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DEVELOPMENT OF A PROTOCOL TO TRACE AND STUDY SCHOOL CHILDREN EXPOSED TO VINYL CHLORIDE

FINAL REPORT

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ABSTRACT

Although a considerable body of occupational and laboratory toxicology data have demonstrated the carcinogenic action of vinyl chloride monomer (VCM), there appears to be little epidemiological literature which examines significant exposure to children. A previous EPA-sponsored pilot study identified a cohort of 1,363 children who attended an elementary school adjacent to a VCM processing plant in Saugus, California. A health status questionnaire was developed and administered to 450 subjects and 270 spouses. Three unusual causes of death were identified. The percentage of pregnancies ending in miscarriage and the proportion of children reported to have had a major illness were significantly elevated in comparison to internal controls (spouses of exposed males) and the published literature. This current study identified a non-exposed control group (N = 979), set up a computer data base management system to facilitate subject tracing, performed an analysis of the mortality experience of the two groups up to 1980, and developed a protocol to validate pregnancy outcome data. Vital status was determined for 76.2 percent of the exposed group and 78.0 percent of the control group. Although the mortality rates up to this point are small, there is some evidence of an increased proportion of non-trauma deaths among the exposed group, and an increased rate among males. There is also evidence of a decreased rate of trauma deaths among the exposed cohort. Reproductive outcome responses were validated for 16 of the 246 married females (pregnant at least once) who had been interviewed. The validation protocol results suggest that the questionnaire is a good instrument capable of recording valid reproductive information.

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DISCLAIMER

The statements and conclusions in this report are those of the contractor and not necessarily those of the California Air Resources Board. The mention of commercial products, their source or their use in connection with material reported herein is not to be construed as either an actual or implied endorsement of such products.

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1.0
INTRODUCTION AND SUMMARY

1.1 PURPOSE AND OBJECTIVES

1.1.1 The Problem

The carcinogenic activity of vinyl chloride monomer (VCM) has been clearly established, and steps have been taken by both the California Air Resources Board (ARB) and the U.S. Environmental Protection Agency (EPA) to limit occupational and general public exposure (ARB, 1977; USEPA, 1975a, 1976). Before the health hazard of VCM was recognized, however, no restrictions other than common zoning practices limited siting of plants producing or handling the monomer.

One such plant is the polyvinyl chloride (PVC) polymerization and phonograph record-producing facility operated by the Keysor-Century Corporation in Saugus, California. Since 1958, the plant has been operating at a nominal 24 hours per day, seven days per week, producing PVC from VCM and vinyl acetate. It was not until 1974 that the plant was directed to initiate significant action to control worker exposure; since then, they have satisfied federal Occupational Safety and Health Administration (OSHA) requirements for reporting worker health records, and have installed some process controls, including a fume incinerator.

The Saugus Elementary School, which was built in 1938, is located approximately 1,000 feet (300 m) from the plant. The proximity of the plant and school is believed to be unique in the United States. The latency period for, and the effects in, children could differ from those resulting from adult exposure. It has been postulated (Hefner, 1975; Watanabe, 1976) that risk to young children may be greater because of the reduced activity of several enzyme systems which are thought to be important in the metabolic processes that facilitate body elimination of VCM. For these reasons, and because VCM concentrations above the current occupational standard of 1 ppm had been measured at the school site, the EPA sponsored a two-year pilot study (1979-1981) of the health status of the students who had attended the

school during the first six years of plant operation. Science Applications, Inc. (SAI) was the contractor, and the findings of the pilot study were submitted to the EPA (Ziskind et al., 1981).

1.1.2 Summary of the EPA Pilot Study

1.1.2.1 Objectives and Methods

The objectives of the EPA-sponsored pilot study were to (1) evaluate the incidence of possible carcinogenic and non-carcinogenic health effects among a cohort of former students at the Saugus Elementary School; (2) establish tracing and registry mechanisms to maintain contact, update health status, and permit reexamination of the study cohort; and (3) estimate ambient VCM concentrations at the school site during the exposure period.

The maximum time between initial exposure and the pilot study was 21 years. Since the latency commonly associated with VCM exposure is 15 to 29 years (USEPA, 1975b), it was hoped that a significant portion of any resulting health impact would be observable in the oldest student population. The pilot study cohort was selected to be the 1,363 children who attended Saugus Elementary School for at least one year during the academic years between 1958/1959 and 1964/1965, inclusive. The minimum time between first exposure and the pilot study was therefore 16 years.

Initial information on the study cohort was obtained from pupil records provided by the Saugus Union School District (SUSD). Names, addresses, birthdates, periods of attendance, and other useful data were placed in computer files, which served as a registry for the study. Since only one measurement of ambient VCM levels at the school site had been made before introduction of emission controls at the plant, estimation of student exposure during the study period was problematical. Emission factors from the literature were combined with limited plant-specific information to estimate what uncontrolled VCM emissions would have been, and then dispersion modelling was used to estimate average exposures during school hours on those days when the school was in session. The uncertainty in these exposure estimates was so great, however, that it was decided to use months of attendance as a

surrogate measure for exposure. Production levels at the plant are believed to have been fairly steady throughout the time of interest; over the long run, therefore, our assumption appears to be reasonable.

In the pilot study, 586 members (43 percent) of the exposed cohort were located. Since it was not known in advance what type, if any, of pathology may be induced in children under the circumstances under study, it was decided to administer a comprehensive questionnaire covering a wide range of symptoms, reproductive outcomes and disease states. Data on smoking, drug use, and occupational history were also obtained. Specially trained interviewers administered the questionnaire to 450 subjects and 269 spouses over 10 months.

1.1.2.2 Pilot Study Findings

Our pilot study findings were:

- Risks of fetal deaths, induced abortion and major illnesses in children of exposed women were higher than those corresponding to unexposed spouses of male members of the cohort; and
- Three deaths among the study cohort were from causes unusual for the age group: malignant lymphoma, malignant melanoma and erythema multiforme (etiology unknown).

It should be borne in mind that these findings are very tentative; both the small study population and the lack of controls prevent us from being more conclusive. In addition, confounding factors which may have influenced the results were not explored in depth. The findings were, however, sufficiently suggestive to warrant further investigation.

1.1.3 Objectives of the Present Study

The objectives of the ARB-sponsored study were to build upon previous research by:

(1) Defining, locating and setting up a data base for a suitable control group;

(2) Designing and implementing a computerized registry to facilitate tracing of subjects and controls during this study and in any future studies;

(3) Conducting a mortality study of the exposed cohort and the controls;

(4) Developing and testing a protocol for validating the reproductive outcome results of the pilot study.

1.2 OUTLINE OF THE RESEARCH

1.2.1 Selection of the Control Group

It was determined that a suitable control group could be selected from students who had attended schools in Lancaster, about 50 miles from Saugus, since the two areas have similar socioeconomic characteristics, elementary school records were available for the pertinent time period, enough students were potentially available to serve as controls, and Lancaster School District officials were willing to cooperate. The size of the control group was 979.

