PLAINTIFF'S EXHIBIT

DOW-695

EPIDEMIOLOGY
HEALTH AND ENVIRONMENTAL SCIENCES
DOW CHEMICAL U.S.A.

PROTOCOL STATUS: PRELIMINARY-DRAFT FINAL 7th DRAFT

TITLE: A RETROSPECTIVE COHORT MORTALITY STUDY OF MICHIGAN DIVISION EMPLOYEES WITH PAST WORKPLACE EXPOSURE TO ASBESTOS.

PROTOCOL NUMBER: EPI-DR-00270713-0380 DATE: December 1, 1980

PROPOSED STARTING DATE: January 1, 1981

ESTIMATED DATE OF FINAL REPORT: January 1, 1982

SIGNATURES:

Primary Investigator: _____ 5 Dec 1980
P. F. D. VanPeenen, M.D. (Date)

Approvals: _____ 17 Dec 1980
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Distribution:

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7th DRAFT December 1, 1980

PROPOSAL: EPI-DR-00270713-0380

TITLE: A RETROSPECTIVE COHORT MORTALITY STUDY OF MICHIGAN DIVISION EMPLOYEES WITH PAST WORKPLACE EXPOSURE TO ASBESTOS

SHORT TITLE: Asbestos Cohort

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ABSTRACT

Persons with past workplace exposure to asbestos are known to experience higher mortality from certain diseases, primarily cancer of the lung, than those without such exposure. For this reason, for Dow epidemiological studies designed to measure mortality and morbidity in groups with workplace exposure to certain chemicals, it has been the practice to identify employees within such groups who have worked in the pipe coverers job category and to consider them separately. In addition, pipe coverers are provided special surveillance by the Michigan Division Medical Department. It is not certain, however, that individuals in this job classification at Dow have, in fact experienced increased age-specific mortality or, if so, whether such increases are the same for all pipe coverers. In addition, it is quite possible that persons in other job classifications may have experienced significant asbestos exposures. The purpose of this project is (a) to identify, through industrial hygiene measurements and extrapolations, Michigan Division job classifications with past workplace exposures to asbestos, (b) to attempt to quantify exposures, and (c) to determine whether the overall mortality, mortality from lung cancer, and mortality from the generic rubric of pulmonary diseases of such employees has been significantly greater than that of comparable segments of the U.S. population.

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OBJECTIVE.

To learn which Michigan Division job classifications may have involved workplace exposures to asbestos and to learn whether those in such classifications have experienced increased standard mortality ratios (SMRs) for certain asbestos-associated diseases.

INTRODUCTION.

Michigan Division employees who were pipe coverers prior to 1970 have been considered separately in past epidemiological studies, because it was thought they might be at potential risk to asbestos-related diseases and thus would not be suitable for inclusion in studies of effects of other chemicals. However, it is possible that employees in certain other job classifications were also exposed to asbestos; or that important differences in exposure (and hence in asbestos-related outcomes) exist within the pipe coverers category.

The human health hazards of asbestos exposure have been well documented and publicized in recent years. Prior to recognition of these hazards, the material was widely used for pipe insulation in a variety of industries, including Dow as well as the other members of the chemical industry. As dangers of asbestos exposure became known, use of asbestos was curtailed. At the Michigan Division, use of asbestos for pipe insulation was discontinued between 1969 and 1973 and use of

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asbestos-containing weather-proofing paper was stopped in 1976. Use of asbestos-containing panels of "Transite" for construction was restricted in 1976-1977, and industrial hygiene recommendations for rip out of old pipes, including wetting-down, use of shrouds and use of respirators, have been in effect since the early 70's. Therefore, if, in fact, asbestos exposure in the Michigan Division were associated with health effects, these would be expected in individuals who worked with the material prior to 1970. Furthermore, any associations would be via airborne routes of exposure. Such effects have been anticipated by offering pipe coverers special medical surveillance program examinations. In addition, it has been assumed that the mortality experience of such employees was not typical of other Dow employees, so they have been considered separately in published reports from the U. S. Area Epidemiological group. Our proposed research is specifically designed to test appropriateness of this latter assumption.

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REVIEW OF LITERATURE.

