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UNIVERSITY of LOUISVILLE

January 12, 1996

Dr. Hasmukh Shah
Chemical Manufacturers Association
1300 Wilson Blvd.
Arlington, VA 22209

RE: Study of Brain Cancer in Vinyl Chloride Exposed Workers

Dear Dr. Shah:

As per our discussion and recent meeting, you will find enclosed an updated budget and more detailed outline of the timetable required for the project originally submitted (10-27-94). This proposed project will provide an analysis of the 45 year retrospective and 20 year prospective occupational surveillance data of an industrial cohort with regards to the occurrence of brain cancer in vinyl chloride exposed workers.

If there is need for any further information or questions, please feel free to call upon us.

Sincerely,



Carlo H. Tamburro, M.D., M.P.H.
Professor of Medicine
Director, Liver Research Center & Laboratory
Professor of Pharmacology & Toxicology
Chief, Division of Occupational Toxicology

CHT:njh

Enclosure

Carlo H. Tamburro, M.D., M.P.H.
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John L. Wong, Ph.D.
Director
Molecular Laboratory for

BFG 01085

BRAIN CANCER STUDY IN VINYL CHLORIDE EXPOSED CHEMICAL WORKERS

This proposed study will provide an updated analysis of the prospective occupational health surveillance program at the B.F. Goodrich Bells Lane plant in Louisville, Kentucky. The purpose of this study is to evaluate the relationship of vinyl chloride exposure and brain cancer occurrence. Upon completion of the six tasks outlined, each brain cancer case will be paired with all available matched controls and each brain cancer case will be evaluated as a case-control study by non-parametric rank order analysis (Greenburg and Tamburro, JOM, 1981). The study's primary aim is to reaffirm our initial observations of an absence of any causal relationship between vinyl chloride exposure and the development of brain cancer.

In order to accomplish this in a timely fashion (within fifteen months), there are seven organizational and informational tasks that need to be completed before a comprehensive analysis can be conducted:

Task 1: Protocol Development and Review

Upon final agreement of this proposal, anticipated by March 1, 1996, a protocol committee will convene composed of University of Louisville principle investigator and staff and the CMA's working group to review the submitted protocol for concurrence of the objective aims and confirmation of the methodological approach. This will be accomplished by a meeting at the University of Louisville of the participants within two to four weeks of the study's initiation. Final protocol (by April 1, 1996), will be submitted to three external reviewers for comments and recommendations to be completed and returned by May 1, 1996. The protocol will include plans to cooperate and coordinate this study with that of Applied Epidemiological, Inc. Data will be exchanged to the extent needed without ~~breaching~~ confidentiality with either state agencies or industrial participants. *breaching*

Task 2: Update of All Employee Work Histories.

Our data base indicates that approximately 3330 individuals (total cohort) were employed for one or more years at the Bells Lane plant in Louisville, Kentucky, between its initial operation in 1942 until its first offspring companies, i.e., Zeon, Inc., 1990, and Geon, Inc., 1993, were created. Work history data is available on 93% of the total cohort. Over 1400 work histories prior to 1978 are 95% completed. Some 400 to 700 employee work histories (between 1979 and 1993) need updating or verification. Approximately 1900 employees hired before and who did not work after 1974 are being added to the cohort data base. Given the full cooperation that we have enjoyed over the past years from the three existing offspring companies (B.F. Goodrich, Zeon, and Geon) we estimate that completion of Task 2 will require 480 working hours over a eight month period. Six working sessions are estimated to be needed with each of the three offspring company personnel. Each session will be spaced about three to four weeks apart to allow new data entry, data correction, validation, reanalysis for completeness, etc., for all known employees. An interim progress report will be given at seven months.

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Task 3: Updating Job Titles by Activity and Plant Buildings.

All job titles and buildings for this plant for years 1942 through 1979 are 95% completed and verified. Job titles, locations, and buildings for this plant after 1979 are incomplete because of new plant construction, renovations, and manufacturing location changes. This updating is especially important due to the recent changes over the past five or six years related to the separation of the original B.F. Goodrich plant into its offspring companies. These job updates are essential for the proper assessment of exposure rankings after 1980. Given the continued cooperation of all three offspring companies, we estimate this task to take 180 working hours spread over a five month period. Approximately five sessions are estimated to be needed with past or recent personnel management and staff to acquire this information. Status reports of the progress of Task 3 will be given at five months and at its completion (seven months).

Task 4: Chemical Data.

Updating and verification of the original 22 chemicals used on a continuous or intermittent basis between 1942 and 1978 are included in this task. Area and personnel monitoring data (whichever are available) will also need to be incorporated and updated. This is essential for the quantitative confirmation of each rank order estimate. A few new or old chemicals may need to be added to this chemical list for completeness. Verification and inclusion of all such agents will require an estimated 170 working hours spread over a five month period. Status reports will be given at five months and at the completion of Task 4 (seven months).

Task 5: Exposure Rankings.