1.2.2 Establishment of a Cohort Registry

To aid in storing and updating data on the exposed and control groups, and in performing statistical analyses, a data base management system was set up on an Apple II Plus™ microcomputer. (Program listings and operating instructions were submitted to the ARB under separate cover, as Appendix B.) The registry contains basic information on each subject and control, such as name, birthdate and address, as well as the latest information on vital status. It also contains data on the most recent attempts at tracing those individuals not yet found. Floppy disks containing the registry records have been submitted to the ARB.

1.2.3 Mortality Study of Exposed Cohort and Controls

We attempted to trace all exposed subjects and controls from the time of school attendance to 1 January 1980 to determine vital status for the mortality study. The most powerful tool for tracing was a request to the California Department of Motor Vehicles (DMV) for driver record information

forms. These forms provided sufficient data to enable us to locate many individuals immediately; in other cases, they provided valuable leads, such as the states to which people moved after leaving California. In addition, deaths in California are reported on the forms; the majority of deaths in this study were first discovered in this way. On the basis of information obtained through the DMV search, subjects were placed into four categories:

(1) Known to have been alive on or after 1 January 1980
(2) Known to have been alive before 1 January 1980
(3) Suspected deceased
(4) No DMV information found

Controls known to have been alive on or after 1 January 1980 were considered "located." Tracing continued for all others.

For subjects suspected to be deceased, death certificates were requested from the California Department of Health Services, Vital Statistics Branch. Certificate data were checked against school record information.

All exposed subjects for whom DMV records were returned, and control subjects known to have been alive before 1 January 1980, were sent a letter explaining the study and asking for an address verification. Located individuals were also asked to provide information on the whereabouts of friends and relatives who had attended one of the study schools. Subjects and controls who did not respond in writing after two weeks were contacted by telephone whenever possible. Located exposed subjects were also asked to sign and return a follow-up consent form.

The next step in the tracing was to search local telephone directories for the subjects or their parents. Copies of death certificates were requested for subjects reported by relatives or friends to be deceased. Other tracing resources used included the 1981-1982 California Automated Mortality System (CAMLIS), out-of-state motor vehicle departments, California marriage records and Los Angeles County voter registration records.

Mortality study data were entered into the computerized data base management system described above and analyzed by several methods; results are discussed in the next section.

1.2.4 Validation of Certain Pilot Study Results

Married female participants in the pilot study were placed into two categories: those who reported an abnormal reproductive outcome and those who reported none. Our goal was to validate the responses of ten subjects in each category. Questionnaire responses selected for validation included gravida/parity, difficulty conceiving, pregnancy outcome (live birth, stillbirth, miscarriage or abortion), congenital defects, child still alive, and major illnesses in child. For each validation protocol subject, questionnaire responses were compared with information provided by attending physicians. The percentage of normal and problem outcomes which were correctly reported and verified were calculated for each type of response.

1.3 FINDINGS AND CONCLUSIONS

1.3.1 Results of Tracing

(1) Approximately 77 percent of the exposed subjects and controls were followed up, either to 1 January 1980 or to their deaths. Tracing results may be summarized as follows:

Tracing Results	Exposed	Controls
Total persons	1,363	979
Traced	1,039 (76.2%)	764 (78.0%)
Lost to follow-up	324	215
Alive on or before 1 January 1980	1,023	749
Deaths before 1 January 1980	16	15

(2) The percentage of males located exceeded that for females by about 10 percent. This difference in success was probably due to the fact that women usually change their names when they marry but could also be caused by other biases in the tracing methodology.

(3) Spanish-surnamed individuals in both the exposed and control groups were easier to locate than non-Spanish surnamed individuals.

(4) The cumulative probability of not being lost to follow-up was not significantly different for the exposed and control groups.

(5) The actual person-years of observation we achieved were 83 and 86 percent of the total possible person-years for the exposed and control groups, respectively.

1.3.2 Mortality Study

(1) At the end of the tracing effort, we had confirmed 16 deaths among members of the exposed cohort and 15 among the control cohort before 1 January 1980. Death certificates were obtained for all but one case, which occurred during military service.

(2) The majority of deaths in both groups were due to homicide, suicide and accidents (trauma deaths).

(3) The mortality rates for all causes of death have been somewhat lower among the exposed cohort than among the controls.

(4) The mortality rates from non-trauma causes (which are more likely to be associated with an environmental exposure) are elevated among the exposed cohort as a whole. This increase is due to the higher rate for male exposed members, since female exposed subjects do not as yet show any increase. Also, the rate for trauma deaths was lower in the exposed group than in the control group.

(5) Three of the six non-trauma deaths among the exposed cohort were due to malignancies (malignant melanoma, rhabdomysarcoma,

and malignant lymphoma), as was one of the four non-trauma deaths among the controls (astrocytoma).

(6) Observed non-trauma mortality rates for the exposed and control cohorts were approximately 30 and 21 times, respectively, those expected for California residents over the same time of observation. Trauma death rates were similar to those expected.

(7) Mortality rate ratios (RRs) between exposed and control groups were not statistically significant for all subjects, non-Spanish surname subjects, males, females, or non-Spanish surname males.

(8) Insufficient time has elapsed for detection of an RR of 2.0 with 80-percent power at the 0.05-percent significant level.

1.3.3 Validation of Questionnaire Responses

(1) The responses of 14 percent of exposed women who had reported problem pregnancies and 4 percent of the women who had reported no problems were validated by our protocol.

(2) Of the 34 subjects who were requested to sign medical release forms, the responses of 16 were validated.

(3) Of those validated, the agreement between subjects' and physicians' responses for pregnancy outcomes, miscarriages, birth defects, and gravida/parity were 100 percent (except for one unknown for gravida/parity).

(4) Validation of "difficulty conceiving" was less favorable, possibly because a time limit for trying to become pregnant was not specified on the physicians' questionnaires. Although subjects' and physicians' responses for "major illness in child" and "child alive at time of interview" were very simi-

lar, this result should be treated with caution, since physicians could not provide information for a large percentage of the cases.

(5) This validation exercise revealed no evidence to suggest that reproductive outcome information was incorrectly reported in the pilot study.

1.4 RECOMMENDATIONS

1.4.1 Cohort Follow-up Efforts

We recommend tnat the exposed and control group registries set up through this project be maintained and updated annually. Maintenance activities may include:

(1) Updating address and name changes;

(2) Tracing and relocating subjects who are lost between annual updates;

(3) Acquiring death certificates for persons known to have died during each year; and

(4) Intensive tracing of subjects who have been identified as lost to follow-up.

1.4.2 Study of Reproductive and Other Morbidity Outcomes

In order to follow up on the preliminary findings of the pilot study and the present effort, we recommend a study in the exposed and control groups of reproductive outcomes and other morbidity outcomes. We suggest:

(1) Re-using the reproductive history portion of the questionnaire;

(2) Revising procedures for obtaining physician names and medical record release forms, and revising the wording of those forms; and

(3) Analyzing the data in the same manner as in the pilot study.

