EVALUATION OF BERYLLIUM ANIMAL DATA

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A. INTRODUCTION

My name is Andrew L. Reeves. I am Professor of Occupational and Environmental Health at Wayne State University in Detroit, Michigan. My teaching assignments and research interests are in the area of occupational and environmental toxicology. I am a member of the Society of Toxicology with past service on its Nomination Committee and Education Committee and as Vice President of its Specialty Section on Metals; of the American Industrial Hygiene Association with past or present service on its Air Pollution Evaluation Committee, Refresher Courses Committee, Toxicology Committee and Biological Monitoring Committee; and of numerous other scientific and technical societies including the International Commission on Occupational Health.

I obtained my undergraduate and graduate education at the Universities of Budapest, Vienna, and Munich, and I earned a Ph.D. in biochemistry from Wayne State University in 1959. I wrote my dissertation on the toxicology of beryllium, and I have retained a strong professional interest in beryllium ever since. I have authored or coauthored more than 30 research papers, reviews, and book chapters on beryllium, and I served on the Subcommittee on Beryllium of the Toxicology Committee of the National Academy of Sciences. I also have served as Consultant to the Department of Energy and to the Environmental Protection

Agency on questions relating to the toxicology of beryllium. My curriculum vitae is contained in Attachment 1.

A cursory examination of the animal experiments and the reported neoplastic responses suggests that there is little doubt about the link between beryllium and cancer. However, close examination of these animal data raises serious questions about their applicability to human carcinogenicity. The early animal studies on beryllium, while voluminous, were for the most part poorly conducted, incompletely reported, and by today's scientific standards would be unacceptable. In this document, I wish to examine the experimental evidence for the carcinogenicity of beryllium, at the request of beryllium producers in this country. I feel I can do so with more than ordinary expertise because I have been intensively personally involved in that research since 1955.

B. EARLY HISTORY OF BERYLLIUM RESEARCH

In 1945-46, Dr. Leroy U. Gardner, Director of the Saranac Laboratory in upstate New York, in a search to find the cause of an "unusual incidence of pulmonary sarcoid" in the fluorescent light bulb industry, injected zinc beryllium silicate, a phosphor used in the manufacture of the tubes, into rabbits by the

intravenous route. The rabbits developed osteosarcoma of the long bones. The incidence was 100% for survivors of the treatment for 7 months or more (7/7). This having been the first instance of experimental carcinogenesis with an inorganic substance, it evoked great interest. Beryllium was clearly implicated as the causative agent because zinc oxide, zinc silicate or silicic acid did not cause osteosarcoma in a second set of trials, whereas beryllium oxide (a sample obtained at that time from Clifton Prods., Inc.) did. Guinea pigs and rats, similarly treated with either beryllium silicate or beryllium oxide, failed to respond. The dose of beryllium with the two compounds injected ($ZnBeSiO_3$ and BeO) was 60 and 360 mg, respectively, in divided doses during a 20-week period. These results were orally presented to the Federation meetings in 1946, with an abstract printed in the Proceedings (Gardner and Heslington, 1946) but there was no paper published on these studies.

In the fall of 1946, Dr. Gardner suddenly died and Dr. Arthur J. Vorwald became director of the Saranac Laboratory. He recognized the artificiality of the intravenous route and commenced chamber inhalation studies. According to another oral presentation, this time to the American Cancer Society in 1953, primary adenocarcinoma developed in the lungs of rats with a frequency of 80% (4/5) after 14 months of exposure 7 hours daily, 5.5 days/week, to a beryllium sulfate aerosol measured as 33 ug Be/m^3. This study again remained unpublished, although Dr.

Vorwald sent typewritten drafts of the oral presentation to persons requesting information (Vorwald, 1953). An abstract of these and some further data was printed in meeting proceedings of the International Union against Cancer, following a repeat oral presentation (Vorwald et al., 1955).

In 1954, Dr. Vorwald resigned his position as Director of the Saranac Laboratory and came to Detroit to organize the Department of Occupational and Environmental Health at Wayne State University. I joined the Department in January, 1955. Beryllium research was recognized as being in the center of the departmental interest and Dr. Vorwald secured sizable grants from the American Cancer Society to equip the Department and continue the research commenced at Saranac. My initial research as a graduate student involved investigating the kinetics of inhaled beryllium and the pathogenesis of beryllium tumors (Reeves et al., 1958; Reeves, 1959; Vorwald and Reeves, 1959 a,b). The fact that the produced lesions were malignant adenocarcinomas was to be taken for granted.

Dr. G. W. Schepers became the new Director of the Saranac Laboratory. Dr. Schepers published in 1957 the first paper on beryllium carcinogenesis in the lungs of experimental animals, based on 136 rats of which 78 survived to planned necropsy. Only the total number of tumors produced, rather than the number of tumor-bearing animals were counted (76), after 6 months' exposure to $BeSO_4$ aerosol measured as 12 ug/cu. ft. (35 ug Be/m^3) and up

to eighteen months' continued life in normal air. Eight histological variants of neoplasms were noted to occur; lesions interpreted as intrathoracic metastases were seen; and successful transplants were claimed to have been accomplished (Schepers et al, 1957).

Dr. Vorwald believed that Dr. Schepers' published results were based at least in part on his own work that he left behind at Saranac, which he did not feel was ready for publication at that point. There were several unresolved questions with the beryllium-induced lesions.

First, the proliferative response in the lungs of rats was invariably associated with purulent lesions of chronic murine pneumonia, accentuated by the response to the acidity of the $BeSO_4$ aerosol. Whether or not the proliferative reaction was part of the inflammatory reaction complex, or a response to nonspecific irritation, rather than a specific response to beryllium, was not certain. Furthermore, the tumors did not appear to shorten the life expectancy of the host animals significantly. In these, as well as in some later experiments, it was ordinary routine to keep a great majority of exposed animals alive to their scheduled necropsies towards the end of the natural lifespans, even if they were given their exposure to beryllium early in life. The only condition was the scheduled administration of antibiotic medication in their drinking water, in order to control (but never quite eradicate) the epizootic

pneumonia. The significance of this factor in the development of tumors was not investigated. The attritional mortality between tumor-bearing and tumor-free animals was in many experiments comparable.

Second, there was also a question about the metastatic spread of these tumors. Multiple tumor foci in the same lung were frequently observed, but each was associated with purulent lesions of its own and to regard them as metastases was highly questionable. Extrathoracic metastases were never observed, and this was conspicuously admitted in Dr. Vorwald's unpublished paper: "Extrapulmonary foci of epidermoid cancer were not discovered in the rats of the experiments in this report" (Vorwald, 1953).

Third, we at Wayne State University had a completely negative transplant experience with the beryllium-induced pulmonary tumors, which was not for want of trying -- virtually every beryllium-induced tumor that we ever produced we tried to transplant, either as 1 mm^3 solid tissue cube or as carefully macerated cell homogenate, into both non-cortisonized and cortisonized hosts. Not one of them succeeded, and I was then, and am now, completely satisfied that these tumors were nontransplantable. There was great reluctance on the part of Dr. Vorwald to accept this conclusion, because he felt that it contradicted the microscopically visible evidence. His reluctance only deepened when Schepers claimed successful

transplants of the tumors he produced, or claimed to have produced.

