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**ECETOC Statement on US National
Cancer Institute (NCI) Epidemiological
Study on Formaldehyde**

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ECETOC STATEMENT ON US NATIONAL CANCER INSTITUTE (NCI)
EPIDEMIOLOGICAL STUDY ON FORMALDEHYDE

On 13 Feb. 1986 the European Chemical Industry Ecology and Toxicology Centre (ECETOC) issued a Summary Review of recent findings relevant to the question of the carcinogenicity of formaldehyde (ECETOC, 1986). It was known that the NCI had completed an epidemiological study but the results did not become available until the end of February (NCI, 1986). A number of experts from member companies of ECETOC have now analysed the study, and their views are given in this Statement.

1. General Description of Study

The objective of the study was to assess the risk of certain specific cancers (especially of the airways and the brain), leukaemia, and other causes of death among industrial workers occupationally exposed to formaldehyde. It comprised a historical cohort, mortality study of 26,561 persons employed in 10 plants in the USA at which formaldehyde was produced or used. The study population had accumulated more than 600,000 person-years of follow-up. The criterion for inclusion in the study was first employment before 1 January 1966, and the vital status of the subjects was followed to 1 January 1980. The cohort included workers first employed in the 10 plants between 1934 and 1965. Of these, 4396 had died and death certificates were available for 4059 (92%) of the deceased. The vital status of 1357 persons, 5% of the total cohort, was lost to follow-up. Exposures were estimated retrospectively in a very painstaking manner by preparing matrices for each job/ work-area/ calendar-year combination based on 5 categories of exposure ranging from

"non-exposed" to "greater than 2 ppm, TWA". The intensity (level) of exposure, duration, cumulative exposure, peak exposures, time since first exposure and exposure to particulate matter were evaluated. Of the total population exposed to formaldehyde, 97% had been exposed to up to 2 ppm and 3% to greater than 2 ppm.

The NCI point out that the study has a statistical power of 80% for detecting a 4-fold increase in the mortality from nasal cancer since this is such a rare tumour.

In the statistical analysis of the results, standardised mortality ratios (SMRs) developed by comparing the mortality experience of the cohort with that of the general US population and local populations, and directly-standardised rate ratios (RRs) developed by comparing the exposed and non-exposed subjects of the cohort, were used. The 95% confidence intervals were given for the SMRs, which were calculated for three categories of "time since first exposure", ie. less than 10 years, 10-19 years, and 20 years or more. A Chi-square test was used to evaluate the statistical significance of trends in the SMRs.

In comparison with some of the earlier epidemiological studies (see ECETOC, 1986), the NCI findings are based on the largest cohort of any such study, exposure is well-defined and the study period is long (from 1934 to 1979 inclusive). It should be noted that in a mortality cohort study of this size, the likelihood that the smoking habits of the study population differ significantly from those of the general population is very small. This is borne out by the fact that in this study the SMR for lung emphysema was close to 100 in the exposed and non-exposed groups. In case-control studies, however, documentation of the smoking habits of each individual studied is necessary to eliminate this as a confounding factor, but in two recently-published case-control studies on formaldehyde (Olsen et al., 1984; Hayes et al., 1984) such documentation was lacking or insufficient.

B. Results

The most essential finding from this study is that in the total cohort there was no statistically-significant excess in mortality from :

- all causes of death,
- all types of cancer combined,
- any individual type of cancer.

There was no pattern of elevated mortality even in the group exposed to greater than 2 ppm of formaldehyde. There was no excess of mortality from nasal cancer (2.0 observed, 2.8 expected), or cancer of the buccal cavity, pharynx, brain and the lymphatic or haemopoietic system.

The calculation of SMRs and RRs for a large number of different causes of death and types of cancer always results in some statistically-significant findings by chance. To assess the plausibility of such findings it is necessary carefully to analyse dose-response relationships. Such an analysis showed that there was no significant excess mortality due to cancer, and no consistent upward trend in the SMRs related to either the intensity of exposure or cumulative exposure with the exception of Hodgkin's Disease. The mortality from this, while not significantly increased in itself, showed a rising trend with the intensity of exposure but not with cumulative exposure. In ECETOC's view, these findings cannot be interpreted and are most probably due to chance.

Although there was a deficit in mortality from cancer of the buccal cavity and pharynx, the SMRs for cancer of the nasopharynx and oropharynx were elevated. To relate these findings of increased mortality to exposure to formaldehyde, however, is not biologically plausible since there was no dose-response relationship. Furthermore, the grouping together of cancers of the nasopharynx, which could be of several histological types, may be misleading. To draw any definite conclusions from such findings it would be necessary to define the histological type of each tumour more precisely.

There is a substantial difference in the SMRs for lung cancer between the salaried and wage workers, and a clear difference between those of the exposed and non-exposed groups. This latter difference is due to the higher socio-economic status of people in the non-exposed group, consistent with the fact that persons in lower socio-economic groups smoke more heavily than do those in higher groups.

In this study of a very large cohort, no deaths due to cancer of the parotid glands were found, in contradiction to the findings of Stayner et al.(1985).

On page 12 of their report the NCI state that "no explanation for the discrepancy between the case-control studies from Denmark and the Netherlands and this and other cohort or proportionate mortality studies is obvious.....". ECETOC's view is that the discrepancy with the Danish (Olsen et al.,1984) and Dutch (Hayes et al.,1984) results is attributable to several important deficiencies in these two studies which make their findings doubtful (see ECETOC, 1986).

C. Conclusions

The NCI conclude that :

"In summary, deaths from all causes were about as expected among white men indicating little, if any, "healthy worker" effect. Non-significant excesses seen for Hodgkin's disease and cancers of the lung and prostate did not show convincing rising risks with cumulative exposure. This large multi-plant cohort study provided little evidence to suggest that formaldehyde exposures affected the mortality experience of these industrial workers".

ECETOC finds this to be a reassuring study which does not demonstrate any relationship between occupational exposure to formaldehyde and excess mortality due to cancer or any other cause of death.

D. Bibliography

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The TF thanks Dr. G. Paddle of ICI for helpful comments on the NCI report, but notes that he was unfortunately not able to see the text of this present document.



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