2.0
METHODS

In this section we will discuss the methods used in performing the tasks required under this contract. These included the following:

(1) Conduct a mortality study of a cohort of children exposed to vinyl chloride gas in the 1950s and 1960s and a group of non-exposed children. The mortality study is discussed in Section 2.1.

(2) Set up a computerized cohort registry designed to facilitate contacting members of the exposed group some time in the future in order to monitor changes in health status. This is discussed in Section 2.2.

(3) Develop a methodology to obtain current address information and determine vital status. Tracing methods are discussed in Section 2.3.

(4) Develop a protocol to validate reproductive and other questionnaire responses. The validation protocol is outlined in Section 2.4.

2.1 MORTALITY STUDY

The mortality study was conducted using an historical prospective design. A cohort of 1,363 children who attended an elementary School (Saugus Elementary in Saugus, California) located near a plastics factory emitting vinyl chloride gas between 1958 and 1964 was identified retrospectively using school district records. A control group of children who attended elementary school in the nearby Lancaster School District during the same time but who were not exposed to vinyl chloride were also identified retrospectively from school district records. Using information provided in the school records, members of each group were traced and their vital status on or after 1 January 1980 was ascertained. The methods used to trace subjects are common to both the mortality study and establishment of the cohort registry; tracing methods are discussed in Section 2.3. In this section we will discuss all other aspects of the mortality study: selection and comparability of exposed and control groups, methods used to determine vital status, and statistical analysis methods.

2.1.1 Selection of the Exposed Cohort

The exposed cohort was assembled on the basis of information contained in student records provided to us by the Saugus Union School District (SUSD), Saugus, California. These records contain: the student's full name, sex, date of birth, place of birth, address and telephone number, dates of attendance, names of the persons with whom the pupil lives, the pupil's previous school and school of transfer. Criteria for inclusion in the exposed cohort were the following:

(1) Attendance at Saugus Elementary School for a minimum of one academic year (kindergarten through 6th grade)

(2) Attendance during or after the academic year 1958/1959 (after the beginning of operation of the vinyl chloride plant)

(3) Attendance during or before the academic year 1964/1965

Based on school records information 1,363 subjects met these criteria. The oldest students in the cohort would have entered 6th grade in September 1958, while the youngest entered kindergarten before September 1964. The minimum time from first exposure to the present (December 1982) is therefore 18 years; the maximum time since first exposure is 24 years.

Duration of exposure was taken to be months of attendance at the Saugus Elementary School. The school records provided us with beginning and ending dates of enrollment for most students. Months of attendance were calculated by subtracting the ending month from the beginning month and adding one. One academic year (beginning in September and ending in June) therefore comprised 10 months of exposure.

2.1.2 Selection of the Control Group

With the assistance of Dr. J. Foster, SUSD Superintendent, a number of control group possibilities were investigated. It was determined that a suitable control group could be selected from students who attended elementary school in the Lancaster School District (LSD), Lancaster, California. Lancas-

ter is approximately 70 miles northeast of Saugus, and is also in Los Angeles County. The Lancaster School District was selected for the following reasons:

- Socio-economic status of Lancaster is similar to that of Saugus;
- It was thought that the percentage of Spanish-surnamed students in the Saugus and Lancaster groups would be comparable;
- Elementary school records were available for the same years as the Saugus cohort (1958-1964);
- Information contained in LSD and SUSD records was comparable;
- A sufficient number of students were available who could be used as control subjects; and
- School district officials were willing to cooperate.

Since all exposed cohort subjects were selected from one elementary school in the Saugus district - Saugus Elementary - we initially requested school records for students who attended one school in the Lancaster District - Desert View Elementary. Criteria for selection of control group subjects were as follows:

- Attendance at Desert View School for a minimum of one academic year (kindergarten through 6th grade);
- Attendance during or after academic year 1958/59; and
- Attendance during or before the academic year 1964/1965.

We found 796 control subjects who satisfied the above criteria. To increase the size of the control group and to minimize the differences in age distribution between the two groups, an additional 300 school records were requested from the Lancaster School District. Since we had exhausted the pool of Desert View students meeting our selection criteria, we requested that records be selected from among students who attended schools in the Lancaster District other than Desert View School. In an attempt to minimize the difference between groups on birth year, we requested that these records be selected for students with birth years on or before 1950. As before, attendance must have been for a period of at least one school year between academic years 1958/59 to 1964/65. Of the approximately 300 additional records sent to us, 183 met all selection criteria. The total sample size of the control group was therefore 979.

2.1.3 Comparability of Exposed and Control Groups

Table 2.1-1 compares the exposed cohort (N=1,363) with the control group (N=979) on sex, birth year, percent Spanish surname, percent completed 6th grade in the district, and place of birth. Table 2.1-2 compares 1960 census data for the neighborhoods of the exposed and control schools.

2.1.4 Determination of Vital Status

The cutoff date for determining vital status was set at 1 January 1980 to maximize both the percentage of subjects for whom vital status would be determined and the length of time since first exposure. All subjects determined to have been alive any time on or after the cutoff date were categorized as "alive" for the purposes of the mortality study.

A major task in ascertaining vital status was the tracing of subjects from the date last known to be alive according the elementary school records up to the cutoff date. The methods used to trace subjects are fully discussed in Section 2.3. One comment about tracing should be made at this point, however. It is absolutely crucial that the same information, the same tracing methods, and the same amount of effort be used to follow up both the exposed cohort and the control group. If follow-up is not applied equally to both groups it is possible to bias the results of the study. For example, it is possible to find more deaths in one group simply by looking for deaths more energetically in that group. Throughout this mortality study we were careful to apply follow-up methods equally in both groups.

A subject was considered alive if he was determined to be alive on or after 1 January 1980, or deceased if he was discovered to be deceased before that date. The following methods were used to ascertain vital status.

- A letter sent to the subject was answered by return letter or phone call.
- A form sent to a subject's sibling, parent or relative requesting address and vital status information on the subject was answered, by return letter or by phone, providing the information that the subject was alive on or after the cutoff date, or deceased before the cutoff date.