An unfortunate and almost unseemly competitiveness developed between Dr. Vorwald and Dr. Schepers for claiming priority to have first reported pulmonary cancer from inhaled beryllium, for the validity of the model to have produced experimental pulmonary cancer, and for funding from the American Cancer Society. This was the climate in which I commenced independent experimentation with beryllium on Dr. Vorwald's staff after the attainment of my Ph.D. in 1960. In the meantime, both Schepers and Vorwald continued to report on beryllium-induced pulmonary cancers in a most peculiar fashion. Instead of writing papers for peer review, the results were mentioned, or sometimes only hinted at, in reviews (Schepers, 1961; Vorwald et al., 1966). The details of these experiments are therefore not in the public domain.

Careful perusal of all available evidence suggests that Schepers exposed rats to beryllium phosphate and obtained a tumor incidence of 35-60 out of 170 at 32-35 ug Be/m^3 and 7 out of 40 at 227 ug Be/m^3. With beryllium fluoride, he obtained a tumor incidence of 10-12 out of 200 at 9 ug/m^3, and after exposure to zinc beryllium manganese silicate (a fluorescent phosphor in use at that time), he obtained a tumor incidence of 4-20 out of 220 at 0.85-1.25 mg Be/m^3. These incidences are 2-35% of animals exposed, provided that each counted tumor is assigned to a different host (which cannot be definitely determined from the

presented data). There appears to be an inverse dose/response relation. In similarly exposed rabbits and guinea pigs he obtained no tumors.

Vorwald's experiments all involved rats exposed to beryllium sulfate aerosol inhalation, in reported concentrations ranging from 2.8 to 180 ug Be/m^3, on various exposure schedules ranging in length from 3 to 24 months. Pulmonary lesions assumed to be adenocarcinomas were reported in all groups, in incidences ranging from 20% to 100%. Unfortunately, I must state that these data deserve no confidence. The study was extremely loosely controlled, with Dr. Vorwald absent from the University during much of the experiment. The person charged with the responsibility to conduct the study was in a declining state of health and had to be placed on permanent medical leave in 1965. Control of chamber air was virtually nonexistent during much of the exposure. Animal care was sporadic, with substantial attrition and cannibalism. Three quarters of the participating animals were never necropsied, and those necropies that were performed were frequently done by untrained technicians who would readily confuse a pus sac with a tumor. Only the most rudimentary tabulation of these data was ever completed.

Unfortunately, when Dr. Vorwald was asked by Dr. Stokinger in 1965 to contribute a chapter on experimental toxicology to the latter's monograph on beryllium then in preparation, Dr. Vorwald decided to incorporate these data in the chapter -- perhaps as a

means to accord some recognition to the unwell person. That was the only justification to include him as a coauthor of the chapter. I was also included as a coauthor of this chapter for my contribution on the biochemical aspects of beryllium toxicology, but I had no control over other parts of the manuscript. I have been greatly embarrassed by this seeming association with these data ever since. I felt compelled to disavow them at the OSHA hearings in Washington, D.C. in 1977, and I feel compelled to disavow them now.

C. LATER CHAMBER INHALATION STUDIES

When I commenced independent experimentation with chamber exposures in the mid-1960's, it was my resolve to improve the prevailing standards of conduct of studies and their reporting. For the first time in the history of beryllium inhalation toxicology, I insisted on a steady air sampling program in the chambers rather than spot checks, and I reported the mean levels with their standard deviations which showed honestly how imprecise our chamber technology was at that time. (Ironically, some Government reviewers commented unfavorably on my data for this reason, while the hairline precision of a single figure [e.g., 2.8 ugm^3 from Vorwald, or 227 ug/m^3 from Schepers] was accepted at face value.)

I also wished to tighten the standards of pathologic

evaluation. However, Dr. Vorwald was not accustomed to "blind" evaluation of slides (i.e., coded without indication of origin) and considered it professionally improper (comparable to the clinical diagnosis of berylliosis without evidence of history of exposure). Finally, I established a collaboration with Dr. Daniel Deitch, who was trained by Dr. Vorwald but was willing to perform blind evaluation of slides and grading of the neoplastic response in terms of hyperplasia, metaplasia, anaplasia, and frank adenocarcinoma.

We exposed 150 rats of both sexes to $BeSO_4$ aerosol at a mean atmospheric concentration (± 1 S.D.) of 34.25 ±23.66 ug Be/m^3 on a 35 hrs./wk. schedule, and 150 rats to clean air (controls) [Reeves et al., 1967; Reeves and Vorwald, 1967]. The first lung tumors were seen at 9 months' exposure and all animals necropsied at 13 months (43/43) had pulmonary adenocarcinomas. Essentially similar results were obtained 2 years later on another animal group (Reeves and Deitch, 1969). In the later study, a total of 225 female rats were exposed for 3-18 months to 35.66 ± 13.77 ug Be/m^3 (35 hrs./wk.) at various age levels. It was found that tumor yield depended not on length of exposure but on how early in life the exposure was received. Rats exposed at an early age for only 3 months had essentially the same tumor frequency (19/22) as rats exposed throughout the 18 months (13/15), whereas rats receiving 3 months exposure later in life had substantially reduced tumor counts (3-10/20-25). Generally, an incubation time of at least 9 months from commencement of exposure was required

to produce actual tumors, whereas epithelial hyperplasia of the alveolar surfaces commenced after about 1 month progressing to metaplasia at 5-6 months, and to anaplasia at 7-8 months. In guinea pigs, 18 months of exposure (35 hrs./wk.) to 3 different concentrations of beryllium sulfate (3.7 ± 1.5 ug Be/m^3, 16.6 ± 8.7 ug Be/m^3, and 30.4 ± 10.7 ug Be/m^3) produced no tumors, only alveolar hyperplasia/metaplasia in 23 out of 144 animals, all associated with diffuse interstitial pneumonitis. Incidence of hyperplasia/metaplasia in unexposed controls was 3/55 (Reeves et al, 1971; Reeves and Krianek, 1974).

In all of my studies, no metastases were observed, no successful transplants were accomplished, and the microscopic diagnosis of neoplasia was based entirely on Dr. Vorwald's criteria. When these slides were shown at intramural seminar presentations, the D.V.M. pathologists (as contrasted to M.D. pathologists) occasionally commented that some of the lesions looked questionable to them and were, perhaps, complicated by the reaction to aspirated food particles. I developed the opinion then, which I still hold today, that the classification of neoplasms may have species-specific parameters which are not fully explored at present and which require a fundamental large-scale study.

