Methyl Ethyl Ketone and Methyl Isobutyl Ketone Not Carcinogenic

The April 22, 1993, issue of *Environmental Health Perspectives* contained a commentary by Legator and Strawn entitled "Public Health Policies Regarding Hazardous Waste Sites and Cigarette Smoking: An Argument by Analogy." Although the article does not include any discussion of either methyl ethyl ketone (MEK) or methyl isobutyl ketone (MIBK), it does list them in Table 3 as substances that cause cancer in animals and/or humans."

Because MEK and MIBK are both widely used industrial chemicals, they have been studied extensively for possible human health or environmental effects. The Ketones Panel of the Chemical Manufacturers Association has sponsored a number of the studies and surveyed all the pertinent literature on these two compounds. The panel is not aware of any evidence suggesting that either MIBK or MEK causes cancer in humans or animals. Indeed, neither MEK nor MIBK is known or reasonably expected to cause any type of chronic health effect in humans.

MEK has been shown to be inactive in a wide variety of *in vitro* and *in vivo* genetic toxicity assays and was not neurotoxic in five recent studies. Although MEK has not been tested specifically for carcinogenicity, the data on its structure and metabolism, the results of numerous subchronic studies, and the absence of genotoxicity indicate that MEK is highly unlikely to pose a cancer risk.

With respect to MIBK, inhalation studies conducted with rats, mice, dogs, and monkeys all indicate a very low order of subchronic toxicity. The results from a number of different mutagenicity screening assays show that MIBK exhibits very little, if any, mutagenic activity. Existing studies also demonstrate that MIBK is not teratogenic and exhibits low reproductive toxicity. As with MEK, MIBK has not been tested specifically for carcinogenicity because data on its structure and metabolism, subchronic health effects, and genotoxicity indicate that it is highly unlikely to pose a cancer risk.

If you are aware of any evidence that either MEK or MIBK is carcinogenic, please notify the panel. If not, we request that you publish a correction in order to set the record straight. Inaccurate and misleading information, even from a single publication, can have a significant impact. We therefore ask that you take the steps necessary to correct the false impression that has been created by your April 22, 1993, publication.

If you have any questions or wish to provide information on either of these these compounds, please contact Barbara Francis, manager of the Ketones Panel, at (202) 887–1314.

Gordon D. Strickland
Chemical Manufacturers Association
Washington, DC

Response

I am grateful to Gordon Strickland for detecting an error in my commentary in the April 22, 1993, issue of *Environmental Health Perspectives.* To my knowledge, there have been no carcinogenesis studies carried out with methyl ethyl ketone (MEK) in animals. I am aware of only a single unconfirmed study (*1*) that indicated a statistically significant increase in buccal or pharyngeal neoplasms. The Xs in Table 3 were inadvertently placed in the category for cancer for both MEK and methyl isobutyl ketone when they should have appeared under the heading "neurological."

Marvin S. Legator
University of Texas Medical Branch
Galveston, Texas

Reference

1. Alderson M, Rattan N. Mortality of workers on the isopropyl alcohol plant and two MEK dewaxing plants. Br J Ind Med 37:85–89 (1980).

Editor's Note: We regret our error in Legator and Strawn's Table 3 and any confusion this error may have caused. The corrected table is shown below.

Breast Cancer and Menarche in Asian Women

Fortunately for women, the scientific community is finally beginning to become more serious about breast cancer. Because of the recognized association between estrogen exposure and breast cancer, two recent discussions have suggested that lower risk in Asian women may be related to later onset of menses. It has been stated that Chinese women begin menses at an average age of 17 (*1,2*). This statement, which occurs in both *EHP* and *Science*, is unreferenced in both and is contrary to published studies.

Eveleth and Tanner (*3*) have summarized studies finding that well-off Chinese girls from Hong Kong and Singapore begin menses around age 12.4. A recent study from mainland China including 162,902 Han girls (*4*) found that the median age of menarche was 13.17 years for urban girls and 13.83 years for rural girls. Therefore, the lower rate of breast cancer in Asian women must not be related to a late age of menarche since studies find that Asian girls begin menses about the same time as girls in many other cultures (*3*).

At any rate, age of menarche may not be as good a marker of estrogen exposure as age of onset of breast development. The length of time between the onset of development and the beginning of menses may differ in various populations and could be an important factor in breast cancer epidemiology. In general, many studies on the prevalence of secondary sexual characteristics in girls start with subjects at too late an age (for example age 8,10, or even 12) to establish the timing of onset (*5,6*). Better understanding of women's natural growth and development cycles is necessary for the develop-

Table 3. Effects of substances found in cigarette smoke (*16*) and at a hazardous waste site (*18,19*)

Chemical	Cancer	Developmental	Liver/ kidney	Neurological	Blood	Lung	Cardiovascular
Arsenic	X	X	X		X	X	X
Cadmium	X	X	X			X	X
Chromium	X		X			X	
Lead	X	X		X			X
Nickel	X	X				X	
Benzene	X	X	X	X	X		
Toluene		X	X	X			
Xylene		X		X			
Tetracholoroethylene	X	X	X	X			X
Trichloroethylene	X	X	X	X			
Methyl ethyl ketone			X	X	X		
Methyl isobutyl ketone			X	X	X		