The scientific and lay literature on asbestos-associated diseases is extensive. Current thinking was well presented during a New York Academy of Sciences-sponsored Symposium entitled "International Conference on Health Hazards of Asbestos Exposure", the proceedings of which are available as a monograph (Selikoff and Hammond, 1979). Briefly, airborne asbestos exposures have been associated with asbestosis and with excess mortality from chronic respiratory diseases,

pleural mesotheliomas, and lung cancer; and possibly from other cancers as well. In the case of lung cancer, a dose-related increase has been documented, with "latency" (incubation periods) as long as 40 years for those with low exposure.

Because of the widespread use of asbestos pipe insulation in the past, pipe coverers and some maintenance workers in the chemical industry might be considered at increased risk for death from lung cancer and from mesothelioma. We are unaware of mortality studies specific to the U. S. chemical industry, although there has been at least one morbidity study showing evidence of asbestosis among chemical industry maintenance workers (Lilis et al, 1979). To our knowledge, there are no published Dow reports on the health effects of asbestos, although M.G. Ott assembled a list of pipe coverers and considered any one on the list in a separate category when analyzing data from his epidemiological studies.

APPROACH.

Employees of Michigan Division, who, by nature of their jobs, are considered to have had exposure to asbestos between 1940 - 1970 will be identified: they will make up an "exposed" cohort. The mortality experience of this group will be compared with that of U.S. citizens of similar age, race and sex. On the basis of these comparisons, standard mortality ratios (SMRs) will be calculated according to estimates of exposure intensity, to duration of employment, to length of exposure and to broad job classification.

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EXPOSURE DATA.

Preliminary discussions with Dow industrial hygienists reveals general agreement that employees who worked as pipe coverers prior to 1970 were at least potentially exposed to airborne asbestos fibers, but documentation of intensity of exposure is often lacking (de Gesero, 1969 a + b). In addition, there are few records of whether employees in other jobs may also have experienced potential exposure. Therefore, the first step in this project will be to identify process index numbers, and/or job classification titles and codes, of persons considered to have had potential asbestos exposure prior to 1 January, 1970. The 1970 "cut-off" was selected because (a) this permits a latency of at least 10 years and (b) awareness of the dangers of asbestos and measures to control exposures took place about 1970, so subsequent exposures would be less. Exposures will be justified by recorded measurements where possible, or by extrapolations*. Asbestos exposure should no longer occur, and, indeed, the processes which formerly generated exposures may no longer exist, so historical data and/or extrapolations will be necessary.

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*Current techniques for measuring asbestos fibers were not in use prior to 1970: therefore, historical industrial hygiene data will probably be crude by today's standards. Nevertheless, we will attempt to derive estimates of fibers per ml per year.

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EXPOSED COHORT.

After the appropriate job classifications and index numbers indicative of potential exposure are agreed upon, we will identify the master numbers of incumbents between 1940 and 1970. For this purpose, both computer searches of computerized work histories and hand searches of annual employee census lists will be made. Hand searches may be necessary because computer records of work histories prior to 1970 are incomplete as of this date (July 1, 1980).

Industrial hygiene co-investigators for this project have already done considerable checking into jobs and processes which might have involved potential asbestos exposures. In addition to the broad pipe coverers category, there are other job categories which had such potential exposure in the old Chlor-Alkali, new Chlor-Alkali and Cell Maintenance areas, as well as in power plant operations and maintenance areas (particularly Class A). Exposure for the former was because asbestos is used in electrolytic cell diaphragms and exposure for the latter was because of the refractory material made of asbestos which was found on boilers and turbines.

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CONTROLS.

Standardized mortality ratios (SMRs) are usually constructed by dividing observed deaths by the expected number of deaths which are calculated from the mortality experience of all U. S. citizens of the same age, race and sex. Therefore, U.S. mortality, as available in the Monson computer programs (Monson, 1974), will be used as a source for estimating the kinds and numbers of expected deaths for comparison with those we actually identify.

ANALYSES.

