of test-firing facilities.

2. A national air-sampling network for monitoring beryllium in the atmosphere should be instituted immediately to provide background data.

3. Analytical techniques that can be used in the field to rapidly identify the various beryllium compounds are urgently needed.

4. A thorough study of rocket exhaust products containing beryllium is needed to characterize them as to their chemical and physical properties, including at least, particle size, crystallinity, crystallite size, refractive index and solubility.

5. Toxicity studies presently in progress on beryllium oxide prepared by calcining at various temperatures should be continued in order to determine any effects that might develop with time. Well-characterized rocket exhaust products pertinent to the propellant program should be studied in a similar manner.

6. Studies should be initiated to establish a dose-response relationship, as well as a study of the mechanism of action of beryllium compounds.

B. Air Quality Criteria

Until pertinent information from the suggested research becomes available, we recommend the use of the following interim air quality criteria:

1. For continuous exposure to all forms of beryllium arising from industrial sources, the current level of 0.01 μg Be/m^3 averaged over a 30-day period should continue to be used.

2. For intermittent exposure to soluble compounds of beryllium arising from rocket motor firing, a maximum atmospheric exposure of 75 µg-min Be/m^3 may be tolerated within the limits of 10-60 minutes accumulated during any two consecutive weeks.

3. For intermittent exposure to beryllium oxide arising from rocket motor firing and which has the physical and chemical characteristics of "low-fired" beryllium oxide comparable to a product calcined at temperatures around 400°C, a maximum exposure of 75 µg-min Be/m^3 may be tolerated within the limits of 10-60 minutes accumulated during any two consecutive weeks.

4. For intermittent exposure to beryllium oxide arising from rocket motor firing and which has the physical and chemical characteristics of "high-fired" beryllium oxide comparable to a product calcined at temperatures in excess of 1600°C, a maximum exposure of 1500 µg-min Be/m^3 may be tolerated within the limits of 10-60 minutes during any two consecutive weeks.

In applying the above criteria for intermittent exposure to a rocket motor firing, it will be necessary to consider simultaneously the concentration of soluble beryllium compounds, the "low-fired" beryllium oxide and the "high-fired" beryllium oxide and adjust the limits accordingly. For example, if the rocket effluent is composed of acid-soluble beryllium (36% HCl diluted 1:1) in amounts greater than 1% but less than 5%, the "high-fired" limit of 1500 µg-min Be/m^3 should be reduced by a factor of 2; if greater than 5%, the limit for "low-fired" beryllium should be used.

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