Concurrently, Wagner et al. (1969) exposed rats, hamsters, and squirrel monkeys to aerosols of beryl ore and bertrandite ore, at the then "nuisance limit" for all dusts (15 mg/m^3). At

this particle concentration, the beryllium content of the aerosols was 620 and 210 ug/m^3 for beryl and bertrandite, respectively. Exposure was continued intermittently for 17 months. At that point, 18 of 19 rats exposed to beryl dust had bronchiolar or alveolar cell tumors, of which 7 were judged to be adenomas, 9 to be adenocarcinomas, and 2 to be epidermoid tumors. Metastases were not observed, and transplants were not attempted. In the rats exposed to bertrandite dust, and in all hamsters and squirrel monkeys, no undisputable tumors were found. In the bertrandite-exposed rats and hamsters, granulomatous lesions composed of large, tightly packed macrophages as well as "atypical proliferation" of the cells lining the respiratory bronchioles and alveoli were seen. Atypical proliferation was also seen in beryl-exposed hamsters, which "could be considered alveolar cell tumors except for their size". Only the granulomatous lesions were seen in both beryl- and bertrandite-exposed monkeys.

Schepers (1964) found that among 20 female rhesus monkeys exposed to inhalation of $BeSO_4$, $BeHPO_4$, or BeF_2, in concentrations ranging from 0.035 to 8.3 mg Be/m^3, one animal had a small pulmonary neoplasm which appeared to be alveolar carcinoma. The animal was in the $BeHPO_4$ (1.1 mg Be/m^3) exposure group. The tumor, which had a 3 mm maximum diameter, was found on the 82nd day following commencement of exposure. Its connection with the beryllium exposure was judged uncertain.

Vorwald (1968) reported the outcome of a 3-year chamber study on stumptail monkeys inhaling an aerosol of $BeSO_4$ with intermittent exposure averaging about 15 hrs/wk. at a mean atmospheric concentration of 38.8 ug Be/m^3 Eight of 11 surviving animals had pulmonary tumors, with "adenomatous patterns predominating among areas with epidermoid characteristics". Metastases to the mediastinal lymph nodes and in some animals to the liver, bones, and adrenals were seen. No control animals were kept in this experiment.

Sanders et al. (1973) exposed female rats to a submicron aerosol of medium-fired (1000°C) BeO by the nose-only method. Only 1 out of 184 animals developed a lung tumor during the 2-year observation period.

Dutra et al. (1951) exposed 5, 6 and 8 rabbits to BeO aerosols at 1, 6, and 30 mg Be/m^3, respectively, on a 25 hrs/wk. schedule for 9-13 months. One rabbit in the 6 mg Be/m^3 group developed sarcoma of the pubic bone, with extensions to the contiguous musculature. Scattered tumors which were judged to be metastases of the primary bone tumor were seen in the lungs and spleen. The lungs of the same rabbit also exhibited emphysema, interstitial fibrosis, and lymphocytic infiltration. The rabbits in the other groups remained free from malignancies.

D. INTRATRACHEAL INJECTION STUDIES

Intratracheal administration of beryllium compounds was practiced as a shortcut for inhalation experiments by Vorwald (1953), Spencer et al. (1965) and Groth et al. (1980). The fate and effects of these deposits is not necessarily the same as that of identical compounds deposited by inhalation. The intratracheal injection produces an unnatural deposition pattern in the lung and also allows the pulmonary entry of larger particles, which would normally be filtered out in the upper respiratory tract. Dusts of a certain compound therefore frequently show longer pulmonary half-time after intratracheal injections that after inhalation.

One lung tumor after intratracheal injection of 338 ug Be (as $BeSO_4$) was reported by Vorwald (1953); the induction of lung cancer with intrathoracic metastases in rhesus monkeys following intrabronchial injection and/or bronchomural implantation of "pure" BeO was mentioned in Vorwald et al.'s 1966 review, without any original publication.

Groth et al. (1980) injected dusts of metallic beryllium, passivated metallic beryllium (with <1% Cr) and various beryllium alloys, as well as beryllium hydroxide, intratracheally into rats. Lung tumors were observed after injection of metallic beryllium, passivated metallic beryllium, and a beryllium-aluminum alloy containing 62% Be, but not after the other

beryllium alloys in which Be concentration was <4%. The injection of beryllium hydroxide yielded 13 out of 25 cases of neoplasia of which 6 were judged to be adenomas and 7 to be adenocarcinomas. The rest of the animals had various degrees of metaplasia but no frank tumor.

The most detailed studies with intratracheal injections of beryllium were reported by Spencer et al. (1965, 1972). High-fired (1600°C), medium-fired (1100°C) and low-fired (500°C) specimens of beryllium oxide were injected into rats; incidence of pulmonary adenocarcinomas was 3/28, 3/19, and 23/45 in the 3 groups, respectively, corresponding to 11, 16 and 51%. This gradation of response to beryllium oxides of various firing temperatures parallels the antigenicity and conventional toxicity of these specimens.

E. INTRAVENOUS INJECTION STUDIES

Finally, an account must be given of the direct continuation of Dr. Gardner's work with osteosarcoma in rabbits, following intravenous injection. Cloudman et al. (1949) produced osteosarcoma in 4 out of 5 rabbits receiving a total dose of 17 mg Be (as $ZnBeSiO_3$); mice were also injected, with production of "some" tumors (count or incidence % not stated). In this experiment, "substantially 100% BeO by spectrographic standards" produced no tumors. Nash (1950) produced 5 cases of osteosarcoma

among 28 rabbits injected with $ZnBeSiO_3$ phosphor, with about 200 mg phosphor (23 mg Be) appearing to be the minimum effective dose. Dutra and Largent (1950) produced osteosarcoma in rabbits with both $ZnBeSiO_3$ (2/3) and BeO (6/6), and reported a successful transplant in the anterior chamber of the eye of a guinea pig. Barnes et al. (1950) produced 6 cases of osteosarcoma among 17 rabbits injected with zinc beryllium silicate and 1 case of osteosarcoma among 11 rabbits injected with beryllium silicate. The tumors were multicentric in origin; blood-borne metastases were stated to be common. Hoagland et al. (1950) injected rabbits with two samples of zinc beryllium silicate phosphor, containing 2.3 and 14% BeO, and produced osteosarcoma incidences of 3/6 and 3/4, respectively. With uncompounded beryllium oxide, the incidence was 1/8; beryllium phosphate produced no tumors. The osteosarcomas appeared highly invasive but could not be transplanted.

Araki et al. (1964) injected 35 rabbits with zinc beryllium manganese silicate, beryllium silicate, or beryllium phosphate. The incidence of osteosarcoma was 6/24, 2/7, and 2/4 in the three groups, respectively. There were no tumors among three rabbits injected with BeO or for two uninjected controls. There was also a primary thyroid tumor in the ZnBeMn silicate injection group. Liver cirrhosis and splenic fibrosis were observed and the transplant experiments were all negative.

A series of experiments were reported from the Mayo

Foundation (Janes et al., 1954 and 1956; Kelly et al., 1961) regarding the effects of intravenous beryllium on bone. Out of a combined total of 31 rabbits receiving a total dose of 12 mg Be, 22 animals developed osteosarcomas. There was new bone formation in the medullary cavities of the long bones before the malignant changes were apparent. It was of particular interest that there was atrophy of the spleen in those animals in which bone tumors developed, whereas the spleen seemed to be normal in the injected rabbit which did not develop the bone tumors. Following splenectomy, the incidence of bone tumor or new bone formation in the medullary cavity was 100%, whereas the incidence in non-splenectomized rabbits after identical injection was only 50%. The results suggested that a well-functioning spleen performed a protective role against beryllium carcinogenesis in the rabbit. Tibial chondrosarcomas were also produced and successful transplants to the anterior eyes of rabbits were performed (Higgins et al., 1964).

