CertainTeed	Date November 1, 1977	To See Below	Location and mail code
Subject Vinyl Chloride Research Program Manufacturing Chemists Association (MCA)		From J. G. Heil JGH	Location and mail code VF P&PG 2B

TO: W. A. Krivsky--VF P&PG 2B
J. G. Kelso--VF P&PG 2B
T. A. Dougherty--VF P&PG 2B

CC: W. A. Shumaker--VF P&PG 2B

Background

CertainTeed joined the Vinyl Chloride Research Program of the MCA when established in 1974. The Technical Task Group on Vinyl Chloride Research is composed of MCA members and other companies involved in the synthesis and polymerization of vinyl chloride.

The purpose of the Technical Task Group was to support and accelerate research projects that would assure the safety of workers and those who live in the nearby communities of the VCM/PVC manufacturing plants.

Studies Funded by MCA

A number of studies have been funded and several important studies have been completed. The purpose, type, results and/or status of the studies will be discussed.

Teratology

"The Effects of Maternally Inhaled Vinyl Chloride on Embryonal and Fetal Development in Mice, Rats and Rabbits," Dr. B. Schwetz, et al, Dow Chemical.

The pregnant females (mice, rats and rabbits) were exposed to VCM levels of 50, 500 and 2500 ppm to determine the effects on embryonal and fetal development. Although the doses were high enough to cause maternal toxicity, there was not any teratogenesis in any of the species, nor did the levels cause any fetal or embryonal toxicity.

Chronic Inhalation Studies

"Chronic Vapor Inhalation Toxicity Study with Vinyl Chloride in Rats, Mice and Hamsters." Dr. M. L. Keplinger, Industrial Bio-Test Laboratories.

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This long term study, begun in 1973 over the animal's lifetime, exposed 200 of each animal to VCM levels of 50, 250 and 2500 ppm. Partial results of the test have been published, but the final report is not expected until next year. The purpose of the studies is to determine the existence of threshold levels.

Metabolic Studies

"Hepatic Macromolecular Binding Following Exposure to Vinyl Chloride" April 5, 1977, P. G. Watanabe, et al, Dow Chemical.

Metabolites are formed when the body biotransforms vinyl chloride to detoxify the chemical. The study investigated the dose response of the vinyl chloride and the resultant metabolites. The types and levels of reactive metabolites change with the increase of dose levels.

"Resolution of Dose-Response Toxicity Data for Chemicals Requiring Metabolic Activation: Example - Vinyl Chloride by P. J. Gehring, et al, July 12, 1977.

The toxicity of many chemicals results from the biotransformation products formed from the chemical rather than to the chemical per se. The production of a toxic metabolite is dependent upon enzymatically mediated reactions.

Since these reactions are concentration dependent and saturable, toxicity resulting from exposures to chemicals requiring activation to a toxic form cannot be related directly to the magnitude of exposure to dose. It is necessary to determine the amount of the chemical undergoing biotransformation as a function of dose or exposure before a meaningful dose response relationship can be established.

Using the data from the tests on rats, the results were extrapolated to man with the conclusion that for daily eight hour exposure to 1 ppm, the predicted incidence of angiosarcoma would be 1.5 in 100,000,000 which is less than expected to occur spontaneously in the population. This is conservative since there is evidence that a practical threshold exists for both rats and man.

"Summary of the Studies Conducted on the Pharamcokinetics/Metalbolism of Vinyl Chloride in Rats," May 31, 1977 by P. G. Watanabe, et al, Dow Chemical.

The important statement in this study suggests that the body readily detoxifies the reactive metabolites under 50 ppm exposures showing that a threshold or nontoxic level does exist for vinyl chloride.

Epidemiology

Equitable Environmental Health, the final report of VCM/PVC industry workers, will be released shortly for approval. The study covers over 10,000 workers in the industry, going back to 1942.

University of Louisville Studies

A seven part, three year program began in 1976. The first annual report was received in September, the status of each proposal is discussed below.

Proposal I - Immunological Systems for the Detection of Vinyl Chloride and Other Chemical Injury. The purpose of this three part study was to determine early signs of cancer development or identify high risk groups.

Part (a) - A cohort of vinyl chloride and normal workers, diseased and undiseased were analyzed to determine if lymphocytes cells, capable of eliminating growths and tumors, exist in the cohort. The data is being prepared.