Table 2.1-1

COMPARISON OF EXPOSED COHORT AND CONTROL GROUP ON SELECTED CHARACTERISTICS

	Exposed Group (N=1,363)		Control Group (N=979)	
	Number	Pct	Number	Pct
Sex				
M	679	49.8	515	52.6
F	682	50.0	463	47.2
Unknown	2	0.2	1	0.1
Spanish Surname				
Y	191	14.0	23	2.4
N	1172	86.0	956	97.7
Completed 6th Grade In School District				
Yes	685	50.3	710	72.5
No	678	49.7	269	27.5
Birthplace				
L.A. County	369	27.1	450	46.0
CA, Outside L.A. County	80	5.9	182	13.4
U.S., Outside CA	243	17.8	292	21.4
Outside U.S.	51	3.7	16	1.2
Missing Data	620	45.5	38	2.8
Birth year				
Unknown	2	0.14	1	0.10
1945	2	0.14	0	0
1946	11	0.80	0	0
1947	48	3.52	0	0
1948	68	4.98	22	2.25
1949	88	6.45	109	11.13
1950	107	7.85	143	14.61
1951	125	9.17	89	9.09
1952	156	11.44	81	8.27
1953	166	12.18	85	8.68
1954	154	11.30	86	8.78
1955	140	10.27	101	10.32
1956	115	8.44	104	10.62
1957	96	7.04	94	9.60
1958	85	6.24	64	6.54

Table 2.1-2

COMPARISON OF NEIGHBORHOODS OF EXPOSED AND CONTROL SCHOOLS, USING 1960 CENSUS DATA

Characteristics	Exposed Area	Control Area
Census Tract Number	9200	9008
Total Population	4,908	12036
Race		
% White	95	99
% Black	4	<1
% Other	1	<1
% White, Spanish Surname	7	3
Median Years of School (Adults > 25 years of age)	11.4	12.4
Median Income per Family	$6,831	$7,890
Housing		
% of Persons >5 Years of Age Who Resided in Same House in 1955	22	23
% of Housing Units Owner-Occupied	47	60
Median Value of Owner-Occupied Housing Units	$14,000	$14,800

Source: U.S. Bureau of the Census (1962a, 1962b).

- A telephone call was made to a subject and the subject himself was contacted, or a relative or spouse verified that the subject was alive or deceased according to the above criteria.

- A telephone call to a sibling, parent, or relative verified that the subject was alive or deceased.

- A subject was considered alive if a Department of Motor Vehicles (DMV) request for driver record information verified that the subject took one of the following actions on or after the cutoff date:

    - Applied for or renewed a driver's license;
    - Changed address;
    - Had a traffic violation or accident; or
    - Applied for or renewed identification card.

Deaths in the State of California are reported to the California Department of Motor Vehicles and indicated on a person's driver record. Several deaths were discovered in this manner. The identity of the person was verified by obtaining a copy of the death certificate and checking information against the school records.

The names of all subjects for whom vital status had not been determined near the end of tracing were submitted to the California Automated Mortality Linkage System (CAMLIS). CAMLIS is a computer system run by the University of California, San Francisco, Department of Epidemiology and International Health, which matches information from user files against the State of California mortality files for 1966 to 1981. The CAMLIS System reportedly produces results superior to those attainable by manual review of death records. Copies of death certificates were requested for subjects identified as deceased by the CAMLIS System. The identity of the subject was verified by checking death certificate information against school records information. By using the CAMLIS system we are <u>almost</u> positive (no system is fool-proof) that all subjects not traced to 1 January 1980 did not die in California between 1966 and 1981.

We made certain that information was obtained on the correct person when contacting a subject, or a subject's parent, sibling, or relative, by letter or phone by taking the following steps:

- Always using the subject's full name;
- Verifying that the person for whom we were obtaining information attended elementary school in the correct school district between 1958 and 1964;
- Fully explaining the criteria for which the subject was selected as a member of the exposed or control group; and
- When in doubt, verifying the subject's birthdate, names of parents, and names of siblings.

All deaths discovered in this manner were verified to be the subject for whom we were searching by obtaining a copy of the death certificate and checking death certificate information against school record information.

2.1.5 Mortality Study Statistical Analysis Methods

Several epidemiologic analysis techniques have been applied to the data derived from the mortality study. First, as is discussed in Section 3.2.2, the data were treated as in a standard follow-up study where the amount of person-time of follow-up for each subject is known. Mortality rates were calculated as the number of deaths occurring in a group divided by the total number of person-years of observation. For each individual the number of persons-years of observation was derived by subtracting the month and year the subject entered the cohort from the month and year the follow-up on the subject terminated. Termination in this case could be

- The date of death
- The date the subject was last known to be alive, before being lost to follow up, or
- 1 January 1980, the pre-determined date for terminating follow-up for subjects known to be alive.

Mortality rates for the exposed group relative to the non-exposed were expressed as rate ratios (RR), and tested for statistical significance by a Chi-square test based on a binomial approximation for person-time data (Rothman and Boice, 1979; Kleinbaum et al., 1982). When the numbers of deaths were small, so that expected numbers were less than 5, we performed an exact binomial test.

Follow-up mortality was also examined with an actuarial life table (Colton, 1974). In this analysis, each subject's year of entry into the cohort is considered the first year of observation in the life table. During each year, the probability of mortality is calculated for all subjects who began the interval alive, as well as a cumulative risk of mortality from the start of the study. The life table analysis can be considered a refinement over the total person-years rate, because it examines the risk of death in each year of follow-up after entering the cohort. In contrast, the person-years rate is a summary measure that assumes the the rate is constant throughout the study period (Kleinbaum et al., 1982). The overall cumulative risks can be compared between the exposed and non-exposed, and the difference in survival has been tested as described by Colton (1974), using the Greenwood standard error formula.

The life table method was also used (in Section 3.1) to assess the comparability of follow-up between the exposed and control cohorts. For this assessment, we have considered loss-to-follow-up as the "terminal event," and compared both groups for attrition over time.

In Section 3.2.2, we explore the possibility of a dose-response relationship for the deaths in the exposed group. We accomplished this by conducting a case/control analysis of the data derived from the exposed cohort and examining the amount of exposure. This approach has been termed an "ambidirectional" design, and has an advantage over the cohort design in that it makes use of the efficiency of a case/control analysis for studying rare events (Kleinbaum et al., 1982). The observed deaths among the exposed subjects become the "cases," and the "controls" are drawn from the large pool of exposed subjects who did not die. This analysis is particularly useful for controlling extraneous, possibly confounding, factors, because living controls can be matched on these factors to the deceased cases (Smith et al., 1977).

For each deceased exposed subject, we specified the sex, year of birth, type of surname (Spanish or non-Spanish), and year of death. From the computer-based registry, a pool of potential controls was generated for each case, composed of exposed subjects of the same sex, year of birth, type of surname, and who we knew to be alive on the date of the case's death. Three

controls were chosen from the pool by a random numbers table. The result was a matched case/control series, with a 3-to-1 matching ratio.

For each case and control, we recorded the number of months of exposure at the elementary school. We stratified the length of exposure into two levels, using the median of the cohort as the cutpoint: 10-19 months (low exposure), and 20 or more months (high exposure). The analysis was performed by the Mantel-Haenszel procedure, treating each case and the three matched controls as a separate stratum, and deriving an overall summary odds ratio (Schlesselman, 1982). The suitability of the Mantel-Haenszel chi-square statistic for hypothesis testing was examined by the rule of thumb suggested by Mantel and Fleiss (1980).