Beryllium oxide or zinc beryllium silicate were directly introduced into the medullary cavities of bones of rabbits by Yamaguchi (1963), Tapp (1969), and Fodor (1977). Osteosarcoma, chondrosarcoma, and presarcomatous changes (irregular bone formation) were observed; 20-30 injections (20 mg BeO per injection) gave the highest frequency of tumor formation. The tumors developed directly from the medullary bone, sometimes preceded by fibrosis. They metastasized to the liver, kidneys, lymph nodes, and, in especially high frequency, to the lung.

F. CONCLUSIONS

The above discussion summarizes the experimental evidence for beryllium neoplasia following exposure via the respiratory tract. As a general comment on those studies, the following points can be made:

1. The relevance to public health of bone sarcomas from intravenous beryllium or from intramedullary beryllium in rabbits is limited by the artificiality of the routes of administration. It is certain that beryllium concentrations in circulating blood that were achieved by intravenous injection cannot even be approached within a margin of several orders of magnitude by either inhalation or ingestion (Reeves, 1965; Reeves and Vorwald, 1967). The single observation of a bone sarcoma in a rabbit after inhalation exposure needs confirmation. In the human experience, three cases of osteosarcoma among the patients in the Beryllium Case Registry were reported initially, but they turned out to be multiple entries of a single case (Hardy, 1976) and can be considered statistically as a random occurrence. There is no valid medical evidence of beryllium carcinogenicity in humans.

2. The pulmonary adenocarcinomas in rats from inhaled and/or intratracheally injected beryllium, although repeated many times, must still be viewed as questionable. The histopathologic differentiation between adenomas and adenocarcinomas is not at all well established and may have species-related peculiarities, so that sometimes different conclusions on the same compound are reached by pathologists, especially reflecting whether they were trained in human medicine or veterinary medicine. The uncontrolled experiments with monkeys have no significance. The close association of the neoplasms with purulent lesions of chronic murine pneumonia, the questionable or controversial metastasis and transplant experiences, and the ability of the host animals to live out their natural lifespans with the tumor all point to the conclusion that to equate these lesions with conventional lung cancer of humans may be a gross oversimplification.

3. Lack of a neoplastic response from beryllium was established in the lungs of rabbits, hamsters, and guinea pigs, and in the bones of rats and guinea pigs. The negative evidence with guinea pigs was particularly strong and involved both intravenous injection (Gardner and Heslington; Vorwald, 1950) and inhalation (Schepers, 1961; Reeves et al., 1972) at levels that produced

tumors in rabbits and rats. It has been suggested that an immunologic phenomenon may be a factor in determining whether the response to beryllium will be neoplastic or not, and certain species may have resistance to beryllium tumors according to their immunocompetence (Reeves, 1982).

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Personal History

Born on October 13, 1924 in Budapest, Hungary, as András Lajos Révész.

In Nazi Concentration Camp, 1944-45
In Communist Prison, 1949-50
Escaped from Hungary, 1950
Entered the United States, 1954

Naturalized U.S. Citizen 1959, in Detroit, Michigan as Andrew Louis Reeves

Married 1951
Three children (born 1952, 1954, 1956)
Divorced 1974
Remarried 1977, to Shirley Marilyn Roe, M.A.
Former Head, Dept. Technology & Science
Detroit Public Library

Education

Schools Attended:

Primary and Secondary Schools in Budapest, 1930-42
University of Budapest School of Law, 1943-44
University of Budapest School of Science, 1945-49
University of Vienna School of Liberal Arts, 1950-51
University of Munich School of Science, 1951-53
Wayne State University Graduate Division, Detroit, 1954-59

Academic Degrees:

Dipl. Chem. (major in organic chemistry)
University of Munich, 1953

Ph.D. (major in physiological chemistry)
Wayne State University, 1959

Languages (with year of acquisition and present proficiency):

Hungarian (1926; completely fluent)
German (1928; completely fluent)
English (1934; completely fluent)
Latin (1936; reading knowledge)
French (1938; reading and speaking knowledge)
Italian (1942; some reading and speaking knowledge)

Biographical References

American Men and Women of Science (1960 et seq.)
Hungarians in America (1963 et seq.)
National Faculty Directory (1966 et seq.)
National Forensic Center (1980)
Who's Who in Technology Today (1982)

Employment History

F.T. = Full Time
P.T. = Part Time

1942-43	(F.T.)	Dr. Wander Pharmaceutical Factory, Budapest, Hungary. Laborer in Organic Chemistry Plant
1945-48	(P.T.)	Chinoin Pharmaceutical Factory, Budapest, Hungary. Laboratory Trainee
1948-49	(P.T.)	University of Budapest Department of Chemistry, Budapest, Hungary. Teaching Assistant
1951-52	(P.T.)	American Joint Distribution Committee, Schleissheim, F.R.G. Night Watchman in Supply Depot
1952-53	(F.T.)	International Refugee Organization, Children's Village, Bad Aibling, F.R.G. High School Science Teacher
1953-54	(P.T.)	Süddeutsche Zeitung, Munich, F.R.G. Laborer in Newspaper Printing Plant
1954-55	(F.T.)	Detroit Institute of Cancer Research, Detroit, Michigan. Research Assistant
1955-56	(F.T.)	Wayne University College of Medicine, Detroit, Michigan. Research Technician
1956-63	(F.T.)	Wayne State University School of Medicine, Detroit, Michigan. Research Associate
1963-68	(F.T.)	Wayne State University School of Medicine, Detroit, Michigan. Assistant Professor, Occupational & Environmental Health
1968-72	(F.T.)	Wayne State University School of Medicine, Detroit, Michigan. Associate Professor, Occupational & Environmental Health
1972-79	(F.T.)	Wayne State University School of Medicine, Detroit, Michigan. Professor, Occupational & Environmental Health
1979-	(F.T.)	Wayne State University, College of Pharmacy & Allied Health Professions, Detroit, Michigan. Professor, Occupational & Environmental Health

Teaching Assignments, Administrative Assignments, and Committee Service at Wayne State University

CME = Continuing Medical Education
OEH = Occupational & Environmental Health

Member, Faculty Senate, School of Medicine 1963-1979

Advisor, M.Sc. Program in Occupational Health 1964-74

Co-Instructor, OEH 0790 "Seminar in OEH" 1964-1974

Advisor, Ph.D. Program in Physiology, minor in OEH 1966-1974

Chairman, CME course in Industrial Toxicology 1968-

Member, Facilities Committee, School of Medicine 1969-1971

Co-Instructor, OEH 0799 "Directed Study in OEH" 1969-

Lecturer, Gastrointestinal unit, Freshman Medical Class 1971-74

Instructor, OEH 0710 "Principles of Industrial Toxicology" 1972-1973; 1979-

Lecturer, Cardiorespiratory unit, Freshman Medical Class 1972-74

Lecturer, Pulmonary disease unit, Sophomore Medical Class 1972-75

Lecturer, Occupational Health elective, Senior Medical Class 1972-76

Alternate Member, Radiation Safety Committee 1972-

Instructor, OEH 0716 "Fibrogenic Dusts" 1972-

Instructor, OEH 0717 "Toxicology of Metals" 1972-

Instructor, OEH 0718 "Toxicology of Organic Compounds" 1972-

Member, Salary Committee, OEH 1974-1975

Member, Scientific Advisory Committee, OEH 1976-1977

Director, Environmental Toxicology Research Program 1976-1979

Associate, Department of Pharmacology 1976-

Member, Search Committee for Chairman of OEH 1979-1980

Member, Administrative Committee, College of Pharmacy & Allied Health Professions 1981-1982

