

Formaldehyde Council, Inc. (FCI)

Questions and Answers on Formaldehyde Epidemiology Studies

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The Coggon Study

1. What does the Coggon study address?

Coggon and coworkers in the U.K. studied over 14,000 workers exposed to formaldehyde in industrial workplaces. Their research was published in the *Journal of the National Cancer Institute* (November, 2003 issue).

2. What are the findings in the Coggon paper?

The researchers reported no significant findings. Specifically, the study found no excesses of either leukemia or nasal or nasopharyngeal cancer in the exposed workers.

The authors conclude: "The evidence for human carcinogenicity of formaldehyde remains unconvincing."

The Hauptmann Study

1. What does the Hauptmann study address?

Hauptmann and coworkers at the National Cancer Institute examined causes of death in workers at ten U.S. plants producing or using formaldehyde or formaldehyde resins.

The study examined only workers who began work between 1938 and 1966, and followed them through 1994. Nearly all of the exposure studied occurred prior to 1980.

Hauptmann and colleagues published a paper in the *Journal of the National Cancer Institute* (November, 2003 issue) that addresses only the study findings regarding leukemia. Other findings from this study will be reported in a separate paper that is still being prepared (see discussion below).

2. What are the findings in the Hauptmann paper?

The authors suggest caution in drawing any definitive conclusion at this time.

The paper reports that higher levels of peak or average formaldehyde exposure are associated with leukemia. However, the researchers did not find an association between leukemia and cumulative exposure or duration of exposure to formaldehyde. And overall, they found less leukemia or other blood and bone marrow cancer deaths in exposed workers than expected compared to rates in the general population.

The Hauptmann paper notes that a similar study of British plant workers (the Coggon study) did not find leukemia associated with formaldehyde exposure.

3. More specifically, what did the researchers find?

The study population included over 25,000 workers who began work between 1938 and 1966. The researchers examined causes of death listed on death certificates for any of those workers who have died.

Hauptmann did not update the exposure classification work, which was done for a 1986 publication reporting on the same group of workers. Exposure classification is always difficult, especially when researchers try to reconstruct worker exposure levels from many decades ago. All peak exposure values were based on estimates, not actual measured values.

In comparison to the general population, the rates of cancer death in the exposed workers were consistently less than expected. However, there was a higher risk of death from leukemia or possibly other cancers of the bone marrow and blood system to workers at higher peak or average exposure levels when compared to lower-exposed workers.

More specifically, the study uses two types of comparisons:

- General Population Comparison. The study compares causes of death among the exposed workers to causes of death expected in the general population based on national rates. This comparison shows fewer deaths from cancer and other disease in the exposed workers than expected.
 - There were 65 workers exposed to formaldehyde who have died from leukemia among the 25,619 workers studied. This is actually fewer than would be expected in the general population.
 - In the general category of “lymphohematopoietic system cancers”—that is, cancers of the bone marrow and blood system—the study also found fewer cancers observed in workers than expected when compared to the general U.S. population.
 - Deaths from all causes, all cancers, all solid malignant tumors, circulatory diseases, and respiratory diseases occurred at lower rates than expected in both exposed and unexposed workers.
- Comparisons to Other Workers in the Study. The study also compares more highly exposed workers in the study to lower-exposed workers within the study, using four measures of

exposure -- peak, average, and cumulative exposure and duration of exposure. Two of those four measures suggested an association between deaths from leukemia or total lymphohematopoietic cancers (cancers of the blood and bone marrow system) and higher measures of formaldehyde exposure.

- The study found an association between leukemia and high peak or average formaldehyde exposure compared to the internal comparison groups of low-exposed or unexposed workers.
- The study did not find association between cumulative exposure or duration of exposure to formaldehyde and leukemia.

4. What is your assessment of the study?

The Formaldehyde Epidemiology, Toxicology & Environmental Group, Inc. (a predecessor to FCI), on behalf of the plants that participated in the study, assembled a panel of distinguished and independent experts to review a draft of the Hauptmann paper. The peer review group raised significant questions, which were detailed in a document submitted to the authors and summarized in a Letter to the Editor sent to the *Journal of the National Cancer Institute*.

