Quantitative Assessment of Lung and Bladder Cancer Risk and Oral Exposure to Inorganic Arsenic: Meta-regression Analyses of Epidemiological Data

Inorganic arsenic (iAs) in drinking water varies geographically and is prevalent worldwide. Exposures in the US are generally low, while other areas, such as parts of South America and Asia, have higher levels of naturally occurring iAs in water (potentially >100 μg/L). Much of the evidence for the association between iAs and cancer comes from epidemiological studies conducted with more highly exposed populations, which also have distinct underlying characteristics, making extrapolating these studies’ findings to Western populations difficult. To address whether and how one should extrapolate from these high-exposure studies to estimate cancer risk at lower exposures, we conducted an independent analysis of carcinogenicity associated with oral iAs exposure, which included determining the most appropriate cancer endpoints, studies, and models to evaluate for this purpose. We identified bladder and lung cancer as high-priority endpoints and used meta-analysis and meta-regression to pool epidemiological data across studies from different regions of the world to derive oral cancer slope factors and unit risks (excess risk per µg/L) for oral iAs exposure based on background risks of bladder and lung cancer in the US. While we derived these factors assuming a linear, no-threshold relationship between iAs and cancer risk, we also evaluated the evidence for non-linear dose-response relationships and thresholds for each cancer. Our analysis indicated that the incremental risks of bladder and lung cancer associated with iAs exposure were relatively low. The sensitivity analyses we conducted suggested that South Asian populations appeared to drive the pooled cancer risk estimates, but many of the other assumptions we tested did not substantially alter the results of our analysis. Finally, we found that the mode of action evidence supports there being a threshold, but making a robust quantitative demonstration of a threshold using epidemiological data is difficult. When considered in the context of typical exposure levels in the US, our potency estimates suggest that iAs-induced cancer risk is much lower than observed bladder and lung cancer incidences. This suggests that the low iAs levels to which much of the general US population is exposed likely do not result in substantial additional cancer risk above background.