Member, Promotion and Tenure Committee, College of Pharmacy and Allied Health Professions 1982-

Member, Salary Committee, College of Pharmacy and Allied Health Professions, 1982-

Member, Policy Committee on Academic Integrity, College of Pharmacy and Allied Health Professions, 1983-

Teaching Assignment at the University of Michigan

Nonresident Lecturer of Toxicology, School of Public Health 1980-

Sponsored Research

Experimental Pulmonary Cancer from Beryllium (with A.J. Vorwald), American Cancer Society, 1956-68.

Biological Effects of Urban Air Pollution (with R.G. Smith), Public Health Service, 1960-66.

Biological Effects of Inhaled Radioisotopes (with H.L. Berke), Atomic Energy Commission, 1961-66.

Mechanisms of Chemical Carcinogenesis (Principal Investigator), American Cancer Society [institutional], 1961-63.

Pathogenesis of Pulmonary Cancer in Rats (Principal Investigator), Michigan Cancer Foundation [grand-in-aid], 1967-68.

Pulmonary Cancer in Monkeys (continuing after A.J. Vorwald), Public Health Service, 1967-68.

Pathogenesis of Pulmonary Berylliosis (Principal Investigator), Public Health Service, 1968-76.

Experimental Asbestos Carcinogenesis (Principal Investigator), Public Health Service, 1970-73.

Respiratory Toxicity of Diesel Particulates (Principal Investigator), General Motors Corporation, 1976-78.

Cardiovascular Toxicity of Barium (Principal Investigator), Deutsche Forschungsgemeinschaft, 1980-82.

Visiting Appointments

University of Milano Clinica del Lavoro, Milano, Italy
Visiting Fellow, 1973.

University of Würzburg Institute of Toxicology, Würzburg, F.R.G.
Visiting Professor, 1980-81.

Royal Ministry of Health, Laboratory Division, Amman, Jordan.
Toxicology Consultant, 1983.

Recent Major Consulting Engagements
(last 10 years)

General Motors Corporation, Southfield, Mich.
Animal Research Committee, Biomed. Sciences (Chairman), 1974-78
Presentation of Postgraduate Course in Industrial Toxicology, 1976

Brush-Wellman, Inc., Cleveland, Ohio.
Consultant for OSHA Standard on Beryllium, 1975-77
Consultant for EPA Criterion on Beryllium, 1979
Consultant for Vacuum-Schmelze GmbH Beryllium Project, 1982

Dunlap & Associates, Darien, Conn.
Consultant for NIOSH Training Course Development, 1976-78

Department of Energy, Washington, D.C.
Review Group, Kettering Laboratory Project, 1976-78

Environmental Protection Agency, Washington, D.C.
Reviewer of Documents on Beryllium Toxicity, 1977-80; 1983-84
Consultant for Ambient Water Quality Standards, 1979-80

Technical Advisory Service of Attorneys, Fort Washington, Pa.
Consultant for Toxicology, 1977-82

American Mining Congress, Washington, D.C.
Consultant for Diesel Exhaust Toxicology, 1977-78

American Fisheries Society, Bethesda, Md.
Consultant for Water Pollution, 1977-78

American Council on Science and Health, New York, N.Y.
Reviewer of Document on Saccharin, 1979

Ford Motor Company, Dearborn, Mich.
Consultant for Occupational Toxicology, 1979-80

Owens-Illinois, Inc., Toledo, Ohio.
Consultant for Industrial Hygiene & Consumer Safety, 1980-82

World Health Organization, Geneva, Switzerland.
Toxicology Consultant to the Eastern Mediterranean Region, 1983

Recent Invitational Speaking Engagements (last 10 years)

Howard University, Washington, D.C.
Toxicology Short Course, 1977

Frauenhofer-Institute für Aerobiologie, Schmallenberg, F.R.G.
Seminar on Beryllium Carcinogenesis, 1977

Lovelace Foundation, Albuquerque, N.M.
Inhalation Toxicity Workshop, 1978

Wisconsin Alumni Research Foundation (Raltech), Madison, Wisc.
Inhalation Toxicity Seminar, 1978

University Hospital of Wales, Cardiff, U.K.
International Conference on Sarcoidosis, 1978

Gesellschaft Deutscher Chemiker, Würzburg, F.R.G.
Toxicology Short Course, 1981

Deutsche Gesellschaft für Strahlen- und Umweltforschung, Munich, F.R.G.
Seminar on Asbestos, 1981

Karolinska Institute, Stockholm, Sweden
Seminar on the Immunotoxicology of Beryllium, 1981

University of Umeå School of Medicine, Umeà, Sweden
Seminar on Metal Carcinogenesis, 1981

University of Düsseldorf Institute für Umwelthygiene, Düsseldorf, F.R.C
Seminar on Beryllium, 1981

University of Surrey, Guildford, U.K.
International Symposium on Immunotoxicology, 1982

Michigan State University, East Lansing, Michigan
International Workshop on Mesothelioma, 1982

Harper-Grace Hospitals, Detroit, Michigan
Respiratory Diseases Unit Seminar on Asbestos, 1982

Henry Ford Hospital, Detroit, Michigan.
Pulmonary Diseases Seminar on Asbestos, 1983

Membership and Office in Professional Societies

American Association for the Advancement of Science
Member 1956-

American Chemical Society
Member, 1957-
CA Abstractor, Toxicology & Industrial Hygiene, 1959-73
Instructor, Short Course "Toxicology for Chemists", 1978-
Instructor, Audiovisual Lecture "Chemical Structure-Biological Activity Correlations", 1983

American Conference of Governmental Industrial Hygienists
Associate Member, 1968-
Arrangements Committee, 1969-70

American Industrial Hygiene Association
Member, 1961-
Air Pollution Evaluation Committee, 1968-73
General Conference Committee, 1969-70
Teller's Committee (Chairman), 1969-71
Refresher Courses Committee, 1973-79
Toxicology Committee, 1974-80
Instructor, Refresher Course "Fibrogenic Dusts", 1974-
Instructor, Industrial Toxicology Seminar, 1977-79
Chairman, Toxicology of Particulates Session, AIHC, 1979
Session Arranger, Toxicology Sessions, AIHC, 1980

American Institute of Chemists
Fellow, 1969-76

American Society for Testing Materials
Member, Task Group 16 of Committee E-34 (Occupational Health and Safety)

