

A Review of the Science Related to the Association of Beryllium Metal with Lung Cancer - 2014

The most recent and the most relevant study by Paolo Boffetta, Tiffani Fordyce and Jack Mandel “A mortality study of workers exposed to insoluble forms of beryllium” (European Journal of Cancer Prevention March 2014) is supportive of the growing and more recent scientific evidence that beryllium metal is not carcinogenic to humans. This study investigated lung cancer and other diseases related to insoluble beryllium compounds. The paper states: “A cohort of 4950 workers from four US insoluble beryllium manufacturing facilities were followed through 2009. Expected deaths were calculated using local and national rates. On the basis of local rates, all-cause mortality was significantly reduced. Mortality from lung cancer (standardized mortality ratio 96.0; 95% confidence interval 80.0, 114.3) and from nonmalignant respiratory diseases was also reduced. There were no significant trends for either cause of death according to duration of employment or time since first employment. Uterine cancer among women was the only cause of death with a significantly increased standardized mortality ratio. Five of the seven women worked in office jobs. **This study confirmed the lack of an increase in mortality from lung cancer and nonmalignant respiratory diseases related to insoluble beryllium compounds.**”

The following support the conclusions of the above noted cancer experts.

Beryllium was evaluated during the recent review of the European Cancer Directive prepared for the European Commission (*The IOM Project P937/99 2011*). The report stated: “**There was little evidence for any important health impact from current or recent past exposures in the EU**”

A report prepared by the European Commission on beryllium in relation to occupational diseases (*Information Notices on Occupational Diseases: A Guide to Diagnosis, 2009*) states: “**The causal relationship between prolonged or repeated exposure to beryllium and the occurrence of bronchial cancer has not been firmly established, and due to the multi-causality of the occurrence of this type of cancer, the recognition of the occupational origin must lie on a thorough assessment based on rigorous scientific criteria taking into account all possible etiologies.**”

The Industrial Injuries Advisory Council Position Paper 27, December 2009 Beryllium and Lung Cancer states: “**The Council has concluded that at present there is insufficient evidence to recommend that lung cancer in relation to beryllium should be added to the list of prescribed diseases.**”

A study of the United Kingdom’s Beryllium Registry (*Jones Williams W 1996*) that includes all cases of beryllium disease or suspected beryllium disease from 1945 to 1993, stated: “**There were no cases of cancer.**”

In a study of multi-year cancer statistics from the data in occupational disease registries for Germany, Austria, Belgium, Denmark, Spain, Finland, France, Italy, Luxembourg, Netherlands, Portugal, the Czech Republic, Switzerland and Sweden covering 32 million workers (*Eurogip. Work-related Cancers: What Recognition in Europe 2010*), it was reported that: **Only (1) case of cancer related to beryllium was reported. This compares to approximately 2.4 million new cancer cases diagnosed each year in Europe**

The only studies that conclude that beryllium causes cancer were all carried out on one group of beryllium production workers in the United States and nowhere else in the world. Depending upon the study and the authors, the reported risk of cancer varied. The studies that suggest beryllium metal is linked with cancer

(Ward, Sanderson, Schubauer-Berigan), have been found to be flawed by more recent studies and have very serious methodological errors according to scientists with a high level of expertise in cancer studies.

The study (Rothman K.J., Mosquin P.L. *Confounding after Risk-set Sampling in the Beryllium Study of Sanderson et al. Ann Epidemiol 21(10): 773-779 2011*) concluded: **“Simulations and reanalysis show that much of the reported association with lagged exposure is attributable to confounding by year of birth and year of hire. Lagging changes the exposure variable and can thus lead to changes in the amount of confounding.”** The study suggests that the previous studies that indicated a cancer risk did not account for factors that could influence the study conclusions.

A study (Levy, P.S., Roth H.D., Deubner D.C. *Exposure to Beryllium and Occurrence of Lung Cancer: Findings from a Cox Proportional Hazards Analysis of Data from a Retrospective Cohort Mortality Study. J Occup Environ Med 51: 480-486 2009*) concluded **“The patterns observed provide little support for an association of lung cancer with beryllium work factors. This result is likely due to the absence in the original study of a significant overall excess of lung cancer after smoking adjustment.”**

The review by Paola Boffetta of the International Prevention Research Institute, Lyon, France, *Occupational exposure to beryllium and cancer risk: a review of the epidemiologic evidence. Critical Reviews in Toxicology 42(2): 107-118 2012*) concluded: **“The studies of beryllium disease patients do not provide independent evidence and the results from other studies do not support the hypothesis of an increased risk of lung cancer or any other cancer. Overall, the available evidence does not support a conclusion that a causal association has been established between occupational exposure to beryllium and the risk of cancer.”**

Studies by experts in animal toxicology also call into question the carcinogenicity of beryllium in animals. (Hollins D.M., et al. *Beryllium and lung cancer: A weight of evidence evaluation of the toxicological and epidemiological literature. Crit Rev in Tox 39(1): 1-32 2009*) reported **“the vast majority of studies reviewed for beryllium, including the studies that reported a positive tumor response in rats, suffered from incomplete reporting and serious methodological flaws.”**

Dr. Christian Strupp presented new research results in two papers on beryllium metal. The new studies were generated in accord with OECD standards and GLP requirements in order to comply with REACH. According to Strupp, **“The new studies allow a scientific interpretation of the complex database that led to decades of erroneous conclusions that the toxicity of beryllium metal (which is commercially available) and soluble beryllium compounds (not commercially available) are the same.”** The REACH OECD compliant tests for the REACH beryllium dossier determined that **Be was not genotoxic and did not interact with DNA and produce mutations, did not cause structural chromosomal aberrations or forward gene mutations in mammalian cells** (gene mutations are reported to be an initial step in the carcinogenic process), **did not directly damage the DNA of the cells and was not cytotoxic.** (Cytotoxic testing is typically used to determine if a material is suitable for implanting in the human body or placed in contact with body tissues or body fluids on a long-term basis).

Based upon the most recent science as detailed above, the Beryllium Science & Technology Association is seeking support from EU member state authorities to have beryllium metal reclassified as not being known or presumed to have carcinogenic potentials.