

AN EPIDEMIOLOGIC STUDY IN THE CHEMISTRY INDUSTRY

A STUDY PROPOSAL

A. INTRODUCTION

This proposal outlines an epidemiologic study to be undertaken to evaluate the role of vinyl chloride in the development of cancer. The results of Phase I would be available within six months; results of Phase II, which would be conducted concurrently with Phase I, would be available by October 1974. Phases III and IV would be undertaken only if an association between the chemical and cancer was suggested in the data of Phase II. Only Phase I and Phase II are included in this proposal and tentative budget.

B. PHASE I - DESCRIPTION OF CAUSES OF DEATH IN CHEMISTRY INDUSTRY EMPLOYEES

1. Outline: The causes of death of employees who worked in the 50 plants under study and who died in approximately the past five years would be determined. The percentage who died from all cancer and from specific sites of cancer, e.g. lung cancer, would be calculated. These percentages would be compared to the percentages expected based on U.S. Vital Statistics rates. This phase should start immediately.
2. Data Collection: Each company would be responsible for collecting death certificates and sending them to the Study Center at the Harvard School of Public Health. Certificates would be collected for persons who died while still employed as well as for former pensioned employees.
3. No attempt would be made to identify deaths among terminated employees. The mechanism of collection would likely differ among companies. The most efficient mechanism would be to request a Xerox copy of each death certificate from the insurance company which handles death benefits.

If a company maintains a file of death certificates on deceased employees, copies could be obtained from this file rather than through the insurance company. If neither the company nor insurance company maintains a past file of death certificates, they would be obtained from State Health Departments, as outlined in Phase II.

It would be desirable, but not mandatory, in this phase to assemble death certificates for 5-10 fairly large plants which do not use vinyl chloride, but are located in the same geographic area as the 50 plants under study. The employees of these plants would be assumed to be similar to those of the plants under study, except for exposure to vinyl chloride.

3. Data analysis: As certificates are received at the Study Center, relevant information will be abstracted, the cause of death will be coded, and the data will be placed on a computer punch card. Five months after the start

of the study, the percentage of employees dying from each cause of death will be calculated. Earlier analysis will be performed if sufficient certificates are received.

The above observed percentages will be compared to expected percentages based on U.S. Vital Statistics data. In the calculation of these expected percentages, age, year, race and sex will be taken into account. Thus, the expected percentages will reflect the cancer distribution that would have occurred in a comparable, essentially non-industrial, sample of the United States population. This procedure has been used in several studies at the Harvard School of Public Health.

If death certificates have been collected for the 5-10 comparison plants, the cancer distribution for deceased employees from these plants will be computed and compared to that of the study plants.

4. Interpretation of the data: If a specific cause of death, for example lung cancer, is found to have occurred with increased frequency among the employees, this would raise suspicion that some condition of employment at the plant is causing the cancer. However, it would be relatively weak evidence, since it is possible that some underlying characteristics of the employees is responsible for the increased occurrence of lung cancer, for example, cigarette smoking. Thus, it would be helpful to have a comparison series, since the characteristics of the employees in these plants would be similar to those in the study plants. If excess lung cancer is also observed among employees of the comparison plants, it would be less likely that a condition of employment was responsible.

No firm conclusions could be based on the results of Phase I, since no exposure data on individuals would be available. Thus, even if workers as a group in vinyl chloride plants have excess lung cancer, it is not certain that vinyl chloride is causing the cancer.

5. Size of study: At this time it is difficult to estimate the number of death certificates that would be available for Phase I. If, on the average, four employees (active or pensioned) die per year at each of the 50 plants, there would have been 1,000 deaths during the past five years. A minimum acceptable number would be around 500.

C. PHASE II - COMPARISON BETWEEN SPECIFIC CANCERS AND EXPOSURE TO VINYL CHLORIDE

1. Outline: Two primary items of information would be collected on each deceased employee - cause of death and exposure to vinyl chloride. If employees who die from, for example, lung cancer, have been exposed to vinyl chloride more often than employees who die from other causes, vinyl chloride would be suspected of causing the cancer. The exposure history of employees dying over the past 25-30 years would be determined.

2. Data collection: For employees who died during the past five years, the death certificates collected in Phase I would be used. For other deceased employees, each company (or plant) would identify the date and location of death for as many employees as possible. The Study Center would collect these lists and would obtain death certificates from the appropriate State Health Department.

Next, the vinyl chloride exposure history of each of these employees will be determined. A questionnaire would be sent to each plant listing the name (but not the cause of death) of each deceased employee. A request would be made to give an indication as to the degree and length of exposure to vinyl chloride.

This aspect of the study would be the most difficult. The determination of a employee's past exposure history will be imprecise. Two methods seem feasible: (1) a senior employee in each plant or department would be asked to estimate the exposure information. This would work only if he knew the deceased employee. (2) The usual department and job of each employee could be ascertained from personnel records. Some a priori criteria would be set up to estimate past exposure to vinyl chloride in each department.