Part (b) - The purpose of this study is to screen employees to determine abnormal genotypes that would predispose them to cancer after occupational exposures which are harmless to normal genotypes. This research is centered on HLA tissue typing as a genetic marker for identification of VC injury and angiosarcoma. One interesting item that will be followed up is that a HLA-A27 antigen has been found more often in workers suspected of having the occupational disease, asbestosis.

Part (c) - It is theorized that the body creates a specific antigen to combat specific tumor types. The research is aimed at finding the specific antigen for angiosarcoma.

Proposal II - Biochemical Enzymatic Systems for the Detection of Vinyl Chloride Injury and Cancer Development in Industrial Workers.

The purposes of the enzyme studies are to determine if a correlation exists between physical and biochemical changes prior to and during the development of cancer. This study covers humans exposed to VCM and nonexposed workers. Backup animal studies are also included that exposed rats to VCM levels of 10,000-20,000 ppm.

Proposal III - Tissue and Urinary Glycosaminoglycan Changes Related to Vinyl Chloride Injury: Use and Early Detection and Diagnosis.

A number of tests and studies have been performed to determine glycosaminoglycan patterns in normal, VC exposed and diseased individuals with cirrhosis, hepatitis and alcoholic liver injury. Preliminary data suggests that urinary excretion patterns for vinyl chloride injury are distinctly different from other frequently found non-occupational illnesses.

These studies are expected to result in specific tests for early liver damage that would become part of the routine medical screening.

Proposal IV - Electron Microscopic Evaluation of Liver Injury from Vinyl Chloride Workers.

The purpose of this research is to determine the amount of liver damage determined in biopsies of 80 VCM workers. Early results suggest that VCM liver damage differs from other non-occupational liver disease.

Proposal V - Multivariant Analysis of Biological End-Products and Vinyl Chloride Metabolite Synthesis.

When vinyl chloride enters the body, it is metabolized or biotransformed in the detoxification process. The resulting products are known as metabolites and thought to be the actual carcinogens. The purpose of the study is to detect, formulate and isolate the metabolites and then test each for its carcinogenicity. Hopefully, this study will determine actual carcinogens and the threshold levels.

Proposal VI - Analysis and Identification of the Carcinogenic Potential of Industrial Chemicals.

A number of chemicals, including the VCM induced metabolites are being studied to determine the mutagenesis and carcinogensis with the microbial assay method. This screening technique will isolate the most potentially dangerous chemicals.

Proposal VII - Tissue Antigens and Antibodies in the Detection of Vinyl Chloride Injury.

This is a screening technique to determine if specific antigenic system can be utilized for early detection of VCM caused liver damage. This study will utilize some of the results of the earlier studies.

CERTAINTEED'S COMMITMENT TO THE MCA RESEARCH PROGRAM

Year	Funds Committed	Remarks
1974	$4,266	Paid
1975	3,578	Paid
1976-77	4,407	One half of amount paid in 1976 Second installment due in 1977
1977-78	4,770 proposal	Monies will be due in 2 installments 1977 and 1978

The assessments are based on VCM/PVC production for each company.

Benefits to CertainTeed

The results of the University of Louisville studies should provide the following results:

1. Determine threshold levels of safe exposure.
2. Determine if certain individuals are genetically predisposed to cancer.
3. Establish early diagnostic techniques or useful medical screening tests.
4. Establish tests that can differentiate vinyl chloride induced liver damage and other liver damage caused by cirrhosis, hepatitis, alcohol, etc.
5. Determine the mechanism and cause of angiosarcoma.

Summary

All of the proposed studies by the University of Louisville are specifically related to vinyl chloride even though the MCA letter described each phase of the program in general terms.

Unfortunately, the government regulatory agencies, EPA/OSHA, have taken a nonscientific political stand with their one molecule, one hit theory that with a carcinogen there is not any safe threshold level, therefore, exposures must be reduced to nondetectable limits.

It is only with scientifically based data provided with MCA type sponsored studies will industry hope to reach a defensible compromise.

Under present circumstances, with available information, any employee of the polymer and PVC plants who suffers liver disease could claim, under Worker's Compensation, occupational injury. With present methods/tests it would be difficult to dispute that limited VCM exposure did not contribute to or aggravate the disease, thus making CertainTeed liable. If test methods are available that could relate liver damage to specific causes, the savings to CertainTeed would be tremendous.

If CertainTeed does not support the MCA studies, an important and only current source of PVC/VCM information would be lost.

Recommendation

P&PG should continue to support the MCA, University of Louisville Studies. For a relatively small sum, the potential benefits for protecting employees, reducing risks and future compensation costs, will far exceed our investment.

The MCA commitment form is attached.