As described above, expected mortality by cause according to age, sex, race and calendar time will be derived from the Monson tapes, using person-years at risk to dying contributed by members of the exposed cohort. This expected number will then be divided into the number of actual observed deaths to derive standard mortality ratios (SMRs). SMRs will be calculated for the entire exposed population, and for several subsets, including pipe coverers and all others; for several levels of intensity of exposure (fibers/ml); several levels of duration of exposure (months on job); and several levels of cumulative exposure (intensity times duration).

It will be necessary to examine duration of exposure independent of date of hire*, since length of employment correlates with increased SMRs in most occupations. Limits used to define the subsets will depend upon the frequency distribution of exposure levels, the determination of which is an objection of this project. SMRs will be calculated for deaths from all causes, from respiratory diseases, from all malignancies and from lung and colon cancers. If we encounter SMRs in any of the above categories which are significantly higher than 1.0, that is with SMRs whose lower 95% confidence limits (Kleinman, 1977) are greater than 1.0, those in the category will be considered at excess mortality risk and will reinforce the decision to consider them separately in future cohort mortality studies.

*For this purpose, we will use the "creditable service date."

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WEAKNESSES OF THIS PROJECT.

A major weakness of this study will be that excess mortality, if present, cannot with certainty be ascribed to asbestos exposure. For example, smoking is known to cause lung cancer and reportedly dramatically increases the rate of lung cancer in those exposed to asbestos (Hammond & Selikoff, 1973). We cannot determine the frequency of cigarette smokers in cohorts of Dow personnel before the time of our health inventory records. However, every indication is that this frequency was at least as high as in the U.S. population: according to recent health inventory data, the percent of never smokers in the Michigan Division was about 23% which compares to 31.5 in all U.S. males aged 21 or older, or to 22.9% in U.S. males aged 45-54 (DHEW, 1979).

It may also be argued that excess mortality, if present, may be due to other risk factors such as socio-economic level (Ott et al, 1976). Although our study is designed to partially answer such arguments by including sufficient subsets to detect dose-response trends, limitations of this study should be recognized at the outset.

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PERSONNEL AND COSTS.

P. F. D. VanPeenen, Michigan Epidemiologist, will be the primary investigator; Ralph R. Cook of the U.S. Epidemology group, and F. L. Sabel and R. A. Olson of Michigan Division Industrial Hygiene Services, will be co-investigators.

Dale Ducommun, M.D., of the Michigan Division Medical Department will be the consultant for clinical aspects. Work history coding will be by L. O. Baker of U. S. Medical; and obtaining and coding death certificates will be by Jan Cartmill, also of U. S. Medical. Time and costs are estimated as follows:

Individual or Item	Hours	Cost ($)
P. F. D. VanPeenen (epidemiologist)	140	7,700
R. R. Cook (epidemiologist)	120	6,600
F. L. Sabel (industrial hygienist)	40	2,200
R. A. Olson (industrial hygienist)	40	2,200
J. B. Cartmill (nosologist)	100	5,500
B. J. Lasich (computer programmer)	60	3,300
G. G. Bond (Monson tapes)	30	1,650
L. O. Baker (data coordinator)	40	2,200
Computer time, keypunching	—	8,000
	Total	$39,350

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TIME FRAME

Since part of the cohort (pipe coverers prior to 1970) is already identified, this project might not take as long as the one year we usually allocate for retrospective cohort mortality studies. However, the availability of death certificates of other groups is presently unknown; and locating individuals considered exposed (other than pipe coverers) may be difficult because of changes in processes and job classifications which have taken place between 1940 and 1970. In addition, the project will compete with others of higher priority. Therefore, a realistic estimate of the time needed from approval of protocol to submission of a written final report is one year. A chart showing the Project Evaluation Review Technique (PERT) is attached as Appendix 1.

