Reviewer's report

Title: Reanalysis of updated mortality among vinyl and polyvinyl chloride workers: confirmation of historical evidence and new findings

Version: Date: 13 March 2007

Reviewer: Kenneth A. Mundt

Reviewer's report:

General

This manuscript presents results and interpretation of a statistical re-analysis of cohort mortality data previously reported by others using Standardized Mortality Ratio (SMR) analyses. Different from the original report, which employed external comparison groups, this paper compares mortality of employees in various vinyl chloride (VC) and polyvinyl chloride (PVC) production areas with mortality among technicians and clerks, using Poisson regression. The rationale for this is to avoid a potential ‘healthy worker effect’ and to shed additional light on the relationship between employment in VC and PVC and specific health risks. While in theory the additional analyses appear to be justified, and the use of Poisson regression quite appropriate, there are serious limitations that need to be addressed before the results and their interpretation can be considered valid. Specifically, choice of the technicians and clerks as a reference group may be no better than the previous studies’ use of an external referent if that comparison group is inherently different from the ‘exposed’ employees with respect to disease risks. Most notable are potential socioeconomic and educational differences that would lead to different smoking and dietary habits (relevant to cardiovascular diseases and several cancers, including lung cancers). No effort has been made to address these, and therefore the potential for confounding bias remains problematic. That most exposed worker categories demonstrated small increased risks for broad categories of ‘all causes,’ ‘all cancers,’ and ‘cardiovascular diseases’ and that no single cancer (except liver tumors among autoclave cleaners – known for over 30 years) appears significantly elevated supports this notion. Furthermore, this study neither updates the mortality experience of the cohort (last updated through 1999) nor makes any effort to improve exposure assessment – which would have had a much greater impact on improving validity of study results. The authors’ interpretations suggest that serious biases inherent in previous analyses of the same data have been overcome; however, they meanwhile have failed to acknowledge the potential for bias in their own results and interpretation.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Detailed comparisons of the exposed groups with the control group (i.e., technicians and clerks) are most critically needed. Unless compared groups can be demonstrated to be highly comparable with respect to educational level, other socioeconomic status indicators and related health behaviors such as smoking, diet and exercise, these factors should be individually evaluated and controlled.

If the primary problem above could be overcome, some effort to assess individual workplace exposures (or at least validate exposure assumptions) would be valuable. Currently an ecologic-level assessment is made which assumes that all individuals who had worked predominately in the same production area (or large group of ‘other blue collar workers’) had the same exposures (to unspecified substances).

If possible, updating the mortality of the cohort would provide larger numbers for more stable statistical analyses.

The language used in many sections is imprecise and not always accurate, possibly a result of translation from an original version in Italian. For example, the conclusion in the abstract (perhaps reasonably anticipated to be the most-read sentences in published papers) states, ‘This cohort analysis, based on internal comparison, confirmed specific risk excesses previously reported for cancer other than liver angiosarcoma…’ However; no statistically significant cancer result is provided other than for liver angiosarcoma. One exception to this criticism is the description of the statistical methods, which is very clearly and concisely written (likely by a different author than the balance of the manuscript).

Re-defining the alpha-error level in order to derive statistically significant results is inappropriate and not a
standard approach.

Application of attributable risk prior to assessing confounding and possible interaction is questionable and could be misleading.

How this re-analysis has allegedly clarified ‘contradictory results’ needs to be explained, especially in light of the unaddressed limitations stated above.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

This paper currently contains too many larger issues that need to be addressed before comments on more minor items can be offered.

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Discretionary Revisions (which the author can choose to ignore)

Please see previous comment.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

In the past I have conducted and published similar epidemiological research on the North American vinyl chloride industry, all of which was financially supported by the Vinyl Chloride Health Committee of the American Chemistry Council (ACC). Currently, I have no financial relationship with this organization.