

March 17, 1998

Dr. C.W. Jameson
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Dear Dr. Jameson:

The National Toxicology Program's (NTP) plan to review alcoholic beverages for listing in the federal government's Ninth Report on Carcinogens is supported by strong scientific evidence and long overdue. We urge the NTP to continue its review of alcoholic beverages and to recommend listing as a known human carcinogen or reasonably anticipated to be a human carcinogen. The International Agency for Research on Cancer (IARC), another entity that evaluates human carcinogens, took the logical step to list alcoholic beverages as a likely human carcinogen a decade ago.

Numerous studies carried out over several decades confirm a strong association between the consumption of alcoholic beverages and certain types of human cancers. According to an estimate of the National Institute on Alcohol Abuse and Alcoholism, from 2 to 4 percent of all cancer cases in the United States are caused either directly or indirectly by alcohol. Simple calculations reveal that those cancers result in more than 16,000 deaths and economic costs of more than \$3 billion each year.

The use of alcoholic beverages in the United States has important consequences, both for the incidence of cancer and other health effects. Alcoholic beverages are widely used. According to the Substance Abuse and Mental Health Services Administration, more than 109 million Americans consume them each month, in one form or another. Significantly, as many as 18 million Americans, including as many as 4 million under the age of eighteen, suffer from alcohol dependence. A small, but significant number of persons consume alcoholic beverages in massive amounts; the top 10% of drinkers average more than 2.5 drinks per day and consume more than 60% of all alcohol.

Much of the data linking cancer to consumption of alcoholic beverages comes directly from studies of actual human consumers. Dozens of epidemiologic investigations have shown that alcoholic-beverage consumption is associated with the increased risk of certain human cancers, and many excellent reviews are available (much of the current evidence is detailed in the *9th Special Report to Congress on Alcohol and Health*, National Institute on Alcohol Abuse and Alcoholism, June 1997). The studies consistently show a strong association between alcohol use



and cancers of the esophagus, pharynx, and the mouth, and a weaker association with cancers of the liver, breast, and colorectal cancers. Both retrospective and prospective cohort studies, and case-control studies, have all shown significant increased risk of cancers of the oral cavity and pharynx, larynx, esophagus associated with alcohol consumption.

In particular, alcohol consumption together with tobacco use dramatically increases the risks of certain (mouth, esophagus, larynx) cancers. Elevated risk, however, persists even after correction for the effects of tobacco smoking and other potential confounders.

Based on results with actual human consumers of alcoholic beverages, IARC determined that there is *sufficient evidence* for the carcinogenicity of alcoholic beverages in humans. That agency also found suggestive but inconclusive data of a positive association of alcohol consumption with rectal and breast cancer. Recently published studies on the link between alcohol consumption and breast-cancer confirm a linear risk relationship and strengthen findings of a positive association between alcohol consumption and an increased risk of breast cancer, even at relatively modest levels of consumption.

The NTP has appropriately decided to review the listing of *alcoholic beverages* as human carcinogens, rather than to review *ethanol*. Alcoholic beverages are often complex mixtures that contain numerous chemicals in addition to water and ethanol. The epidemiologic studies linking alcoholic beverage consumption to various cancers generally cannot distinguish between the effects of the ethanol itself, versus the effects from other compounds contained in a particular beverage, or even an interaction between the two. IARC found that there was no indication that the effects are dependent on type of beverage, i.e., beer, wine, or distilled spirits. Studies on laboratory animals given only pure ethanol do not provide significant evidence of carcinogenicity of ethanol alone. IARC determined that *inadequate evidence* exists for the carcinogenicity of alcohol in laboratory animals.

However, many studies with laboratory animals show that ethanol enhances the carcinogenic potential of other known carcinogenic materials such as N-nitroso compounds and vinyl chloride. Certain N-nitroso compounds have been detected in some alcoholic beverages. It may be that the ethanol is acting indirectly by enhancing the carcinogenicity of other compounds contained in alcoholic beverages.

Nevertheless, if the observed carcinogenicity of alcoholic beverages results from the action of ethanol to enhance the carcinogenicity of other compounds present in alcoholic beverages then it is likely that this effect occurs at concentrations and exposures experienced by the typical consumer of alcoholic beverages. Thus, alcoholic beverages are human carcinogens, whether the carcinogenicity is due to the ethanol or some combination of compounds they contain.

Other evidence strongly suggests that ethanol by itself can reasonably be expected to be carcinogenic to humans. Ethanol consumed by mammals including humans is metabolized primarily to acetaldehyde by enzymes in the liver and other tissues. The resulting acetaldehyde is subsequently transported throughout the body. According to IARC, there is *sufficient evidence* for the carcinogenicity of acetaldehyde to humans.

A considerable body of evidence supports a strong association between consumption of alcoholic beverages and certain human cancers. From the standpoint of protecting human health it is not necessary to know if it is the ethanol alone that is responsible for this effect, or the ethanol in combination with other compounds in the beverages or other common risk factors, such as tobacco use. Therefore, the NTP should continue the process of listing alcoholic beverages as being reasonably anticipated to be a human carcinogen.

Sincerely



George A. Hacker
Director
Alcohol Policies Project

Mark Brown
Director of Toxicology

References

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