**COMMENTS:** A Morbidity Study of Chemical Workers Who had been Engaged in the Production of Pentachlorophenol

Two general comments seem appropriate. In the first place, the citation "system" used in this paper is cumbersome, and it is almost impossible to find cited references. In the text, the references are cited by author name (last name of first author). Not only does this system look awkward, but in some cases the citations are superimposed on the text. Worse, however, is the fact that in the reference section at the end of the paper, the references are numbered (based on appearance in the text?) and not in alphabetical order! Therefore, in order to find a particular citation, the reader has to scan through the entire list of references. Either the citations should appear in the text as numbers, or the references in the "REFERENCES" section should be alphabetized.

In the second place, although the potential effects of multiple comparisons is mentioned in passing in the section on neurotoxicity (page 32), this paper needs a thorough discussion of the problem of multiple comparisons at the beginning, because the whole paper is subject to this statistical aberration. Essentially every organ system was subjected to multiple tests, not just the CNS. The focus of this paper probably should be the remarkable health status of these workers!

Page 4, paragraph 2: The paper states that "Production of PCP in the United States ceased in 1992." This fact will come as a great surprise to Vulcan Materials Company, Birmingham, AL, which still manufactures pentachlorophenol!

Page 6, paragraph 1 (incomplete at top): The authors persist in their belief that PCBs were manufactured at this plant beginning in 1929. PCB manufacture at this plant was begun in 1940.

Page 6, paragraph 2: Manufacture of NaPCP was discontinued in 1973, not 1975, as stated in the last sentence.

Page 13, paragraph 2 (first full): The excessively high coefficients of variation for the urinary porphyrins make any conclusions based on these results most uncertain. However, a claimed excess in urinary porphyrins among a small subclass of workers is one of the highlighted "findings". The error bars around this "finding" must be exceedingly wide!

Page 19-20: The paragraphs on GGT are very difficult to follow, largely because of the large number of intergroup comparisons and the discussions of adjusted analyses and outliers. It is not clear that there is any clinical significance to the few reported significant findings or that there is any biological plausibility to findings for Only PCP which are not present for Ever PCP.

Page 20-21: The entire discussion of porphyrin levels is difficult to credit in light of the wide CVs for these tests. For example, in light of the fact that the CV for pentaporphyrins was over 80%, one must wonder whether a 1 mcg difference between Ever PCP Chloracne workers and unexposed can have any meaning, even if a test for difference of means suggests statistical significance.

Page 26, last paragraph: What is the significance of a GGT elevation in the absence of any other liver finding, especially one which disappears when outliers are removed? Is it possible that, in light of the many comparisons evaluated, that the multiple comparison effect has manifested itself?

Page 29, first (incomplete) paragraph: While the Maroni citation does report a slight excess in coproporphyrin excretion among Italian capacitor workers, that excess is characterized as "very slight" in a subsequent publication. (Maroni, M. et al., 1987) The paper also reports a study of American workers in which "...the porphyrinogenic effects ...were...totally absent..." Further, the porphyrin levels in the Italian workers did not correlate with blood PCB concentration. It seems inappropriate to only cite the human studies which are consistent with the hypothesis generated in this paper and ignoring other available human studies.

Page 29, last paragraph: The Van Birgelin study cited to suggest the biological plausibility of a synergistic effect on porphyrin excretion between PCBs and "dioxins" is an abstract which has only been printed in a non-peer-reviewed collection of abstracts from a conference. This work has never been published in the peer-reviewed literature. The PCB 153 and TCDD doses in this study were very high, only female rats were used, and liver accumulation, not urinary excretion, was measured. The authors' should be cautious about relying too much on this report for generalization to humans.

Page 30, first (incomplete) paragraph: The producer's composite, which contained 50 ppm hexachlorobenzene, contained PCP manufactured at this plant. What is the comparison on which the characterization of the HCB content as "low" is based?

Page 32, first (incomplete) paragraph: This discussion of the potential effects of multiple comparisons should be expanded and applied to the entire paper.

Page 33, last paragraph: The "study" by Klawans was a report of an examination by the author to support the claims of plaintiffs in a lawsuit. If this report is to be cited, the circumstances should be noted. Further, the chlorinated phenols involved in the spill were predominantly monochlorophenol, not pentachlorophenol. The information is presented in such a way that a reader could conclude that the spill involved PCP.