

Assessment of the Beryllium Lymphocyte Proliferation Test Using Statistical Process Control

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Despite more than 20 years of surveillance and epidemiologic studies using the beryllium blood lymphocyte proliferation test (BeBLPT) as a measure of beryllium sensitization (BeS) and as an aid for diagnosing subclinical chronic beryllium disease (CBD), improvements in specific understanding of the inhalation toxicology of CBD have been limited. Although epidemiologic data suggest that BeS and CBD risks vary by process/work activity, it has proven difficult to reach specific conclusions regarding the dose-response relationship between workplace beryllium exposure and BeS or subclinical CBD. One possible reason for this uncertainty could be misclassification of BeS resulting from variation in BeBLPT testing performance. The reliability of the BeBLPT, a biological assay that measures beryllium sensitization, is unknown. To assess the performance of four laboratories that conducted this test, we used data from a medical surveillance program that offered testing for beryllium sensitization with the BeBLPT. The study population was workers exposed to beryllium at various facilities over a 10-year period (1992–2001). Workers with abnormal results were offered diagnostic workups for CBD. Our analyses used a standard statistical technique, statistical process control (SPC), to evaluate test reliability. The study design involved a repeated measures analysis of BeBLPT results generated from the company-wide, longitudinal testing. Analytical methods included use of (1) statistical process control charts that examined temporal patterns of variation for the stimulation index, a measure of cell reactivity to beryllium; (2) correlation analysis that compared prior perceptions of BeBLPT instability to the statistical measures of test variation; and (3) assessment of the variation in the proportion of missing test results and how time periods with more missing data influenced SPC findings. During the period of this study, all laboratories displayed variation in test results that were beyond what would be expected due to chance alone. Patterns of test results suggested that variations were systematic. We conclude that laboratories performing the BeBLPT or other similar biological assays of immunological response could benefit from a statistical approach such as SPC to improve quality management.