Occupational exposure to formaldehyde was found to be associated with increased death rates from myeloid leukemia in 2 recent studies published by researchers at the National Cancer Institute. Formaldehyde is widely used in construction materials, manufacturing, and consumer products, and for embalming in the funeral industry. Millions of workers and consumers are regularly exposed to various concentrations of the chemical.

The 2 studies, published in the *Journal of the National Cancer Institute* (2009;101:751-761 and 2009;101:1696-1708, respectively), found an elevated mortality rate from myeloid leukemia in individuals exposed to formaldehyde in manufacturing settings or the funeral industry. In both studies, the risk was associated with high peak exposure levels before 1980.

“Duration of embalming practice and related formaldehyde exposures in the funeral industry were associated with statistically significantly increased risk for mortality from myeloid leukemia,” writes Michael Hauptmann, PhD, lead author and a biostatistician in the department of bioinformatics and statistics at the Netherlands Cancer Institute in Amsterdam, the Netherlands.

“The significance of these findings,” Dr. Hauptmann says, “is that an enormously economically important chemical that is very useful for producing many things seems to be carcinogenic. There are bodies like the [World Health Organization] that have accepted that there is sufficient evidence that [formaldehyde] is carcinogenic. It not only causes a very rare cancer, nasopharyngeal cancer, but also leukemia. That means there is, in essence, a problem and this chemical should be replaced.”

According to the Hauptmann et al study of embalmers, the mortality rate from myeloid leukemia increased significantly with the number of years of embalming (*P* for trend, .020) and with increasing peak formaldehyde exposure (*P* for trend, .036). Compared with study subjects who had conducted fewer than 500 lifetime embalmings, mortality from myeloid leukemia was found to be elevated among those who performed embalmings for more than 34 years (odds ratio [OR], 3.9; 95% confidence interval [95% CI], 1.2-12.5 [*P* = .024]), those who performed more than 3068 embalmings (OR, 3.0; 95% CI, 1.0-9.2 [*P* = .057]), and those whose estimated cumulative formaldehyde exposure exceeded 9253 parts per million (ppm)-hours (OR, 3.1; 95% CI, 1.0-9.6 [*P* = .047]).

In 2003, Dr. Hauptmann’s team conducted a cohort study of industrial workers who worked with formaldehyde in manufacturing and production (*J Natl Cancer Inst.* 2003;95:1615-1623). “We also found about a 3-fold risk for those in the highest category of peak exposure to formaldehyde compared to people who had little exposure to formaldehyde. They tripled their risk of dying from myeloid leukemia,” he says.

“So far, we only have studies among people who are occupationally exposed,” adds Dr. Hauptmann. “Often people who are occupationally exposed have higher levels of exposure than people who are environmentally exposed in their homes. Among people who work with formaldehyde, we have now from several different types of work evidence that they carry increased risk if they work long with formaldehyde. That is not trivial.”

**Occupational Exposure**

More than 2 million workers in the United States are exposed to formaldehyde, including anatomists and pathologists, professionals who are employed in the funeral industry and who handle bodies or biological specimens preserved with formaldehyde, those in the construction industries, and others who use or produce the chemical.

BarbaraJean Magnani, MD, PhD, says there have been improvements in the regulations of exposure limits to formaldehyde and solutions that contain it, such as formalin. Among pathologists, steps have been taken to monitor and limit laboratory workers’ exposure to formaldehyde, she notes.

Formaldehyde vapor concentrations are monitored in surgical pathology gross dissection rooms, in histology labo-
 laboratories, and in the autopsy room. “If those initial monitorings exceed 0.5 parts per million [ppm; 8-hour, time-weighted exposure], then you need to take action” to reduce exposure, she explains. “Or, if in a single short-term average exposure limit, then [concentrations] can’t exceed greater than 2.0 parts per million.” Dr. Magnani is associate professor of pathology at Tufts University School of Medicine in Boston, Massachusetts, and chair of the Toxicology Resource Committee at the College of American Pathologists in Northfield, Illinois.

Formaldehyde exposures in the range of 0.1 to 0.5 ppm have been linked with airway irritation and allergic-type reactions. According to the US Environmental Protection Agency (EPA) Web site, “effects seen from exposure to high levels of formaldehyde in humans are coughing, wheezing, chest pains, and bronchitis.”

Evidence regarding the carcinogenicity of formaldehyde has been accumulating over time, says Michael Thun, MD, vice president emeritus of epidemiology and surveillance research at the American Cancer Society, and adjunct professor of epidemiology at the Emory Winship Cancer Center and the Rollins School of Public Health in Atlanta, Georgia.

In 2004, the International Agency for Research on Cancer (IARC) classified the evidence as “sufficient” linking formaldehyde with nasopharyngeal cancer, based on studies in humans and animals. Then “in October 2009, IARC upgraded the classification by adding leukemia as a second site for which the evidence for a causal relationship in humans was designated as sufficient,” notes Dr. Thun. “This is important, because myeloid leukemia is a much more common cancer in the US than nasopharyngeal cancer. The regulatory agencies are still digesting the ramifications of this change for quantitative risk assessments and regulatory limits. The EPA still has formaldehyde classified as a ‘probable’ human carcinogen.”

“This issue has major potential implications for consumer products and building materials in new homes,” says Dr. Thun. The EPA cites 1 survey demonstrating a range of formaldehyde levels from 0.10 to 3.68 ppm in homes. “Although individuals can reduce exposure to formaldehyde from building materials such as particle board, medium-density particle board, and hardwood plywood by buying higher quality materials, a more systematic approach is needed,” Dr. Thun adds.

Dr. Hauptmann says several alternatives to formaldehyde have been developed for many industrial and biological applications and that it is important to evaluate the toxicity of these substitutes and to recommend the use of those which are found to be safer, especially in situations in which protective equipment is not effective or efficient in preventing exposure to hazardous levels of formaldehyde.

**Exposure Limits**

According to the EPA Web site, “The Agency for Toxic Substances and Disease Registry has established a chronic inhalation minimal risk level [MRL] of 0.003 ppm based on respiratory effects in humans.” The MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration.

The Occupational Safety and Health Administration (OSHA) defines the current “action level” for formaldehyde exposure at a concentration of 0.5 ppm calculated as an 8-hour, time-weighted average (TWA). OSHA requires that employers “shall assure that no employee is exposed to an airborne concentration of formaldehyde which exceeds 0.75 ppm as an 8-hour TWA.” OSHA currently sets the short-term exposure limit at 2.0 ppm for 15 minutes.

The National Institute for Occupational Safety and Health’s recommended exposure limit is a TWA of 0.016 ppm, with a ceiling limit of 0.1 ppm TWA exposure for 15 minutes.