

Formaldehyde, Hematotoxicity, and Chromosomal Changes—Letter

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Zhang and colleagues (1) compared hematological parameters and prevalence of aneuploidy (monosomy 7 and trisomy 8) between groups of workers exposed to "relatively high levels" of formaldehyde and those occupationally unexposed. The International Agency for Research on Cancer identified this study as "particularly relevant to the discussions regarding sufficient evidence" in classifying formaldehyde as leukemogenic (2). Similarly, the EPA IRIS Draft Toxicological Review of Formaldehyde noted that this study's findings "support the biological plausibility of formaldehyde effects on the hematopoietic system" and provide "the best evidence for bone marrow toxicity, where they report not only a reduction in white blood cell counts, but reductions in cell counts of all the blood cells, as well as increased mean cell volume" (3). However, important methodological limitations have been reported, including the lack of evidence that group differences in aneuploidy are significant to leukemogenesis, that personal monitoring data were collected but not analysed and presented, and failure to adhere to the study protocol. Additionally, the cross-sectional study design precludes identification of "changes" or "reductions" as claimed, as individual outcome parameters were measured only once (4).

NCI recently provided us the mean (but not raw) formaldehyde measurements described by Zhang and colleagues (1). Exposure-response analyses adjusting for sex and smoking found no relationship between formaldehyde exposure level and any of the hematologic parameters. Statistical analysis of monosomy 7 and trisomy 8 prevalence by formaldehyde expo-

sure was impossible after applying standard 2% background rates and strictly adhering to the study protocol criterion of counting >150 cells (clinical evaluations commonly require 200–400). Even disregarding minimum counting criteria, no association between concentration and aneuploidy was seen among formaldehyde exposed workers (4).

Findings based on these new analyses of original study data contradict the conclusions and interpretation of Zhang and colleagues (1) and progeny publications using the same data. In one of these, Lan and colleagues (5) claimed it was "a relatively narrow range of [formaldehyde] exposure that precluded their assessment of exposure-response relationships." However, the 10th to 90th percentile formaldehyde exposure concentration range reported by Zhang and colleagues was 0.78 to 2.51 ppm (1), extending more than 3-fold above the U.S. OSHA permissible exposure level of 0.75 ppm. Reliance on Zhang and colleagues (1) to support biological plausibility of an association between formaldehyde exposure and leukemia should be tempered until its scientific validity can be verified and its findings properly replicated, the need for which was acknowledged in the Draft Formaldehyde Assessment (3).

Disclosure of Potential Conflicts of Interest

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