It was assumed that the effect (if any) of vinyl chloride exposure would be manifest in deaths other than those caused by trauma. However, the majority of deaths in young adults are normally deaths due to trauma causes (e.g. suicide, homicide, and accidents). Therefore, one further analytic strategy was invoked (in Section 3.2.3) to cope with the small number of deaths due to non-trauma causes. The proportion of deaths due to trauma and non-trauma in the study groups was compared to the proportion of trauma and non-trauma deaths occurring the State of California, by the mortality odds ratio method of Miettinen and Wang (1981).

Analogously to a stratified case/control study, the deaths from the study cohorts were stratified by age, sex, and ICD code revision number. For each stratum, the distribution of non-trauma and trauma deaths among the study subjects was compared to the distribution of deaths in California in the same five-year age group, sex, and ICD coding period (either 1960-68 for the ICD 7th Revision, or 1969-78 for the ICD 8th Revision). The mortality odds ratio was summarized by the Mantel-Haenszel method.

2.2 COHORT REGISTRY

The cohort registry is a collection of information for each member of the exposed cohort. The registry was established to facilitate tracing of subjects during this study and in the future.

Figure 2.2-1 is an example of a subject's cohort registry record, showing the different pieces of information we have collected (when available) for each exposed subject. Collected information includes personal data (I.D.#, name, sex, birthdate, Spanish surname code), school attendance data (entry date into school, transfer code), address and telephone information, tracing information (date letter sent, letter no., phone book, phone call, DMV, vehicle registration, property tax, voter registration, and contact code), and date last alive and source of that data (vital status). The meaning of each of the codes used are presented in Table 2.2-1.

The heart of the cohort registry is a set of data base management software designed by SAI staff members Michael Rogozen, D.Env., and George Maldonado, MSPH. The data base management software is written in Applesoft BASIC and is designed to be run on an Apple II Plus™ microcomputer. The cohort registry data base management system has the following capabilities.

- Entry and storage of data to floppy disk
- Data update
- Sorting of data on the following characteristics:
  - Sex
  - Date last alive
  - Spanish surname
  - Exposed group versus control group
  - Type and number of letters sent
  - Date last letter sent
  - Status of DMV search
  - Contact code
  - Alive vs. deceased
- Printing subject information in various formats, including:
  - Individual subject record (e.g., Figure 2.2-1)
  - List of subject I.D. numbers and names (and various other information) meeting a specified sorting criterion

SURVEY I.D.#: 2 REVISION DATE: 12-82

FIRST NAME:	FIRST
ORIGINAL SURNAME:	MAIDEN
PRESENT SURNAME:	MARRIED
SEX (M,F,U):	M
BIRTHDATE (XXYYZZ):	052853
TRANSFER CODE (Y,N):	Y
STREET ADDRESS:	STREET
CITY:	CITY
STATE :	CA
ZIP :	90067
TEL(XXXYYYZZZZ):	2135532705
LETTER SENT (DATE) :	121582
LETTER NO.:	1
PHONE BOOK:	0A
PHONE CALL:	0A
DMV:	4A
VEH. REG.:	0A
PROPERTY TAX:	0A
VOTER REGISTRATION:	0A
CONTACT CODE:	0
DATE LAST ALIVE:	1282
VITAL STATUS:	1
SPANISH SURNAME:	1
ENTRY DATE:	0957

Figure 2.2-1. Cohort Registry Subject Data Record.

Table 2.2-1

COMPUTER DATA BASE MANAGEMENT SYSTEM CODES

LETTER CONTACT CODES

Letter Sent	MM/DD/YY
Letter No.	1 = 1st Letter sent 2 = 2nd Letter P = Letter sent to parents A = Letter answered R = Letter returned, incorrect address, search Q = Letter to parents, 1 Letter to S (Name submitted with name of Sib) S = Letter to parent answered, S+ T = Letter to parent answered, S- U = Letter to Parents, letter to subject returned undelivered V = Validation study: Letter to S W = Validation study: Letter to P X = Validation study: Letter to P & S Y = Letter to parents returned unanswered Z = Letter to Sibling

CODES FOR DMV, VEHICLE REGISTRATION, PHONE BOOK, PHONE CALL, PROPERTY TAX AND VOTER REGISTRATION SEARCHES

1st Digit	0 = Subject, not tried 1 = tried, CA, results pending 2 = tried, out of state, results pending 3 = S- 4 = St 5 = Multiple S+ 6 = S+, search out of state 7 = S+, expired info. 8 = S? 9 = Info. from Phase 1
2nd Digit	A = Parent, not tried B = Tried, CA, results pending C = Tried, out of state, results pending D = P- E = P+ F = Multiple P+ G = P+, search out of state H = P+, expired info. I = P? J = Info. from Phase 1

Table 2.2-1

COMPUTER DATA BASE MANAGEMENT SYSTEM CODES
(Continued)

CONTACT CODES	
Phase 1	A = Not contacted B = Found, interviewed, signed follow-up consent C = Found, interviewed, follow-up consent not signed D = Found, contacted, not interviewed E = Found, refused interview F = Deceased G = Armed forces H = Out of country or out of state with no phone
Phase 2	A, B, C, D, E, G, H = Exposed, not located in Phase 2 Z = Non-Trauma death F = Trauma Death 0 = Control, not located 1 = Found, alive, follow-up consent signed 2 = Found, alive, F-U Consent not signed 3 = Suspected deceased
Date Last Alive	Last date known to be alive
Vital Status	Evidence to support Date Last Alive 0 = Vital status not ascertained 1 = DMV 2 = Return mail from S 3 = Contact in Phase 1 4 = Vehicle registration 5 = Suspected deceased 6 = Death certificate 7 = Phone contact, Phase 2 (talk to S) 8 = Information from friend on "Friends and Relatives Who Attended Saugus School" form; no actual contact 9 = Information from phone contact with friend/relative, Phase 2, in response to calling S A = Letter to parents answered; vital status of subject determined; subject not contacted B = Information from sibling on "Friends and Relatives" form (no actual contact) C = Phone call to parents, sibling
Rev Date	= Mo/Yr address information known to be correct

- Letter heading
- Mailing label
- DMV request form information label (to be attached to DMV form DL-254)

- Compiling and printing group summary information such as frequency distributions of sex, birth year, entry year into cohort, year last known to be alive, and type and number of letters sent
- Statistical analysis of follow-up data by person-years and life table methods. (The design of the analysis software was supervised by SAI staff member Daniel Smith, MS, and written by George Maldonado, MSPH.)

The data base management software we designed has proven to be flexible, efficient and very inexpensive to run. It will be a powerful and efficient tool in future follow-up efforts. Program listings and operating instructions are contained in Appendix B, which was provided to the ARB as a separate document under this contract (Maldonado, 1984).