Comprehensive Cancer Center of Metropolitan Detroit
Advisory Committee, Environmental Carcinogenesis Program, 1976-8
Instructor, Environmental Carcinogenesis Conference, 1979

Detroit Physiological Society
Member, 1959-
Secretary, 1971-73
President, 1975-76
Councilor, 1976-78

Deutsche Forschungsgemeinschaft
Guest Member, Senatskommission z. Prüfung Gesundheits-schadlicher Arbeitsstoffe, 1980-81

Engineering Society of Detroit
Member, 1970-77
Judge, Metropolitan Science Fair, 1971-77

International Association of Bioinorganic Scientists
Member, 1976-

National Academy of Sciences/National Research Council
Subcommittee on Beryllium, Assembly of Life Sciences, 1971-76
Subcommittee on Geochemical Environment in Relation to Health and Disease, Assembly of Mathematical and Physical Sciences, 1979-82

New York Academy of Sciences
Member, 1961-

Permanent Commission & International Association of Occup. Health
Member, 1965-

Society of Toxicology
Member, 1969-
Member, Specialty Section on Metals, 1981-
Vice President, Specialty Section on Metals, 1984-
Nominating Committee, 1973-74
Education Committee, 1976-78

Fellowships, Scholarships, Awards, Honor Societies

1956 - Associate Member, Sigma Xi

1957 - Member, Phi Lambda Upsilon

1958 - Graduate Scholar, Wayne State University

1959 - Full Member, Sigma Xi

1973 - Senior NATO Science Fellow, National Science Foundation

1978 - Recognition Award, Short Course at Wayne State University

1980 - 25-year Service Award, Wayne State University

1980 - Sabbatical Leave (2 semesters), Wayne State University

1981 - Visiting Research Fellow, Deutsche Forschungsgemeinschaft

1983 - WHO Toxicology Consultant, Eastern Mediterranean Region

Nonprofessional Affiliations and Activities

Consumers Union
Member, 1959-69

Council for Basic Education
Member, 1960-70

Founders Society, Detroit Institute of Arts
Member, 1966-71

Grosse Pointe Sail Club
Member, 1970-77

Grosse Pointe Ski Club
Member, 1965-
Treasurer, 1983-

Grosse Pointe Unitarian Church
Member, 1966-
Nominating Committee, 1967
Religious Education Committee, 1969-71
Instructor, Sunday School, 1968-71

National Geographic Society
Member, 1957-

University Center for Adult Education
Instructor, "Wines of the World", 1974-76
Instructor, "The Nine Symphonies of Beethoven", 1974-76
Instructor, "Introduction to Exobiology", 1976

Publications
(in chronological order with type code)

A: Research Papers in Refereed Journals
B: Invited Reviews
C: Books; Chapters in Books
D: Other Research and Review Papers
E: Intramural Documents
F: Short Communications
G: Published Abstracts

Type Code	No.	
E	1.	Reeves, A.L.: Über das Triacetat der 1,2-Diamino-D-Glucose. Diplomarbeit. Ludwig-Maximilian-Universität, München, 1953.
A	2.	Bertho, A. and Reeves, A.L.: Über 1-B,2-Diamino-3,4,6-Triacetyl-D-Glucose. Liebig's Ann. 581(3),161-67 (1953)
A	3.	Johnson, R.M., Albert, S., and Reeves, A.L.: In Vitro Activation of Cysteine Desulfhydrase by Rat Liver Microsomes. Proc. Soc.Exp.Biol.Med. 88(4), 594-96 (195
G	4.	Reeves, A.L., Smith, R.G., and Vorwald, A.J.: The State of Beryllium in Blood Plasma. Fed.Proc. 17(1), 1785 (1
A	5.	Vorwald, A.J. and Reeves, A.L.: Pathologic Changes Induced by Beryllium Compounds: Experimental Studies. Arch. Indust. Health 19 (2), 190-99 (1959).
A	6.	Vorwald, A.J. and Reeves, A.L.: Inhaled Atmospheric Pollutants in the Genesis of Lung Cancer--An Experimental Study of Biochemical Changes Induced by Beryllit Acta Union Internat.Contre le Cancer 15 (3-4), 715-22 (1959).
G	7.	Reeves, A.L. and Vorwald, A.J.: Effect of Intratracheal Injected Beryllium Oxide on the Cytoplasmic Composition of Pulmonary Tissue. Am.Chem.Soc. 135th Mtg. Abst. C-66 No. 136 Boston, 1959.
E	8.	Reeves, A.L.: Studies on the Biochemical Behavior of Beryllium. Dissertation. Wayne State University, Detroi 1959.
G	9.	Reeves, A.L., Dibley, D.B., and Vorwald, A.J.: Effects Polynuclear Hydrocarbon Carcinogens on the Lungs. Am.Chem.Soc. 138th Mtg.Abst. C-63, No. 168 New York, 19
D	10.	Vorwald, A.J. and Reeves, A.L.: An Equipped Horizontal Cold Cabinet. Chemist-Analyst 50(3), 119-20 (1961).

Type Code	No.	
E	11.	Vorwald, A.J. and Reeves, A.L.: Toxic Characteristics of Beryllium--Experimental Findings. Kettering Laboratory Workshop on Beryllium, pp. 59-64, Cincinnat 1961.
A	12.	Reeves, A.L. and Vorwald, A.J.: The Humoral Transport of Beryllium. J.Occup.Med. 3(12), 567-74 (1961).
G	13.	Reeves, A.L., Vorwald, A.J., Urban, E.C.J., and MacEwe J.D.: The Kinetics of Pulmonary Deposition and Clearan of Inhaled Beryllium Sulfate in the Rat. Fed.Proc. 21(446 (1962).
A	14.	Reeves, A.L.: The Absorption of Beryllium from the Gastrointestinal Tract. Arch. Environ. Health 11(8), 209-14 (1965).
C	15.	Vorwald, A.J., Reeves, A.L., and Urban, E.C.J.: Experi mental Beryllium Toxicology. In: Beryllium--Its Industrial Hygiene Aspects (H.E. Stokinger, Editor). pp. 201-34. Academic Press, New York, 1966.
A	16.	Reeves, A.L., Busby, E.K., and Scotti, L.: Gel Electro phoresis in the Study of Pneumoconioses. Am. Indust. Hyg.Assoc.J. 27(3), 278-87 (1966).
G	17.	Reeves, A.L.: Biochemical Features in Beryllium Car- cinogenesis. Am.Indust.Hyg.Conf.Abst. p. 90 Pittsburgh, 1966.
G	18.	Reeves, A.L.: Lung and Lymph Node Isozymes During Beryllium-Induced Pulmonary Carcinogenesis. Proc.Am. Assoc. Cancer Research 7, 227 (1966).
D	19.	Reeves, A.L.: Pulmonary Isozyme Profiles During Experi mental Beryllium Carcinogenesis. Proc. 15th Internat. Congr. Occup. Health 3, 133-36 (1966).
A	20.	Reeves, A.L., Deitch, D., and Vorwald, A.J.: Beryllium Carcinogenesis. I. Inhalation Exposure of Rats to BeSO Aerosol. Cancer Research 27(I), 439-45 (1967).
A	21.	Reeves, A.L. and Vorwald, A.J.: Beryllium Carcinogenes II. Pulmonary Deposition and Clearence of Inhaled BeSO in the Rat. Cancer Research 27(I), 446-51 (1967).
A	22.	Reeves, A.L.: Isozymes of Lactate Dehydrogenase During Beryllium Carcinogenesis in the Rat. Cancer Research 27 (I), 1895-99 (1967).
G	23.	Smith, R.G., Vorwald, A.J., Reeves, A.L., and Mooney, Summary of Health Effects Resulting From Long-Term Exposure of Animals to Urban Air. Am.Indust.Hyg.Conf. Abst. p.100. Chicago, 1967.