Our peer reviewers concentrated on determining whether the suggested association with leukemia is valid. At this time, it does not appear justified to say leukemia is causally related to formaldehyde, but we take any finding regarding worker health seriously, and research will continue.

The Pinkerton Study

1. What does the Pinkerton study address?

Pinkerton and coworkers at the National Institute for Occupational Safety and Health (NIOSH) examined causes of death in workers at three U.S. garment plants that treated fabrics with formaldehyde resins to impart crease resistance.

The study examined workers who were exposed to formaldehyde for at least three months after formaldehyde was introduced in 1959. The NIOSH study population included roughly 11,000 workers.

2. What are the findings?

The authors caution that the results are not conclusive.

There seemed to be an increased risk of deaths from myeloid leukemia among workers with 10 or more years of formaldehyde exposure compared to the general population.

The authors found no association with cancers of the respiratory tract, nasal cavity, or nasopharynx. Their data show an increased risk in cancer of the buccal cavity but they pointed out the results are weak and not supported by other studies.

The authors note that a similar study of British plant workers (Coggon) did not find leukemia associated with formaldehyde exposure.

Interpreting the Studies

1. Do you agree with the suggestion that formaldehyde may cause leukemia?

The three studies, all by government researchers, are conflicting. They are not conclusive, either individually or collectively. However, we are certainly very interested in reviewing any study concerning employee health and safety.

An association between formaldehyde and leukemia is inconsistent with previous studies and our understanding of the biology of how formaldehyde acts in the body. There is a substantial amount of scientific evidence about how formaldehyde acts in the body. Inhaled formaldehyde is expected to act on the upper respiratory tract, not at distant sites in the body.

In addition, excesses of leukemia or other lymphohematopoietic cancers were not seen in the earlier study of the population studied by Hauptmann, and have not previously been observed in industrial workers. The findings in the Hauptmann study are internally inconsistent, with some measures suggesting an association and not others.

Hauptmann and colleagues at NCI have proposed further research to investigate their findings. Industry intends to cooperate with NCI in identifying additional research needs. Both NCI and the industry will further analyze the data from the three studies.

In any event, almost all of the exposure studied by all these researchers occurred during the 1940s, 1950s, 1960s, and 1970s. The levels of formaldehyde exposure in today's workplaces have declined substantially. So while all these studies are important, particularly in a historical sense, they should be evaluated in the context of current exposure levels.

2. All three studies sound very thorough because they covered thousands of workers over many years. Doesn't that make them authoritative studies?

The studies are important, but they are pieces of a large body of scientific evidence. Epidemiologists examine the entire body of literature before drawing conclusions about causation. Hauptmann and coworkers cautioned against drawing any definitive conclusion at this time, and proposed further research. Pinkerton and colleagues stated that their results are inconclusive. Coggon and his coauthors concluded that the evidence for human carcinogenicity of formaldehyde remains unconvincing.

3. What have prior studies shown, and how are these studies different?

Small excesses of leukemia have previously been observed in studies of embalmers, pathologists and anatomists, but a link between those observations and formaldehyde has been considered biologically implausible. Researchers did not expect to find increased leukemia in industrial workers. The results were unanticipated in light of our understanding of the biology of how formaldehyde acts in the body.

Other Types of Cancer

1. What about Nasopharyngeal Cancer?

Earlier studies have found a possible link between formaldehyde exposure and nasopharyngeal cancers.

- Hauptmann and colleagues will address this issue in another forthcoming paper, but have told us that the results are generally consistent with prior results finding an excess of nasopharyngeal cancer in exposed workers.
- The Coggon and Pinkerton studies did not find an excess of nasopharyngeal cancer.
- Marsh and coworkers investigated an excess of nasopharyngeal cancer at one of the plants in the Hauptmann study, and found that it was not associated with formaldehyde. The Marsh paper is in press.

Evaluating prior studies, experts and regulators have focused on nasopharyngeal cancers specifically or on potential respiratory cancer generally. A recent review by the Chemical Industry Institute of Toxicology (CIIT) noted that increases in tumors at sites other than the respiratory tract have been reported sporadically, with little consistent pattern.

