BeST

Beryllium Science & Technology Association

OVERVIEW OF CANCER PAPERS

The Annals of Occupational Hygiene by Oxford University for the British Occupational Hygiene Society

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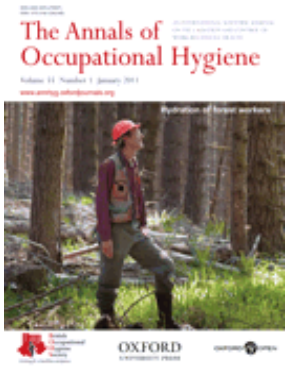

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http://annhyg.oxfordjournals.org/

Beryllium Metal I. Experimental Results on Acute Oral Toxicity, Local Skin and Eye Effects, and Genotoxicity – Ann Occup Hyg (2011) 55(1): 30-42

Beryllium Metal II. A Review of the Available Toxicity Data – Ann Occup Hyg (2011) 55(1): 43-56

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Summary

- Papers resulted from REACH requirements
- All tests were conducted using OECD test standards and under Good Laboratory Practice requirements (GLP)
- Tests results showed that the toxicity of beryllium metal used in commerce differs from that reported for soluble beryllium compounds which are not involved in commerce.
- Test results demonstrate that the current classification of beryllium metal is inaccurate because it has historically been lumped with the toxicity associated with soluble beryllium compounds
- Quality analysis of the body of literature showed that most of the older animal studies do not meet today's quality standards for reliability
- Quality analysis of the body of literature refutes the accepted belief that beryllium metal caused cancer in various laboratory animals
- A critical review of the epidemiology studies showed that cancer studies focused basically on the same group of beryllium production workers
- Cancer risk assessments had different outcomes depending on the individual investigator
- Test results demonstrate the need to change current classifications for beryllium metal

These papers combine new research results on acute and genetic toxicity with a comprehensive summary and analysis of the huge and often misinterpreted available database. The papers are current state-of-the-art documents relative to the toxicity of beryllium metal for acute toxic properties and the findings also reflect a need to reconsider the carcinogenicity classification. The new studies were generated in accord with OECD standards and GLP requirements in order to comply with REACH. The new studies finally 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 quote from the paper, *"It is clear that the often maligned REACH regulation does provide a unique opportunity for toxicologists, authorities, and industry to truly assess the quality of past data and the opportunity to generate new high-quality data that can and should be used to guide our future risk management initiatives."* articulates this point. Additionally, a detailed quality analysis of all of the available literature, using a globally accepted protocol,

clearly demonstrated that the existing animal data on carcinogenic properties is conclusive only for rats and not for any other species. It is well known in the scientific community that the rat has a propensity to develop cancers and is not a good model for predicting carcinogenicity in humans because of the anatomical and physiological differences between rats and humans with regard to particle deposition and retention patterns as well as breathing rates. The review paper summarizes the latest conclusions of the epidemiological expert discussion ongoing for years in the scientific community that delivers only controversial evidence for a carcinogenic potential of beryllium and its soluble compounds. The review paper highlights the fact that the epidemiology focuses on the same cohort (highly exposed beryllium production workers) and depending on the reviewer an excess cancer risk is found or not found. The paper points out that no initiatives to collect data to build up a new cohort reflecting current exposures with detailed investigation of smoking habits has been taken even though exposure to beryllium exists in other worker populations and in the general population due to its occurrence as a natural element.

Details:
New Tests Confirm:

- Beryllium metal does not interact with DNA to mutate cells
- Beryllium metal does not cause aberrations in chromosome
- Beryllium metal does not induce gene mutations
- Beryllium is not cytotoxic
- Beryllium metal does not cause skin irritation
- Beryllium metal does not cause eye irritation
- Beryllium metal does not cause skin sensitization (allergic skin reactions)
- Beryllium metal is not toxic by oral ingestion

A battery of OECD compliant tests focused on genotoxicity and assessed the ability of beryllium to interact with DNA and produce mutations, to detect the ability of beryllium to cause structural chromosomal aberrations, and to detect the forward gene mutations in mammalian cells since gene mutations are reported to be an initial step in the carcinogenic process. Thus, beryllium metal does not directly damage the DNA of the cells. Tests also confirmed that extracts of beryllium metal were 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.

It was suggested that beryllium could theoretically inhibit DNA repair synthesis and morphological cell transformation. To investigate this potential, extracts of varying beryllium metal concentrations were tested. The results showed that beryllium metal did not cause DNA damage in this study, but at the highest dose exerted an effect on the repair of pre-existing DNA damage. DNA repair occurs continuously in the body as cells are assaulted by common environmental agents that cause cell damage. The relevance to human toxicity of the effect noted at very high concentrations is considered rather low, because the general as well as the occupationally exposed population do not have such high exposure. The relevance of these findings for humans is difficult to evaluate as the assays are relatively new and it is not known if the results of high dose testing in-vitro have any relevance to realistic exposures to humans. However, the test results do indicate that beryllium metal would have a threshold if there were sufficient evidence to support carcinogenicity in humans. This means that it would take some level of exposure to cause an effect and that the no-dose carcinogen model is not applicable to beryllium metal.

In addition to the genotoxicity tests, skin irritation, eye irritation, skin sensitization, and oral toxicity tests were conducted that clearly show that the current classifications for beryllium is not correct.