Type Code	No.	
A	24.	Reeves, A.L: Über die Retention von Eingeatmetem Berylliumsulfat-Aerosol in Rattenlungen. Internat. Arc Gewerbepath.Gewerbehyg. 24, 226-37 (1968).
E	25.	Reeves, A.L. (Editor): Principles and Practice of Industrial Toxicology. Syllabus for a Postgraduate Course. Wayne State University, Detroit, 1968.
G	26.	Reeves, A.L.: Effect of Age on the Severity of Toxic Response. Am.Indust.Hyg.Assoc.J. 30(2), 110-11 (1969).
G	27.	Davis, H.V. and Reeves, A.L.: Pulmonary Fibrogenesis in Rats Exposed to Asbestos. Am.Indust.Hyg.Assoc.J. 30(2), 156-57 (1969).
D	28.	Reeves, A.L. and Deitch, D.: Influence of Age on the Carcinogenic Response to Beryllium Inhalation. Proc. 16th Internat.Congr.Occup.Health F6-66, pp.651-52 Tokyo, 1969.
D	29.	Reeves, E.H., Reeves, A.L., and Nedwicki, E.G.: Milia: Tuberculosis and Silicosis. Proc. 16th Internat.Congr Occup. Health F6-81, pp. 678-79. Tokyo, 1969.
F	30.	Reeves, A.L.: Typical Pathways of Hepatic Detoxicatio: In: Biochemistry (8th Ed.), by J.M. Orten and O.W. Neuhaus. p. 749. C.V. Mosby, St. Louis, 1970.
F	31.	Reeves, A.L.: Discussion of "Effect of Shape on Parti: Penetration and Retention in Animal Lungs" by V. Timb: and J.W. Skidmore. In: Inhaled Particles III (W.H. Wa Editor). p. 57. Unwin Bros. Ltd., Old Woking, Surrey,
F	32.	Reeves, A.L.: Discussion of "Long-Term Storage, Migra and Elimination of Dust in the Lungs of Animals" by W Klosterkötter and F. Gono. In: Inhaled Particles III (W.H. Walton, Editor). p. 281. Unwin Bros. Ltd., Old Woking, Surrey, 1971.
F	33.	Reeves, A.L.: Discussion of "Observations on the Mech of Silicotic Fibrogenesis" by A.G. Heppleston. In: Inhaled Particles III (W.H. Walton, Editor). p. 370. Unwin Bros. Ltd., Old Woking, Surrey, 1971.
F	34.	Reeves, A.L.: Discussion of "Biochemical and Biophysi Reactions of Rat Lung Tissue to Quartz and Corundum, With and Without PVN-Oxide Treatment" by M. Grünspan and H. Antweiler. In: Inhaled Particles III (W.H.Walt Editor). p. 378. Unwin Bros. Ltd., Old Woking, Surrey 1971.
F	35.	Reeves, A.L.: Discussion of "Biological Action of Dif ferent Asbestos Dusts With Respect to Fibre Length ar Semiconductor Properties" by K. Robock and W. Kloster kötter. In: Inhaled Particles III (W.H. Walton, Editc p. 475. Unwin Bros. Ltd., Old Woking, Surrey, 1971.

Type Code	No.	
F	36.	Reeves, A.L.: Discussion of "Immunoglobulin Levels in Berylliosis" by H. Resnick and W.K.C. Morgan. In: Inhal Particles III (W.H.Walton, Editor). p. 598. Unwin Bros. Ltd., Old Woking, Surrey, 1971.
C	37.	Reeves, A.L., Swanborg, R.H., Busby, E.K., and Krivanek, N.D.: The Role of Immunologic Reactions in Pulmonary Berylliosis. In: Inhaled Particles III (W.H. Walton, Editor). pp. 599-606, Discussion 607-608. Unwin Bros. Ltd., Old Woking, Surrey, 1971.
A	38.	Davis, H.V. and Reeves, A.L.: Collagen Biosynthesis in Rat Lungs During Exposure to Asbestos. Am.Indust. Hyg.Assoc.J. 32(9), 599-602 (1971).
A	39.	Reeves, A.L., Puro, H.E., Smith, R.G., and Vorwald, A.J Experimental Asbestos Carcinogenesis. Environ. Research 4(6), 496-511 (1971).
A	40.	Krivanek, N.D. and Reeves, A.L.: Effect of Chemical For of Beryllium on the Production of Immunologic Response. Am.Indust.Hyg.Assoc.J. 33(1), 45-52 (1972).
C	41.	Reeves, A.L.: Effect of Air Pollution on Animal Health. In: The Air Pollution Manual 2nd Ed. (P. Giever, Editor pp. 45-59. American Industrial Hygiene Association, Westmont, N.J., 1972.
G	42.	Reeves, A.L., Swanborg, R.H., and Krivanek, N.D.: Immunological Factors in the Etiology of Pulmonary Berylliosis. Soc.Tox.11th Mtg.Abst, No. 126, p.93 Williamsburg, 1972.
G	43.	Reeves, A.L., Puro. H.E., Smith, R.G., and Vorwald, A.J Fibrogenicity and Carcinogenicity of Amosite, Crocidol and Chrysotile in Animal Experiment. Am.Indust.Hyg.Assc 33(2), A79 (1972).
A	44.	Reeves, A.L., Krivanek, N.D., Busby, E.K., and Swanborg R.H.: Immunity to Pulmonary Berylliosis in Guinea Pigs Internat.Arch.Occup.Health 29, 209-20 (1972).
A	45.	Roy-Chowdhury, A.K., Mooney, T.F., and Reeves, A.L.: Trace Metals in Asbestos Carcinogenesis. Arch.Environ Health 26(5), 253-55 (1973).
G	46.	Krivanek, N.D. and Reeves, A.L.: Suppression of Delayed Hypersensitivity to Beryllium in Guinea Pigs by Cyclophosphamide. Soc.Tox.12th Mtg.Abst. No. 99, p.75 New York, 1973.

