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TOXICOLOGICAL REVIEW OF FORMALDEHYDE - INHALATION ASSESSMENT

(CAS No. 50-00-0)

In Support of Summary Information on the Integrated Risk Information System (IRIS)

VOLUME I of IV

Introduction, Background, and Toxicokinetics

June 2, 2010

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U.S. Environmental Protection Agency
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OR[2] = 1.13 per GSD and the result for mold is OR[3] = 1.02 for a comparison of risks at the GSM to 10*GSM and OR[4] = 1.06 for a comparison of risks at the minimum value of total molds ($5*10^3/m^3$) to 10*minimum. As it appears that the magnitude of the formaldehyde effect is substantially stronger than that of the mold effect (following standardization of exposure increment) it can be concluded that the reported formaldehyde effect could not have been the spurious result of uncontrolled confounding by mold. Unfortunately the logistic regression models did not account for the correlated formaldehyde concentrations for children by classroom.

A recent meta-analysis of formaldehyde exposure and asthma in children (McGwin et al., 2010) identified seven peer-reviewed studies providing quantitative results and summarized those findings. Odds ratios and confidence intervals were abstracted and effect estimates were standardized to odds ratios per 10 $\mu g/m^3$. Funnel plots were used to assess publication bias and did not show such a bias. Fixed- and random-effects models were used to calculate pooled ORs and 95% confidence intervals following a test of heterogeneity. A fixed-effect model assumes that all the individual studies provided estimates of the same effect or slope while the random-effect model allows for different effects or slopes in the source studies that may reflect difference in baseline risk factors within in the study populations. The authors preferred the fixed-effect model when heterogeneity was lower and the random-effect model was preferred when the data were more heterogeneous. Both models were presented as the degree of heterogeneity, measured by the Q test and I^2 statistic, which indicated the presence of moderate heterogeneity. However, the Q test value of 14.28 ($p < 0.0001$) and the I^2 statistic of 51% met the authors definition of sufficiently heterogeneous to prefer the random-effect model results.

Of the seven studies that were included in the meta-analysis, six reported increased risks of asthma associated with exposure to formaldehyde. The results of the random-effect model results showed an overall effect estimate of OR = 1.17 (95% CI: 1.01-1.036) (see Figure 4-2). The three studies with the highest statistical weights based on the inverse of the variance of the study ORs were for the studies by Rumchev et al. (2002), Garrett et al. (1999) and Krzyzanowski et al. (1990). Higher weights are reflected by narrower confidence intervals in these studies which implied that they were able to estimate effects with greater precision and so were assigned greater weight in the meta-analysis. The authors (McGwin et al., 2010) noted that an influence plot revealed that the study by Rumchev et al. (2002) may have had 'undue influence on the study data' and recomputed the random effects model without that study. The authors suggest that one difference is that this study is unique in focusing on very young children. Excluding

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[2] OR per GSD = exp[ln(OR per $\mu g/m^3$)/10 $\mu g/m^3$ * 2.3 $\mu g/m^3$] = exp[ln(1.7)/10*2.3] = 1.13.
[3] OR per GSD = exp[ln(OR per 10-fold increase)/(9*GSM)*1.6 $\mu g/m^3$] = exp[ln(4.7)/162*1.6] = 1.02.
[4] OR per GSD = exp[ln(OR per 10-fold increase)/(9*Minimum)*1.6 $\mu g/m^3$]=exp[ln(4.7)/45*1.6] = 1.06.

Rumchev et al. (2002), the OR = 1.24 (95% CI: 1.07-1.45) was somewhat higher than the OR = 1.17 for all the studies.

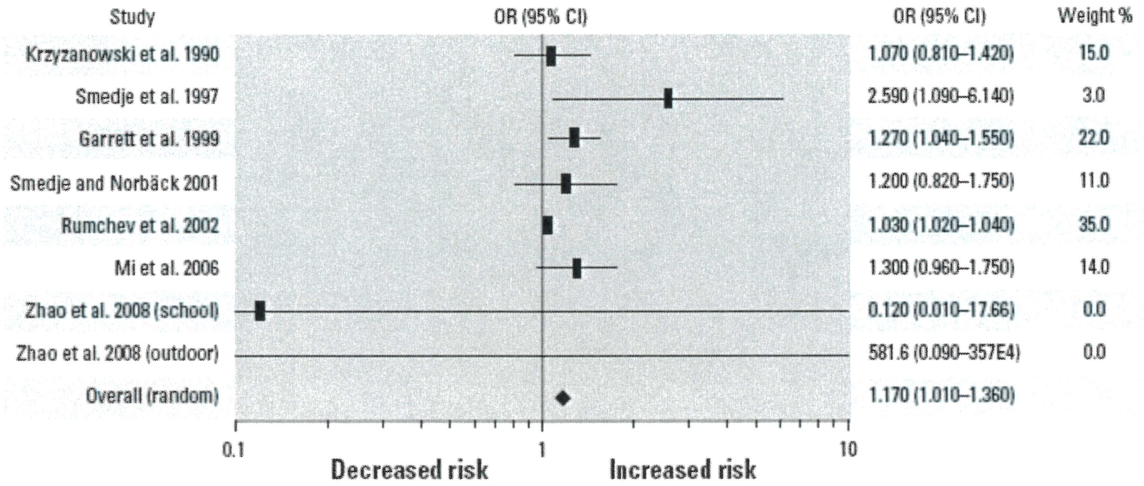

Figure 2. Forest plot of the relative risk estimates and their 95% CIs from the studies included in the meta-analysis of the association between formaldehyde exposure and asthma in children based on a random-effects model.

Figure 4-2. McGwin Forest plot of relative risk estimates and 95% CIs from studies included in a meta-analysis of formaldehyde exposure and asthma in children based on the random effects models.

Source: McGwin et al. (2010).

Separate random-effects were fit for the six studies in which the ORs were for self-reported asthma yielding an OR = 1.26 (95% CI: 0.97−1.64) and for the two studies that used diagnosed asthma OR = 1.12 (0.88−1.44). Meta-analytic results stratified by study design yielded an OR = 1.25 (95% CI: 1.08−1.44) for the cross-sectional studies. This systematic review of the literature on asthma and formaldehyde provide evidence of a concentration-dependent increased risk of asthma (prevalence and incidence) associated with increased concentrations of formaldehyde.

Garrett et al. (1999) also evaluated the prevalence and severity of allergic sensitization to 12 common allergens and reported increased prevalence with increasing formaldehyde concentration in the home. A respiratory symptom score, developed using responses by parents to a validated respiratory questionnaire during an interview, also was increased. The frequency of each respiratory symptom reported during the past year was categorized into four groups