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Dr CW Jameson
National Toxicology Program
Report on Carcinogens
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RE: Comments on *Draft Report on Carcinogens, Background Document for Trichloroethylene*

Dear Dr Jameson:

In response to reading the Draft Report on Trichloroethylene (TCE), please find enclosed a letter to the editor of *Environmental Health Perspectives* that we wrote in response to the recent epidemiologic overview and evaluation of trichloroethylene and cancer by Wartenberg et al. (Trichloroethylene and cancer: epidemiologic evidence. *Environ Health Perspect* 108 (suppl 2):161-176, 2000). We are submitting this letter together with our comments since the Draft Report on TCE relies heavily on Wartenberg et al.'s review of the epidemiologic data on TCE.

Wartenberg et al. incorrectly report information regarding TCE and cancer from our study of aircraft manufacturers (Boice JD Jr, Marano DE, Fryzek JP, Sadler CJ, McLaughlin JK. Mortality among aircraft manufacturing workers. *Occup Environ Med* 56:581-597, 1999). Incorrect SMRs and/or confidence limits for a number of cancers were presented in the Wartenberg et al. report and these were incorporated into several of the summary analyses.

We trust that you will consider the correct values from our paper when making your deliberations.

A further point: One of us (JKM) was the principal investigator of an international case-control study of renal cell cancer[1,2]. It involved six study centers in five countries, a shared protocol, and standardized methods and interview instruments[1]. Wartenberg et al. treats the pooled results on occupation from this study[2] and the separately published center-specific results[3,4,5] as independent observations, which, of course,

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[1] McLaughlin JK, Lindblad P, Mellemgaard A, McCredie M, et al. International renal cell cancer study. I. Tobacco use. Int J Cancer 60:194-198, 1995.
[2] Mandel JS, McLaughlin JK, Schlehofer B, Mellemgaard A, et al. International renal cell cancer study. IV. Occupation. Int J Cancer 61:601-605, 1995.
[3] McCredie M, Stewart JH. Risk factors for kidney cancer in New South Wales. Br J Ind Med 50:345-354, 1993.
[4] Mellemgaard A, Engholm G, McLaughlin JK, Olsen JH. Occupational risk factors for renal cell carcinoma in Denmark. Scan J Work Environ Health 20:160-165, 1994.
[5] Schlehofer B, Heuer C, Blettner M, Niehoff D, et al. Occupation, smoking and demographic factors, and renal cell cancer. Int J Epidemiol 24:51-57, 1995.

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they are not. We believe this should also be taken into consideration. Along the same lines, the patients in the Vamvakas et al. case-control study (1998) of renal cancer include the renal cancer cases from the earlier cohort study by Henschler et al. (1995). Hence, these two studies from Germany are not independent observations of TCE and risk of renal cancer.

Respectfully,

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Editor-in-Chief
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Dear Sir:

We read with interest the epidemiologic overview and evaluation of trichloroethylene (TCE) and cancer recently published by Wartenberg et al. *(1)*. Unfortunately, there were a number of errors in table 5 concerning risks reported in our study of workers exposed to TCE during the manufacturing of aircraft *(2)*. For instance, the SMR and the confidence interval (CI) presented for multiple myeloma were actually those for Hodgkin's disease. There were also serious errors in the listed SMR and CI for stomach cancer as well as discrepancies in the presentation of confidence intervals (CIs) for 10 other sites (see attached tabular comparison). These incorrect values were included in the meta-analyses to make inferences regarding the carcinogenic potential of TCE and thus should be revised.

We also found it peculiar that the reported CIs from our study were recalculated. We computed exact CIs which are methodologically superior to the recalculated ones. The method of re-computation assumed that our upper but not lower confidence limit was correct. These recomputations had the unusual property of exaggerating the lower CI, i.e., making the results appear more statistically significant (or closer to statistical significance) than they actual were.

Table. Discrepancies between TCE and cancer risks as reported in the original article of aircraft manufacturers (2) and as listed in Table 5 of the recent review paper (2).

Cancer site		Original Article (2)	Review Article Incorrect listing (1)
Multiple myeloma	SMR (# cases) 95% CI	0.9 (6) (0.3-2.0)	2.8 (4) (1.1-7.1)
Stomach	SMR (# cases) 95% CI	1.3 (17) (0.8-2.1)	0.8 (7) (0.4-1.7)
Cervix	SMR (# cases) 95% CI	0.0 (0) (0.0-5.5)	- -
Leukemia	SMR (# cases) 95% CI	1.1 (12) (0.5-1.8)	1.0 (12) (0.6-1.8)
Breast	95% CI	0.5-2.7	0.6-2.7
Buccal	95% CI	0.2-1.4	0.3-1.4
Colon	95% CI	0.7-1.5	0.8-1.5
Esophagus	95% CI	0.3-1.7	0.4-1.7
Hodgkin's disease	95% CI	0.8-7.1	1.1-7.1
Kidney	95% CI	0.4-2.0	0.5-2.0
Larynx	95% CI	0.3-2.8	0.4-2.8
Rectum	95% CI	0.6-2.5	0.7-2.5

References and Notes

1. Wartenberg D, Reyner D, Scott CS. Trichloroethylene and cancer: epidemiologic evidence. Environ Health Perspect 108 (suppl 2):161-176 (2000).

2. Boice JD Jr, Marano DE, Fryzek JP, Sadler CJ, McLaughlin JK. Mortality among aircraft manufacturing workers. Occup Environ Med 56:581-597 (1999).

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