Type Code	No.	
G	47.	Roy-Chowdhury, A.K. and Reeves, A.L.: Trace Metals in Asbestos and Their Effect on Crystal Structure. Am. Indust.Hyg.Conf.Abst. No. 78, p. 145. Boston, 1973.
E	48.	Reeves, A.L., Krivanek, N.D., and Roy-Chowdhury, A.K.: Study of Municipal Waters in Selected Communities. Report, Reserve Mining Co., Silver Bay, Minn., 1973.
E	49.	Reeves, A.L., Krivanek, N.D., and Roy-Chowdhury, A.K.: Study of the Origins of Particulate Contaminants in Duluth Tap Water. Report, Reserve Mining Co., Silver Bay, Minn., 1973.
A	50.	Reeves, A.L. and Krivanek, N.D.: The Influence of Cutaneous Hypersensitivity to Beryllium on the Development of Experimental Pulmonary Berylliosis. Transact. N.Y.Acad.Sci 36(1), 78-93 (1974).
B	51.	Reeves, A.L.: Umweltgefährdung durch Beryllium. Zentr. Arbeitsmed.Arbeitsschutz 24(2), 46-56 (1974).
G	52.	Reeves, A.L.: Fibrogenic Dusts. Refresher Course No. 31, Am.Indust.Hyg.Conf.Abst. p. 20. Miami Beach, 1974. et seq.
A	53.	Reeves, A.L., Puro, H.E., and Smith, R.G.: Inhalation Carcinogenesis from Various Forms of Asbestos. Environ. Research 8, 178-202 (1974).
F	54.	Reeves, A.L.: Discussion of "Die Tumorerzeugende Wirbung Faserförmiger Staube" by F. Pott, K.H. Friedrich and F. Huth. In: Proc. Internat. Symp. Recent Advances in the Assessment of Health Effects of Environmental Pollution Vol. 2, p. 724. Commission of European Communities (EUR 5360). Luxembourg, 1975.
D	55.	Reeves, A.L., Mooney, T.F., and Smith, R.G.: Exposure of Laboratory Animals to Urban Air Pollution--Physical Plant, Experimental Difficulties, Observed Effects. In: Proc. Internat. Symp. Recent Advances in the Assessment of Health Effects of Environmental Pollution Vol. 3, pp. 1637-1643. Commission of European Communities (EUR 5360) Luxembourg, 1975.
F	56.	Reeves, A.L.: Discussion of "Assessment of the Influence of Environmental Pollutants on Cancer and Other Chronic Diseases" by S.S. Epstein. In: Proc. Internat. Symp. Recent Advances in the Assessment of Health Effects of Environmental Pollution Vol. 4, p. 2385. Commission of European Communities (EUR 5360). Luxembourg, 1975.

Type Code	No.	
G	57.	Palazzolo, M.J. and Reeves, A.L.: Hypersensitivity to Beryllium in Guinea Pigs. Soc.Tox. 14th Mtg.Abst. No. 13. p. 11, Williamsburg, 1975.
G	58.	Reeves, A.L. and Puro, H.E.: Experimental Carcinogenesi from Inhaled Asbestos. Europ.Soc.Tox. 17th Mtg.Abst. p. 53. Lyon, 1975.
G	59.	Reeves, A.L., Krivanek, N.D., and Palazzolo, M.J.: Cuta neous Hypersensitivity to Beryllium and Pulmonary Berylliosis. 18th Internat.Congr.Occup.Health Abst. p.430. Brighton, U.K., 1975.
B	60	Reeves, A.L.: The Toxicology of Arsenic--Noncarcinogeni Effects. In: Health Effects of Occup.Lead and Arsenic Exposure--A Symposium (B.W. Carnow, Editor). pp. 234-24 Discussion 253-262. U.S.Dept.Health, Education & Welfar (NIOSH 76-134). Washington, 1976.
B	61.	Reeves, A.L.: The Toxicology of Arsenic--Carcinogenic Effects. In: Health Effects of Occup. Lead and Arsenic Exposure--A Symposium (B.W. Carnow, Editor). pp. 265-27 Discussion 279-283. U.S.Dept.Health, Education & Welfar (NIOSH 76-134). Washington, 1976.
F	62.	Reeves, A.L.: Discussion of "Epidemiology of Arsenic" b G. Ott, W.S. Ferguson, S. Milham, and C. Hine. In: Health Effects of Occup. Lead and Arsenic Exposure--A Symposium (B.W. Carnow, Editor). p. 312. U.S.Dept. Health, Education and Welfare (NIOSH 76-134). Washingtc 1976.
A	63.	Reeves, A.L.: Berylliosis as an Autoimmune Disorder. Ar Clin.Lab.Sci. 6, 256-262 (1976).
A	64.	Reeves, A.L.: The Carcinogenic Effect of Inhaled Asbest Fibers. Ann.Clin.Lab.Sci. 6, 459-466 (1976).
B	65.	Reeves, A.L.: Beryllium in the Environment. In: Toxicology Annual (C.L. Winek, Editor) Vol.2, pp. 37-4 Marcel Dekker, New York, 1977; also Clin. Tox. 10(1), 37-48 (1977).
C	66.	Reeves, A.L.: Barium. In: Handbook on the Toxicology of Metals (L. Friberg, G. Nordberg, and V. Vouk, Editors) pp. 321-328, Elsevier/North Holland, Amsterda 1979; also in Toxicology of Metals Vol. 2 (R.J.M Horto Project Ofcr.) pp. 71-84, U.S. Environmental Protectio Agency (EPA-600/177-022), Research Triangle Park, N.C. 1977.

Type Code	No.	
C	67.	Reeves, A.L.: Beryllium. In: Handbook on the Toxicology of Metals (L. Friberg, G. Nordberg, and V. Vouk, Editors) pp. 329-343, Elsevier/North Holland, Amsterdam, 1979; also in Toxicology of Metals, Vol. 2 (R.J.M. Horton, Project Ofcr.) pp. 85-109, U.S. Environmental Protection Agency (EPA-600/1-77-022), Research Triangle Park, N.C., 1977.
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OVERVIEW OF BERYLLIUM ANIMAL TOXICOLOGICAL DATA

OSTEOSARCOMA FROM BERYLLIUM

- NOT OBSERVED IN HUMANS
- NEGATIVE EVIDENCE WITH GUINEA PIGS AND RATS
- RABBITS ONLY
  - INTRAVENOUS OR INTRAMEDULLARY INJECTION ONLY
  - REQUIRED THRESHOLD DOSE 5 mg BERYLLIUM PER ANIMAL
  - HIGHEST CIRCULATING BERYLLIUM AFTER INJECTION OR INHALATION IS 5 μg
  - NATURAL SAFETY MARGIN OF 1000-FOLD

PULMONARY TUMORS FROM BERYLLIUM

- NEGATIVE EVIDENCE WITH GUINEA PIGS AND RABBITS
- SOME UNCONTROLLED EXPERIMENTS WITH MONKEYS
- RATS ONLY
  - ASSOCIATED WITH PURULENT LESIONS
  - HIGHLY QUESTIONABLE METASTASES EXPERIMENTS
  - NOT TRANSPLANTABLE
  - NOT LIFE-SHORTENING

THE SPECIES RESPONSE OR SPECIFICITY TO BERYLLIUM

SPECIES	IMMUNOLOGICAL REACTION	TUMORS
RATS	NOT MEASURABLE	QUESTIONABLE LUNG
RABBITS	WEAK	NO LUNG BONE FROM MASSIVE I.V. DOSING ONLY
GUINEA PIGS	STRONG	NO LUNG NO BONE EVEN FROM I.V. DOSING
HUMANS	STRONG	SEE EPIDEMIOLOGY