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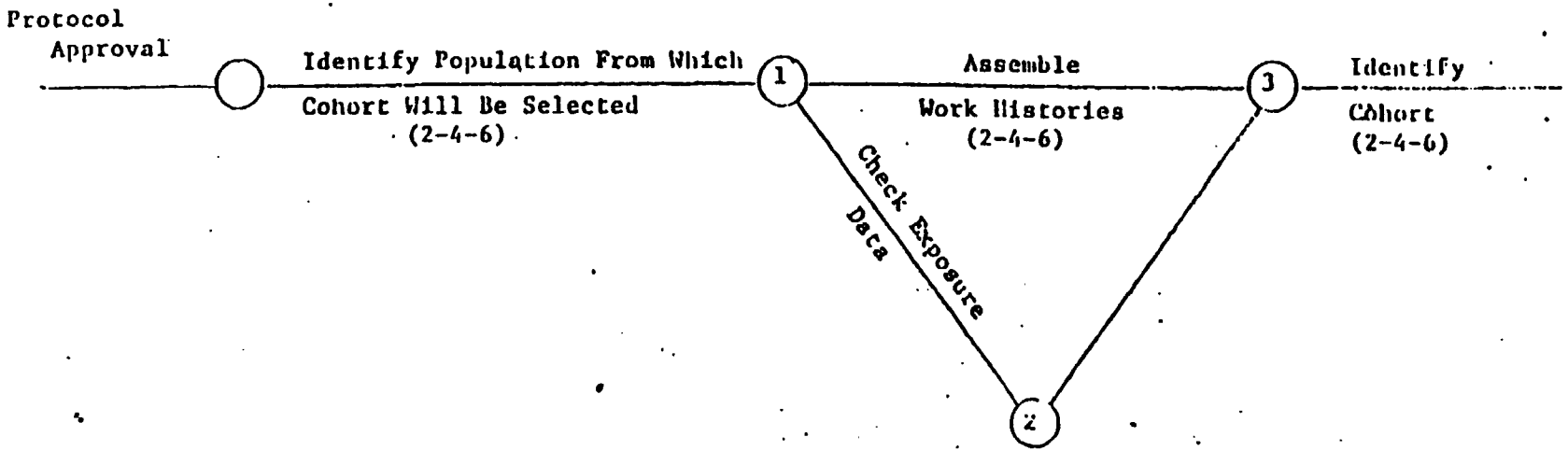
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ASBESTOS COHORT

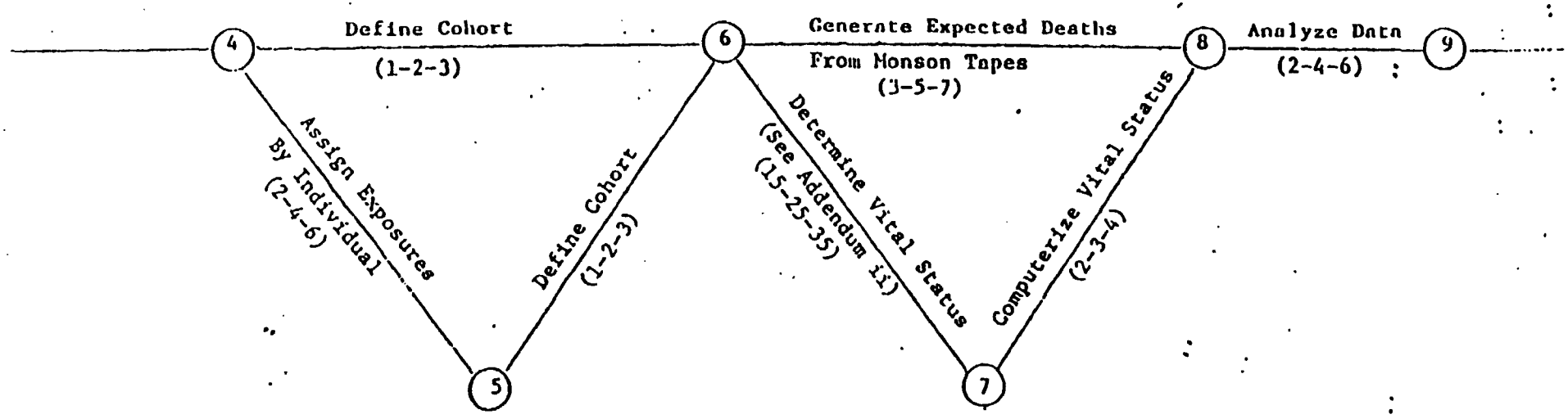
Appendix 1.

