Reviewer’s report

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

Version: 4 Date: 8 October 2007

Reviewer: Kenneth A. Mundt

Reviewer’s report:

General

I appreciate the opportunity to review this paper again - it has been considerably improved. Nevertheless, two of my main criticisms, while partly addressed in the covering letter, have not been meaningfully addressed in the manuscript. These are detailed below, and basically have to do with the appropriateness of the comparison group and the impact that an inherent inability to control for confounding might be exerting on study results as presented. I have offered practical suggestions on how the authors might address both of these issues.

I look forward to seeing the paper after these improvements are made.

Thank you.

----------------------------------------------------------------------------------

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

1. Comparison of the exposed group (blue collar) with the reference group (technicians and clerks) - other than age at hire - appears not to be possible. This may be due to lack of data available to the authors on which these groups can be compared. Unfortunately, this leaves unaddressed the key issue of whether and how the technicians and clerks might differ from the exposed workers in ways important to health and other than the exposures of interest (VC and PVC).

Therefore it would be important, in the interest of isolating and evaluating risks possibly related to VC and PVC exposure, to compare VC and PVC exposed groups (autoclave, PVC compounding and bagging) to the "other blue collar" employees as a second comparison group. These other blue collar employees presumably are not exposed to VC and PVC and may be more similar with respect to socioeconomic and baseline health than the somewhat more white-collar comparison group. This will also help the reader assess directly the potential for confounding introduced by the specific choice of referent group. An added benefit of using the other blue collar group as a referent (alone or combined with the technicians and clerks) is statistical stability. Currently, RR’s may be compromised by very small numbers observed in the referent group.
2. The notion that smoking may not be an important confounder has been misrepresented. Even if 20 or 40% the observed effect reported is due to confounding by smoking, the interpretation would change for many or most of the results. Since the authors appear to be familiar with the Axelson approach to indirect adjustment for a confounder, I urge them to apply these techniques to their data. This will provide the reader with a sense of how much of the observed results could have been due to confounding by smoking (or other risk factors such as alcohol consumption for liver cirrhosis and cancer).

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

The stated rationale for using and reporting 90% confidence intervals for some results is still quite unusual. I suggest a clearer explanation in any case, perhaps indicating that such as a method might be used to screen large numbers of results for promising hypotheses to be pursued with more rigorous approaches. Technically, where many evaluations are performed, smaller alpha errors (i.e., 97.5 or 99% confidence intervals) often are chosen to reduce the number of false-positive results generated (i.e., a Bonferroni-like correction). However, I am not recommending this approach, but mention it to highlight why I believe the 90% CI's presented in this paper might be confusing, and possibly contradictory to traditional statistical thinking.

Discretionary Revisions (which the author can choose to ignore)

The manuscript and its credibility would be strengthened if the political arguments regarding previous studies and the alleged influence of industry were removed or made more specific. Having conducted one of the largest epidemiological studies of VC-exposed workers, which was sponsponsored by the VC industry in the US, I can definitively state from my first-hand experience that the industrial study sponsors of my research made no effort whatsoever to interfere or influence the results. Therefore insuations to the contrary would be untruthful and of no scientific value. The approach of greatest integrity would be to stick to the science, and leave the political perspectives out of the scientific article.

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: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests:

no change from previous reviews of this paper