A component of the cohort registry that was proposed was the obtaining of signed follow-up consent forms. Though follow-up consents were requested for the majority of exposed subjects, we were informed by consultant Gary H. Spivey, MD, MPH (Associate Professor of Epidemiology, UCLA) that he knows of no legal requirement for a signed follow-up consent form; it is, however, required by Human Subjects Protection Committees at many academic institutions. Since the ARB has no Human Subjects Committee specifically requiring this form, we did not invest a great deal of time and resources in following up subjects who had not returned this form. This was especially true when there was no other reason to make further contact with a subject.

The establishment of a cohort registry was proposed and funded only for the exposed cohort. However, the same data base management system was used to collect and manipulate data for the tracing of the control group as for the exposed group. Also, the same tracing methods were used and the same pieces of information were collected for both groups. The only differences between the exposed cohort registry and the control registry were:

- All available address information has been input for exposed subjects; for controls, address information, although collected and available, was input into the computer system only when needed to facilitate subject tracing (e.g. when needed to produce letter headings and mailing labels).

- Signed follow-up consent forms were requested only from exposed subjects. As explained above, this difference is of no practical significance for future follow-up efforts.

In essence, with only a few hours of entry of address information, we will have a Control Registry comparable to the exposed Cohort Registry, which could be used to trace control subjects anytime in the future. Both groups were traced to determine vital status as of 1 January 1980. The exposed group, however, was traced one step further, since exposed subjects were sent letters requesting follow-up consent forms even when vital status had been determined on or after the cut-off date. The updated address information resulting from the additional step was entered into the registry. Thus, address information is likely to be slightly more current for exposed subjects than controls.

2.3 TRACING METHODS

We attempted to trace all subjects from the time of school attendance to 1 January 1980 to determine vital status for the mortality study. Only exposed subjects were sent a letter requesting a signed follow-up consent form and address verification for the purposes of the Cohort Registry. Therefore, tracing ended for control subjects when vital status was determined, while tracing for exposed subjects ended with the return of a signed follow-up consent. However, since we determined that the significance of a follow-up consent form is of little practical significance in our situation, exposed subjects who failed to return follow-up consent forms were not contacted and influenced to do so when there was no other reason to contact the subject.

2.3.1 Basic Tracing Methods

In the first phase of this study, sponsored by the U.S. Environmental Protection Agency (EPA), the efficiency of various tracing methods was determined. In the first phase, 586 member of the exposed cohort (41 percent)

were located and contacted; of these, 450 were interviewed (Ziskind et al., 1981). Drawing from the tracing experience gained in the EPA-sponsored phase, a tracing methodology was designed. It is diagrammed in Figure 2.3-1. It is important to point out that the same methods were used to locate and determine vital status for both the exposed cohort and the control group.

The first step in the tracing scheme was the entry of the following information from school records for each subject into the Computer Data Base Management (CDBM) system: subject identification number, name, birthdate, sex, and date last known to be alive. Using the CDBM system, California Department of Motor Vehicles (DMV) DL-254 forms (Figure 2.3-2) were completed with the subject's identification number, name and birthdate. California driver record information was requested by submitting these forms to the DMV.

DMV requests were clearly our most powerful tracing method. The DMV uses a name and birthdate match -- a combination so unique that of the 2,388 names we submitted to DMV, multiple driver records were returned for only one subject's name-birthdate combination. Figure 2.3-3 is a copy of a returned DMV driver record information form. (The name and address has been changed to preserve the subject's anonymity.) This information was checked against school records to verify that we had identified the correct person.

The driver record information form provides several items of information which we found very useful:

- Full name
- Both maiden and married names for females who originally applied for a driver's license under their maiden names and informed DMV of their name changes after marriage
- Birthdate
- Subject identification number
- Last date of license issuance or renewal
- Date of traffic accident or violation
- State of residence of persons who have moved from California and applied for a license in a new state. (Sometimes a full address in the new state is provided. This proved invaluable in tracing subjects who had moved out of state.)
- Deaths in the state of California. (The majority of deaths in this mortality study were first discovered via this method.)