Exposure ranking updates are required for 1979 through 1994 for all previous job classifications and verifications are needed for all new jobs created between 1979 and 1994 (Task 3). We estimate Task 4 to require 510 working hours spread over an eight month period. Some participation by experienced employees will be required (estimated time 30 to 35 hours). This will be done through a number of one to two hour sessions spaced two to three weeks apart. In between sessions, new data entry, correction, validation, and some data checking will be done to avoid duplication and misclassification. Status reports will be given at the time all needed data has been obtained (five months), and after data has been computerized and validated (seven months). A final report after the cumulative exposure ranks have been calculated for each job for each year will be given at ten months.

Task 6: A Death Certificate Confirmation.

Certification and documentation of the cause of death is available in approximately 490 of the 530 known deaths in this cohort. Forty-six individuals have incomplete data which needs further verification. Some non-vested employee data will need to be confirmed and checked. This task is estimated at taking 330 working hours spread over nine months. A status report will be provided at five and seven months identifying how many employee deaths have been verified at each time interval. Final report at eleven months.

Task 7: Cancer Records and Tissue Confirmation.

The histology, where and when available, will be examined for all "brain cancer" cases identified. The histological examination by nationally recognized expert brain pathologists (Armed Forces Institute of Pathology (AFIP) and University of Louisville faculty) will be performed and the computerized analysis of the pathology will be obtained for final analysis. A verification and confirmation of the histological cell type for each brain cancer case will have been conducted by two independent nationally-recognized pathologists. This task is estimated to take 640 working hours over a nine month period. This task involves both (a) the identification, by death certification and pathological report, of each cancer cell type for all 178 cancer cases (to exclude any misdiagnosed brain cancer cases) and (b) the acquisition of the brain cancer pathological material for examination and analysis by the two independent pathology groups. This will be a very time consuming task and in some cases it will require us to obtain consent from the employee's relatives (cases before 1974). We feel confident, however, that this task can be totally accomplished due to our excellent rapport with both the industrial workers, the unions and their family members. Status reports will be given at the completion of the death certificate verifications, at the completion of the biopsy tissue collection, and finally after the pathological analysis has been completed.

The data analysis for this study will begin at approximately halfway through the data collection (Month 7-8) and will continue through completion of the study (Month 12). A draft report is to be submitted by Month 13. Allowing 60 days for the draft report to be disseminated, reviewed and returned, we expect that this study's data will be ready for submission for publication approximately Month 15 from the onset of the study's initiation.

A tabular outline of the above tasks and the timing of their progress reports is shown in Study Timetable I.

BUDGET FOR CMA

PERSONNEL NAME	TIME ON PROJECT	ROLE ON PROJECT	SUMMARY COST
Carlo H. Tamburro, MD, MPH	10%	Principle Investigator	\$13,680
H. Philip Fortwengler	75%	Occupational Data Manager	34,730
Lark Reynolds, BS	75%	Data Coordinator	18,985
Carl Hall, Ph.D.	45%	Histological Procurement	14,025
Stephen W. Looney, Ph.D.	10%	Biostatistician	9,530
			\$90,950
Consultative Costs ¹			2,750
Supplies, Support Services ²			1,200
Travel ³			1,100
Subtotal			4,450
TOTAL (Direct Costs)			96,000
Indirect Costs (25%)			24,000
GRAND TOTAL			\$120,000

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1. Consultative cost for past and present key employee needed to work with U of L staff in work and environmental record data collection and verification, and cost for independent pathological review and analysis.
 2. Includes use of university main frame (computer time), telephone, mailing, secretarial support services cost.
 3. Costs that will be encountered to check all regional hospitals for tissue collection and verification of tumor diagnosis, especially for the 100 employees who do not have complete cause of death data. In addition, enclosed in the travel is the cost for a trip for personal presentation of interim reports to the Chemical Manufacturers Association office in Washington, DC, at a time to be designated.

**REQUESTED BUDGET FOR
STUDY OF BRAIN CANCER IN VINYL CHLORIDE EXPOSED WORKERS**

DATA UPDATE:	TIME ESTIMATED* (HOURS)	ESTIMATED COST
1. Work history update: Employee/staff work time Data transfer and storage	3-4 months (480)	15,600
2. Job titles update and verification Employee/staff work time Data transfer and storage	1 month (180)	5,850
3. Job exposure ranking Employee/staff work time	4-5 months (510)	16,575
4. Chemical data updating Employee/staff work time	1-2 months (170)	5,525
5. Death certificate verification and updating Staff work time	2-3 months (330)	10,725
6. Cancer case record analysis Staff work time Pathological verification	4-5 months (640)	20,800
		75,075
ANALYSIS:		
1. Consultative cost and time	1-2 months (90)	2,925
2. Support services, publication costs, phone, supplies, misc.	1 month (45)	1,460
3. Statistical computation Statistician time, programming needs Computer mainframe time, etc.	2-3 months (475)	15,440
4. Travel for tissue collection	1 month (15)	1,100
		20,325
TOTAL	(2935)	96,000
U of L overhead 25%		24,000
TOTAL		\$120,000

*Estimated time in (hours) or months needed to complete each task or activity during the estimated total study period.

Study Timetable 1