PROJECT EVALUATION REVIEW TECHNIQUE (PERT)

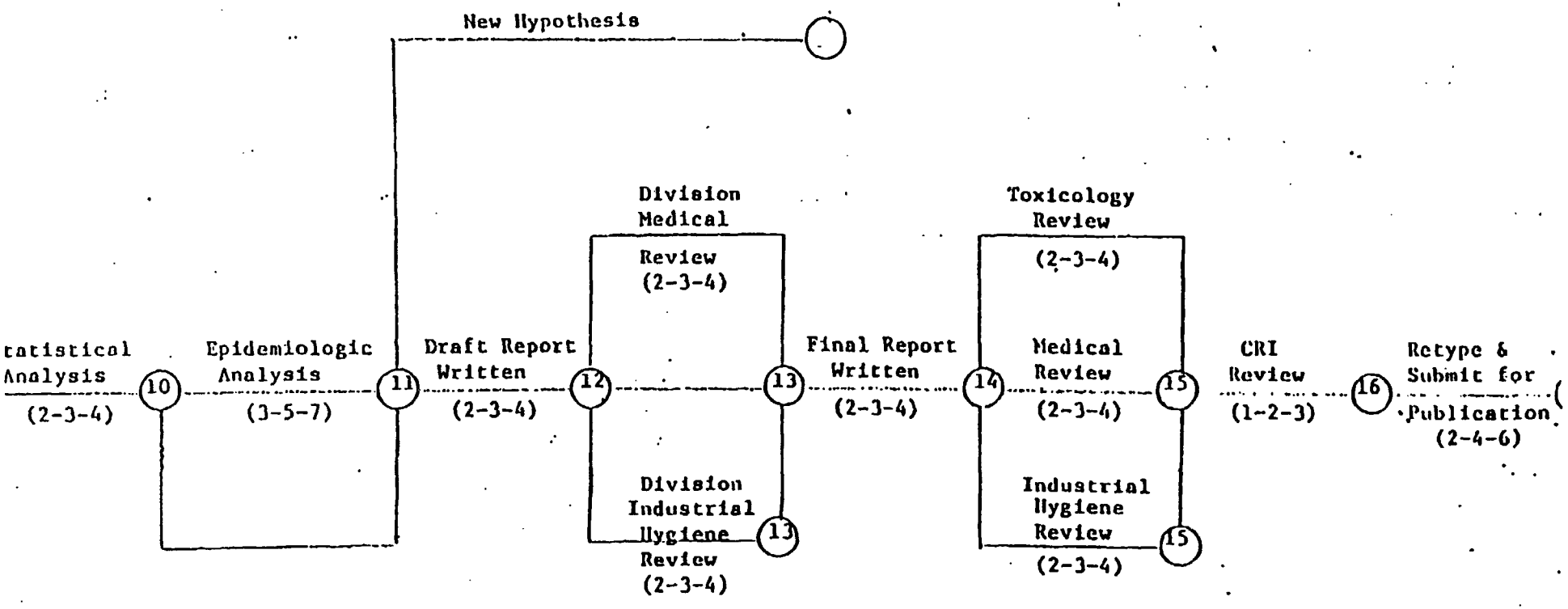
(Time in Weeks: Optimistic-Pragmatic-Pessimistic)



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4
Define Cohort
(1-2-3)
6
Generate Expected Deaths
From Monson Tapes
(3-5-7)
8
Analyze Data
(2-4-6)
9
Assign Exposures
By Individual
(2-4-6)
5
Define Cohort
(1-2-3)
Determine Vital Status
(See Addendum ii)
(15-25-35)
7
Computerize Vital Status
(2-3-4)

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New Hypothesis
tatistical Analysis
(2-3-4)
10
Epidemiologic Analysis
(3-5-7)
11
Draft Report Written
(2-3-4)
12
Division Medical Review
(2-3-4)
13
Division Industrial Hygiene Review
(2-3-4)
13
Final Report Written
(2-3-4)
14
Toxicology Review
(2-3-4)
Medical Review
(2-3-4)
15
Industrial Hygiene Review
(2-3-4)
15
CRI Review
(1-2-3)
16
Retype & Submit for Publication
(2-4-6)

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