In 1999, the CIIT, with input from the Environmental Protection Agency, Health Canada and peer reviewers, performed a thorough evaluation of twenty years of formaldehyde research. Using modeling based on human and animal data, CIIT found negligible risk of respiratory cancer to either employees who may be exposed in the workplace or people exposed to the lower levels found in the environment.

Numerous other authoritative groups from around the globe, including the Organisation for Economic Cooperation and Development (OECD), the German MAK Commission (which sets occupational exposure levels), and the U.S. Consumer Product Safety Commission have reached similar conclusions.

The recent OECD and World Health Organization reviews found that formaldehyde is unlikely to cause cancer at doses that are not cytotoxic (high enough to kill cells). Thus, cancer is not expected to occur at the levels to which humans are exposed.

Current Workers, OSHA Standards, General Concerns

1. What does all this mean to employees in today's workplace?

Authors of all the new or forthcoming papers cautioned against drawing any definitive conclusions at this time, but we will closely review any study concerning employee health and safety.

All of the epidemiologic studies looked at workers who were exposed decades ago. Levels of formaldehyde in the workplace have declined dramatically, and appropriate safeguards are in place. The levels of formaldehyde exposure in today's workplaces have declined substantially since the 1930s, 1940s, 1950s, 1960s and 1970s. Thus, the work conditions represented by the time period of the study do not reflect experience under today's working conditions.

Based on a vast body of research, we are confident that workers are safe. Formaldehyde is one of the most extensively studied chemicals in industrial use.

2. OSHA reduced the occupational exposure limits twice. With these new studies, should OSHA consider lowering the allowable exposure even more?

Based on the enormous amount of other research on formaldehyde and the input from our expert peer reviewers, we believe the current OSHA standards are appropriate, and we are confident that our workers are safe.

3. Why have exposure levels declined?

Levels of formaldehyde in the workplace have declined dramatically over the last several decades in response to advances in technology, improvements in industrial hygiene, and OSHA workplace exposure limits. Like a lot of chemicals, improved manufacturing technology has resulted in lower emitting products. Employers have continued to improve industrial hygiene measures, and industry has also worked with OSHA and labor to set appropriate protective standards.

4. How will these studies impact non-occupationally exposed individuals?

The levels to which workers were exposed in the 1930s, '40s, '50s, 60s and '70s were substantially higher than today's occupational exposures, and *many, many* times higher than the levels to which the general population is exposed. We do not expect to see any increased cancer in the general population.

5. Are there other resources available describing the risks associated with formaldehyde?

There are thousands of published papers on formaldehyde. One of the most complete and authoritative sources of information is a comprehensive review done by the CIIT Centers for Health Research with input from the US EPA and Health Canada. That work is addressed in a number of publications, and an executive summary can be found at www.ciit.org/newsrs/formaldehydesummary.

General Questions

1. What is FCI?

The Formaldehyde Council, Inc. (FCI) is a group of leading formaldehyde producers and users. FCI is dedicated to promoting the development and use of science in understanding the effects of formaldehyde and highlighting the many societal benefits formaldehyde provides.

2. What companies belong to FCI?

Members include:

Borden Chemical, Inc
Celanese, Ltd.
Cytac Industries Inc.
Dynea
DuPont Engineering Polymers
Georgia-Pacific Corp.
Surface Specialities, Inc

3. How is formaldehyde used?

Formaldehyde serves many purposes in products. It is used as a part of:

- the glue or adhesive in pressed wood products (particleboard, hardwood plywood, and medium density fiberboard (MDF));
- preservatives in some paints, coatings, and cosmetics;
- the coating that provides permanent press quality to some fabrics and draperies; and
- the finish used to coat paper products.

4. What are the general objectives of epidemiology studies?

Epidemiology studies look for patterns of disease or causes of death in human populations.

5. How do epidemiologists evaluate causation?

Epidemiologists look at the entire body of literature, not any single study, in order to evaluate causation. An epidemiology study examines the statistical association between exposure and causes of death. Just because a study finds an association (i.e., that two things occur together in the same population) does not mean that one thing causes the other.

Epidemiologists look at a number of factors in order to evaluate whether an exposure causes cancer, including the strength and statistical significance of any association, whether the risk increases with higher dose, whether current biologic knowledge supports the finding, the time sequence of events (exposure occurs before disease), and whether other similar studies found similar results.

