The statement by Steenland and Stayner that we have analysed the data from the study conducted by NIOSH is a gross exaggeration. Our study was based on employment records microfilmed by NIOSH, additional employment records from member companies (microfiche, hard copies, and computer tapes), vital status information from various sources (SSA, NDI, DMF, member companies), and death certificates from state health departments. All these data sources were equally important in our study, and we have properly identified and acknowledged every source in our paper.

The discrepancy in cohort size between our study¹ and the NIOSH study² is most likely the result of additional information we obtained from the participating companies. As stated earlier, the NIOSH microfilms contained both illegible and incomplete work history information. It was necessary for us to obtain additional information from member companies to resolve these data gaps. To our knowledge, NIOSH had never gone back to the member companies for additional information.

Steenland and Stayner criticised our study for lack of detailed exposure information. Although we recognised the value of *valid* exposure data in epidemiological studies, that is not to say that a study is better simply because it has some exposure estimates, valid or otherwise. One of us (OW) participated in some of the walk through surveys and in reviewing the NIOSH exposure classification. Although much resources (from both NIOSH and HIMA member companies) were spent on historical exposure estimates, the validity of the estimates provided by the NIOSH model is questionable. Several member companies have expressed their concerns regarding the inaccuracy of such estimates. For example, at one facility, the NIOSH model predicted that the exposure for a steriliser/operator in 1977 was 19.3 ppm, but industrial hygiene measurements based on 17 samples indicated that the actual exposure was 45.2 ppm. We are strongly of the opinion that the NIOSH exposure estimates were inaccurate and would have been a major source of misclassification if they were incorporated in the analysis.

As we stated in our paper,¹ average

duration of exposure was only about one year shorter than average duration of employment. Thus duration of employment was a close surrogate measure for exposure. We defined latency as time since first employment. NIOSH defined latency as time since first exposure. The difference was minor. The statement by Steenland and Stayner that we failed to observe a "trend" for all haematopoietic cancer by latency was inaccurate. Our data *did* show an "upward trend" for all haematopoietic cancer. As this broad International Classification of Disease (ICD) category consists of several heterogeneous diseases, however, we attached little interpretation to it. It would be far more meaningful to examine the individual cancer categories within this broad category. Such analyses were done. In particular, as noted in our paper, as there was a significant increase of non-Hodgkin's lymphoma in men, we performed a latency analysis of non-Hodgkin's lymphoma for men, and no trend was detected. Similar to our results, NIOSH's analyses also failed to show any trend by latency for more specific individual disease categories.

The statement by Steenland and Stayner characterising our study as "an essentially duplicate analysis" of the data is inaccurate. Data sources aside, we have presented far more analyses than the NIOSH paper. To start with, we presented standardised mortality ratios (SMRs) for 50 causes of death in most analyses, whereas a much smaller number of causes of death was presented by NIOSH (most tables in the NIOSH's paper had only 10 causes of death). Furthermore, as previously pointed out by one of us (OW), the category "non-Hodgkin's lymphoma" used in the NIOSH study (ICD 202 only) was incorrect.³ In the 8th ICD, non-Hodgkin's lymphoma consists of both codes 200 and 202. Our analysis of non-Hodgkin's lymphoma was based on the proper ICD categories. Finally, we also provided analyses for all four major histological cell types of leukaemia.¹ NIOSH did not analyse leukaemia data by cell type.

Steenland and Stayner accused us of "downplaying" the carcinogenic risk of ethylene oxide. It should be pointed out that nowhere in their own paper did Steenland and Stayner conclude that their data had shown a

carcinogenic effect of ethylene oxide. In fact, even though Steenland and Stayner found that "overall there was no significant increase in mortality from any cause in the study cohort," they concluded that, because of the small sample size, "our (NIOSH's) findings are therefore not conclusive."² Thus with regard to whether ethylene oxide is carcinogenic to humans, the only conclusion that NIOSH could offer was no conclusion.

NIOSH's conclusion of their study being not conclusive begs the question why NIOSH conducted the study in the first place. As stated in the letter by Steenland and Stayner, a feasibility study was conducted by NIOSH before the actual mortality study. Based on the results of the feasibility study, NIOSH estimated that the mortality study would have adequate statistical power (80% at $\alpha = 0.05$) to detect a risk ratio as small as 2.0 for all haematopoietic cancer and 2.7 for leukaemia. Our calculation indicated that the NIOSH study actually had adequate power to detect risk ratios as small as 1.47 and 1.79 for all haematopoietic cancers and leukaemia, respectively. Thus the actual power of the NIOSH mortality study was much higher than what was anticipated based on the NIOSH feasibility study. We can only assume that the NIOSH mortality study was given a "go ahead" only after a careful consideration of the anticipated statistical power.

- 1 Wong O, Trent LS. An epidemiological study of workers potentially exposed to ethylene oxide. *Br J Ind Med* 1992;50:308-16.
- 2 Steenland K, Stayner L, Greife A, et al. Mortality among workers exposed to ethylene oxide. *N Engl J Med* 1991;324:1402-7.
- 3 Wong O. Mortality among workers exposed to ethylene oxide. *N Engl J Med* 1991;325:1254.

Neuropsychological performance and solvent exposure among car body repair shop workers

Sir,—In the article by Daniell *et al* (1993;50:368-77) reference is made to NIOSH Method 1500 as applied to methyl ethyl ketone. Methyl ethyl ketone is unstable on coconut shell charcoal: this finding led to the development of Method 2500 (2-butanone), dated 15 February 1984.¹ The compound has never been

included in Method 1500 (hydrocarbons, BP 36–126°C).¹ Therefore, the estimates of methyl ethyl ketone concentrations made by Daniell *et al* are probably biased low.

PETER M ELLER
*Quality Assurance and Statistics Activity,
Division of Physical Sciences and
Engineering, Centers for Disease Control,
National Institute for Occupational Safety
and Health, Robert A Taft Laboratories,
4676 Columbia Parkway, Cincinnati,
OH 45226-1998, USA*

- 1 National Institute for Occupational Safety and Health. *NIOSH manual of analytical methods*, 3rd rev ed. Cincinnati, OH: US Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, DHHS (NIOSH) 1984. (Publication No 84-100.)

Authors' reply

Sir,—Eller's comments are generally correct. Methyl ethyl ketone (2-

butanone) is not among the analytes specified in NIOSH Method 1500, and it could undergo degradation on coconut shell charcoal leading to a negative bias in air sampling results. Certainly, Method 2500 would have been a more appropriate choice if a dedicated assay for methyl ethyl ketone were intended.

The volatile organic vapour samples for the study reported were collected with commercially available charcoal tubes and dosimeter badges (and assayed according to Method 1500), with the recognition that this approach was a compromise that might not yield equal performance for all of the multiple anticipated analytes.

The potential problems in using Method 1500 for methyl ethyl ketone were mitigated by storing the samples at -5°C or lower and by minimising the period of storage before desorp-

tion, nominally 24–48 hours. Control samples were prepared at the beginning of the study and stored under identical conditions for assay with each batch of field samples throughout the course of the study. A total of 41 such samples were assayed for 2-butanone spiked at concentrations equivalent at typical air sampling volumes to air concentrations of 15–150 mg/m³. These samples showed desorption efficiency corrected 2-butanone recoveries of 102% for charcoal tubes and 98% for dosimeters, with standard errors of 3.3% and 3.1% respectively. No time trend was evident in these results throughout the course of the study. We interpreted this as indicating that instability of 2-butanone under these conditions did not lead to unacceptable degradation, or bias field results sufficiently to affect major study findings.