

2019 SOT Conference
Poster: Metals II
Tuesday March, 12, 2019
9:15AM-4:30PM

Critical Evaluation of Human Evidence for the Potential Reproductive and Developmental Toxicity of Nickel and Nickel Compounds

Nickel and nickel compounds were recently considered by the California Office of Environmental Health Hazard Assessment (OEHHA) for listing as reproductive toxicants under Proposition 65. There is a large body of evidence in humans and experimental animals regarding the potential reproductive and developmental toxicity of nickel and nickel compounds. We critically evaluated 42 epidemiology studies that assessed potential associations between nickel exposure and female reproductive, male reproductive, and developmental outcomes. We followed a systematic approach and used the National Toxicology Program (NTP) Office of Health Assessment and Translation (OHAT) Risk of Bias Rating Tool to assess potential sources of bias in the studies across nine domains: exposure assessment, outcome assessment, confounding, selection bias, attrition bias, statistical methods, exposure levels, form of nickel, and temporality. We also critically evaluated the results of the studies, considering how the factors that can affect the risk of bias and study quality may have impacted the interpretation of the results. In addition, we integrated the evidence across studies, placing more weight on higher quality studies with lower risks of bias, and we considered the form of nickel to which the study populations were likely exposed. In the risk-of-bias analysis, we found that all 42 studies have a moderate risk of bias, indicating generally low quality. This was due to the lack of appropriate statistical approaches to assess potential confounding, the use of area-level exposure measurements or indirect exposure measures that were not validated, and an inability to assess the temporal relationship between nickel exposure and the outcome of interest. We found that the majority of studies evaluated exposures to soluble and oxidic forms of nickel, and the results of these studies were largely inconsistent or null. In nickel refinery studies, workers had additional exposures to sulfidic and metallic nickel, and the results of these studies were largely null or not reproducible in more reliable studies. Overall, our analysis indicates that these epidemiology studies do not provide consistent evidence for associations between any form of nickel and reproductive or developmental outcomes; therefore, they do not provide sufficient evidence for recommending nickel and nickel compounds for listing as reproductive toxicants under Proposition 65.