A Novel TLV for Inorganic Manganese Compounds

Karen R. Obenshain, Martha M. Marrapese, and David G. Sarvadi
Keller & Heckman LLP

ABSTRACT

The Ferroalloys Association (TFA) has proposed that the American Conference of Government Industrial Hygienists (ACGIH) Dust and Inorganic Subcommittee revise the Threshold Limit Value (TLV) for manganese and its compounds of 0.2 mg/m^3 as Mn, changing it from a total dust standard to one based on respirable manganese levels. Although the exposure metric would be based on an eight-hour time-weighted-average (TWA_8), the available data suggest that a 30-day moving average more accuratley correlates to the risk of developing the sentinel event of non-clinical, non-progressive, non-material altered neurological responses.

Respirable manganese appears to be the key exposure metric to predicting the occurrence of these neurological responses which can only be observed in exposed groups and which appear not to be indicators of progressive neuorological disease. The respirable dust fraction that portion of inhaled manganese that penetrates the deep lung appears to be the key to controlling manganese toxicity because of its availability for direct transport via the bloodstream to the brain where, in current theory, manganese exerts its toxic effect. The respirable fraction is also considered more important because non-respirable dusts will be absorbed via the gut where normal hepatic homeostatic control can take over. Data on occupational cohorts suggest that variation in manganese body burden, as measured by blood or urine manganese, is not significant at exposures of 0.2 mg/m^3 respirable dust, TWA_8. Chronic low-level human exposures to inhaled manganese at this level have not produced clinical effects, as demonstrated by several recent epidemiological studies.

Rigorous analysis by Clewell and Crump (2000) of BMDs using a variety of data sets is the primary source for the recommendation that a respirable dust standard of 0.2 mg/m^3 will adequately protect exposed employees. The majority of neurological test endpoints were associated with levels of 0.2 mg Mn/m^3 and below. The BMD method offers several advantages in relation to other methods. BMD modeling does not require grouped data and therefore its use can eliminate the artificiality and loss of dose-response information associated with characterizing a range of individual exposures by summarized data. The BMD method also allows comparability of BMDs obtained from studies with continuous endpoints (e.g., neurological test scores) to those obtained from quantal (prevalence) data (e.g., animal toxicity studies).

Given that the recorded observations used in establishing the BMD are in humans and not in animals, and the lack of manifest illness associated with neurological effects at low levels, additional safety factors cannot be justified on scientific grounds as being necessary to provide adequate protection to exposed workers. No uncertainty factor is needed to account for inadequacies in the human toxicology database, given the voluminous amount of existing information on multiple endpoints and routes of exposure, which has now been supplemented by new information that confirms the reversibility of low level neurological measurements. There appears to be a clear, significant difference between exposure levels that produce the signal effect and those that produce clinical manganism. It appears that there is sufficient information in the literature for ACGIH to conclude that the difference in toxicity across routes of exposure is predictable from route-specific bioavailability and that differences in the valence and chemical

form of manganese affect relative bioavailability but not toxicity. This means that a single TLV for different forms of inorganic manganese is appropriate.

Thus, it is a reasonable premise, supported by current scientific evidence, that, if these apparently insignificant CNS effects are prevented, other effects, such as pulmonary and reproductive effects, and the irreversible neurological effects of manganism seen at far more massive doses, will also be prevented.

This work was supported by The Ferroalloys Association Manganese Committee, as part of its ongoing efforts to support research in developing occupational exposure limits.