The details of this part of the study would have to be worked out with each plant. It is unlikely that precise exposure information would be obtained. However, since the person who estimates the exposure would be unaware of the cause of death, no bias would be expected to be introduced.

3. Data analysis: For each cause of death, the distribution of exposure to vinyl chloride will be determined. Age, race, sex and duration of employment will be taken into account. If vinyl chloride is causing any disease, persons dying of that disease would have been more heavily exposed than persons dying from other causes. If vinyl chloride is not associated with a specific cause of death, the distribution of exposure would be random.
4. Size of study: It is desirable to have Phase II be as large as possible. The determination of exposure to vinyl chloride will be relatively imprecise, and large numbers will to a degree accomodate this imprecision. Also, there are always problems in locating death certificates for employees who are known to be dead. Therefore, to the extent possible, death certificates should be collected for the past 25 years or so. The limit as to how far back to go will depend upon the availability and content of personnel records and/or the presence of a senior employee who knew many of the employees. There will likely be a great diversity among plants. A desirable number would be around 5,000 deceased employees.

5. Interpretation of the data: If vinyl chloride and specific cancers are not found to be associated with each other, belief that vinyl chloride is safe would be strengthened. Any positive association between vinyl chloride and a cancer would be suggestive evidence that the vinyl chloride is causing the cancer. While it is possible that there is some unknown factor which is causing the association, this would seem unlikely, assuming that within each plant the employees are relatively similar except for conditions of employment.

Any positive association between vinyl chloride and cancer would be examined in terms of calendar time. It would be expected that employees exposed many years ago would have been at greater risk of developing cancer than those of only a few years ago. If no excess cancer is noted among recent employees, this would be strong evidence that current standards of exposure are safe.

6. Duration: Preliminary results would be available in October 1974. Further analyses and presentation of the data would extend into early 1975. The total time for Phase I and Phase II would be two years.

D. PHASES III AND IV

The implementation of these Phases will depend upon the outcome of Phase II. If no evidence is found to suggest an association between vinyl chloride and a cancer, the study will cease.

If, however, there is evidence from Phase II that a vinyl chloride is associated with cancer, further data may be needed. Phase III would determine cancer rates of past employees who were exposed to vinyl chloride. Phase IV would involve clinical examination and follow-up of currently exposed employees.

These phases are not included in the present proposal. Should they become necessary, new commitments would be expected both from the Manufacturing Chemists Association and the Harvard School of Public Health.

E. HUMAN REQUIREMENTS

1. MCA - The details of the study would be worked out in collaboration with one person from the MCA. He would serve as a liaison between the companies and the H. S. P. H.
2. The 19 participating companies - There should be an overall coordinator who would know all the details of the study. He would be responsible for locating individuals at each plant who would collect the desired information. However, he should not be involved in the data collection. The Director of Industrial Hygiene or his representative would seem to be a logical choice for this position.

3. The 50 participating plants

- a. Collector of death certificates - This person would either be at the company or plant level, depending upon local procedures. In Phase I, he would be responsible for contacting the insurance companies to obtain the desired death certificates, or would arrange to have them collected locally. In Phase II, he would be responsible for assembling lists of names of deceased employees to be sent to the Study Center. He should not be aware of the reason for the study, and specifically should not know the exposure histories of the employees, so that the collection of death certificates will be unbiased.
- b. Collector of exposure information - this person will receive lists of names from the Study Center and will be responsible for determining the exposure information as outlined above. He should not be aware of the reason for the study, and specifically should not know the cause of death of the employees.

4. Harvard School of Public Health (See attached curricula vitae)

- a. Dr. Richard Monson - Assistant Professor of Epidemiology. Study Director.
- b. Dr. Lawrence Fine - Research Fellow in Occupational Medicine. Study Assistant Director.
- c. Dr. John Peters - Associate Professor of Occupational Medicine. Study Advisor on Occupational Medicine.
- d. Dr. Jane Worcester - Professor of Biostatistics. Study Advisor on Biostatistics.
- e. A research assistant to be named.

5. Fiscal requirements

	<u>% of time</u>	<u>First year</u>	<u>Second year</u>
1. Dr. Monson	25%	6,300	6,700
2. Dr. Fine	50%	9,600	10,100
3. Dr. Peters	20%	6,000	6,350
4. Dr. Worcester	10%	3,600	3,850
5. Research assistant	100%	8,500	9,000
6. Reimbursement to State Health Depts. and Insurance Companies for death certificates		10,000	0

7. Computer/programming costs	3,000	7,000
8. Travel	4,000	2,500
9. Miscellaneous supplies	500	500
	51,500	46,000
Indirect costs (45%)	23,175	20,700
	74,675	66,700

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