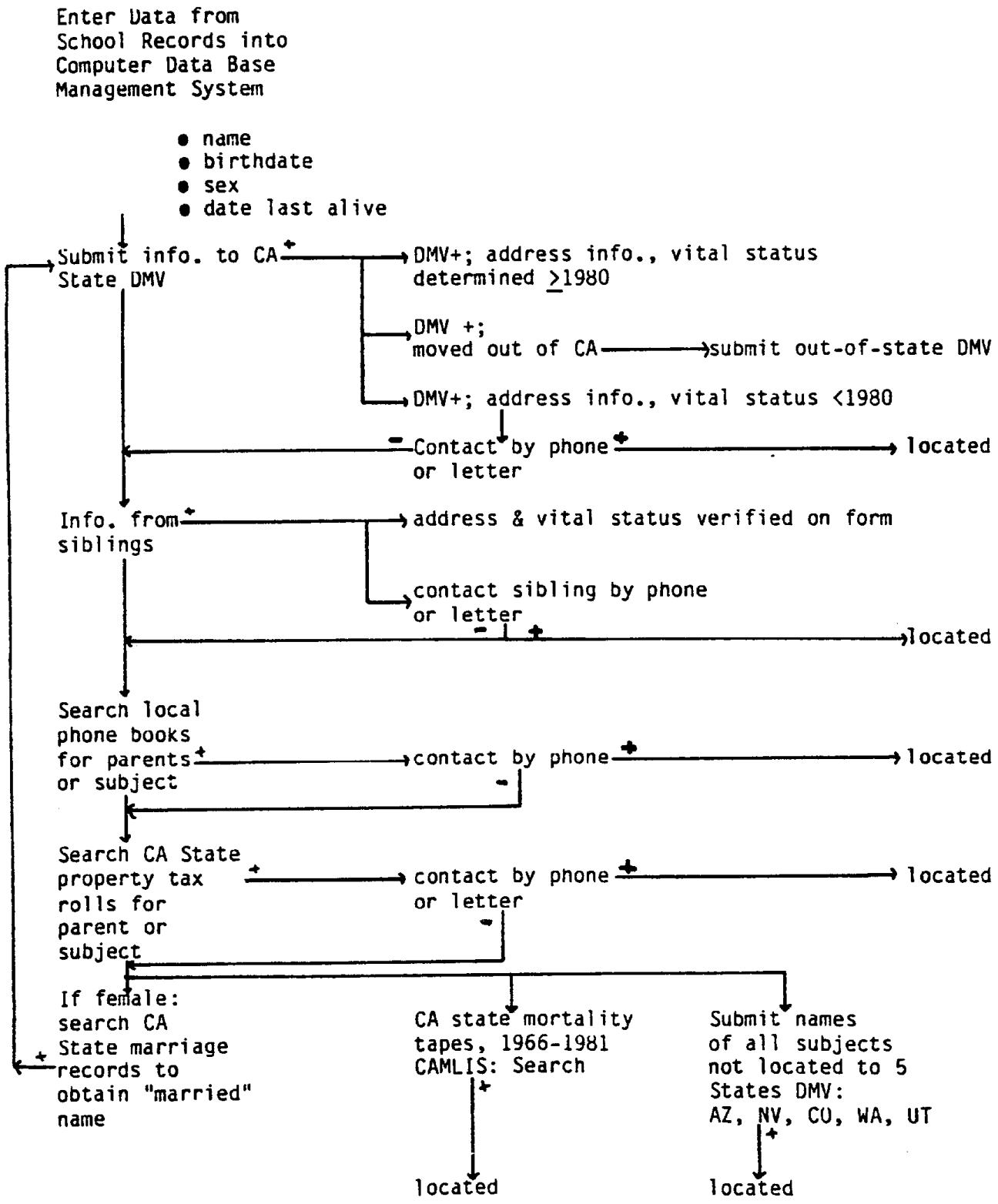
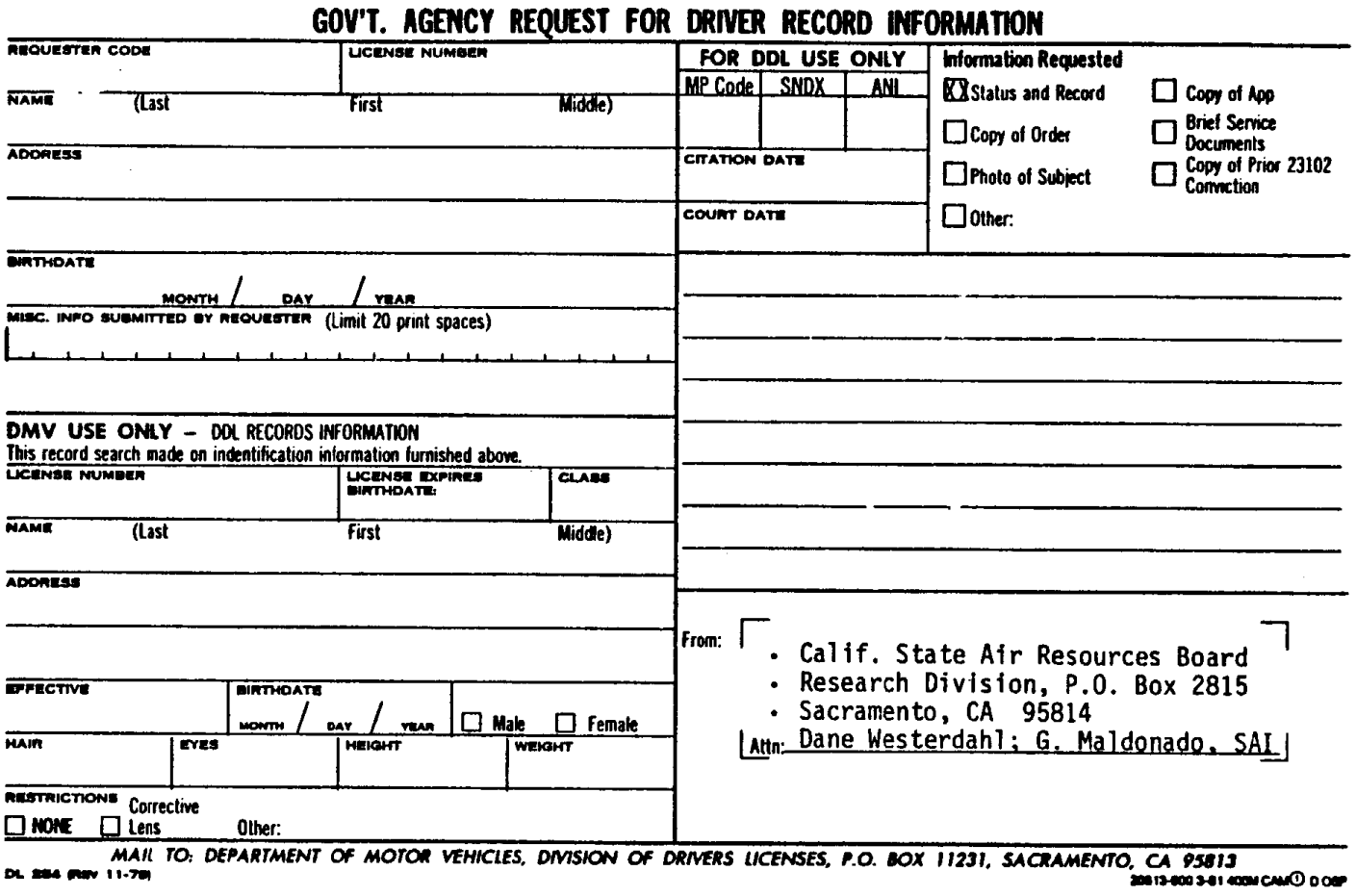


Figure 2.3-1. Tracing Diagram



GOV'T. AGENCY REQUEST FOR DRIVER RECORD INFORMATION

REQUESTER CODE | LICENSE NUMBER

NAME (Last First Middle)

ADDRESS

BIRTHDATE MONTH / DAY / YEAR

MISC. INFO SUBMITTED BY REQUESTER (Limit 20 print spaces)

DMV USE ONLY – DDL RECORDS INFORMATION
This record search made on indentification information furnished above.

LICENSE NUMBER | LICENSE EXPIRES BIRTHDATE: | CLASS

NAME (Last First Middle)

ADDRESS

EFFECTIVE | BIRTHDATE MONTH / DAY / YEAR | ☐ Male ☐ Female

HAIR | EYES | HEIGHT | WEIGHT

RESTRICTIONS ☐ NONE ☐ Corrective Lens Other:

FOR DDL USE ONLY

MP Code	SNDX	ANI

CITATION DATE

COURT DATE

Information Requested

☒ Status and Record
☐ Copy of App
☐ Copy of Order
☐ Brief Service Documents
☐ Photo of Subject
☐ Copy of Prior 23102 Conviction
☐ Other:

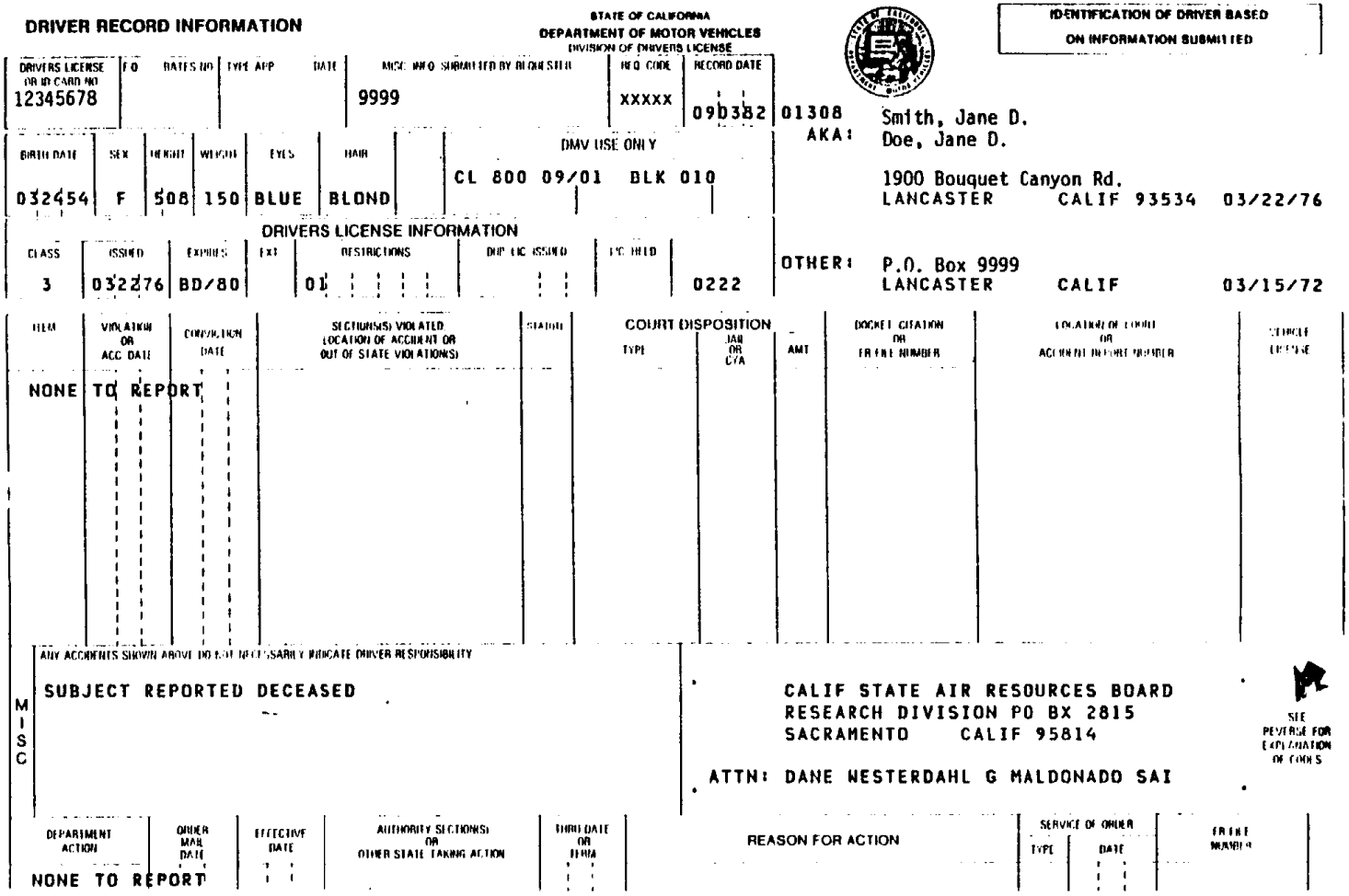
From:
- Calif. State Air Resources Board
- Research Division, P.O. Box 2815
- Sacramento, CA 95814

Attn: Dane Westerdahl; G. Maldonado, SAI

MAIL TO: DEPARTMENT OF MOTOR VEHICLES, DIVISION OF DRIVERS LICENSES, P.O. BOX 11231, SACRAMENTO, CA 95813

DL 254 (REV 11-79)

Figure 2.3-2. Driver Record Information Request Form (DL 254).



DRIVER RECORD INFORMATION

STATE OF CALIFORNIA
DEPARTMENT OF MOTOR VEHICLES
DIVISION OF DRIVERS LICENSE

IDENTIFICATION OF DRIVER BASED ON INFORMATION SUBMITTED

DRIVERS LICENSE OR ID CARD NO	FO	DATES NO	TYPE APP	DATE	MISC INFO SUBMITTED BY BLOCK STEP	REQ CODE	RECORD DATE
12345678					9999	XXXXX	09/30/82

BIRTH DATE	SEX	HEIGHT	WEIGHT	EYES	HAIR	DMV USE ONLY
032454	F	508	150	BLUE	BLOND	CL 800 09/01 BLK 010

01308 Smith, Jane D.
AKA: Doe, Jane D.

1900 Bouquet Canyon Rd.
LANCASTER CALIF 93534 03/22/76

DRIVERS LICENSE INFORMATION

CLASS	ISSUED	EXPIRES	EXT	RESTRICTIONS	DUP LIC ISSUED	LIC HELD	
3	032276	BD/80		01			0222

OTHER: P.O. Box 9999
LANCASTER CALIF 03/15/72

ITEM	VIOLATION OR ACC DATE	CONVICTION DATE	SECTION(S) VIOLATED (LOCATION OF ACCIDENT OR OUT OF STATE VIOLATIONS)	STATUS	COURT DISPOSITION TYPE	JAIL OR CYA	AMT	DOCKET CITATION OR FR ENF NUMBER	LOCATION OF COURT OR ACCIDENT BEFORE ORDER	VEHICLE LICENSE
NONE TO REPORT										

MISC

ANY ACCIDENTS SHOWN ABOVE DO NOT NECESSARILY INDICATE DRIVER RESPONSIBILITY

SUBJECT REPORTED DECEASED

CALIF STATE AIR RESOURCES BOARD
RESEARCH DIVISION PO BX 2815
SACRAMENTO CALIF 95814

ATTN: DANE WESTERDAHL G MALDONADO SAI

SEE REVERSE FOR EXPLANATION OF CODES

DEPARTMENT ACTION	ORDER MAIL DATE	EFFECTIVE DATE	AUTHORITY SECTION(S) OR OTHER STATE TAKING ACTION	THRU DATE OR TERM	REASON FOR ACTION	SERVICE OF ORDER TYPE	SERVICE OF ORDER DATE	FR ENF NUMBER
NONE TO REPORT								

Figure 2.3-3. DMV Driver Record Information Form.

Based on the results of the DMV search, subjects were placed into one of four categories:

(1) Known to have been alive on or after 1 January 1980
(2) Known to have been alive before 1 January 1980
(3) Suspected deceased
(4) No California DMV information found

Controls known to have been alive on or after 1 January 1980 were considered "located." Tracing continued for all others.

In the cases when the driver record information form indicated the subject had moved out of state, a request for driver record information was sent to the new state of residence.

For subjects suspected to be deceased based on DMV record information, death certificates were requested from the California Department of Health Services, Vital Statistics Branch. Information on the death certificate was checked against school record information (e.g., full name, birthdate, name of parents, birthplace).

All exposed subjects for whom driver record information was returned, and control subjects known to have been alive before 1 January 1980, were sent a letter explaining the study, asking for an address verification, and requesting information on friends and relatives who attended elementary school with them. In addition, exposed subjects were requested to sign a follow-up consent form. All envelopes were stamped "Address Correction Requested;" this instructs the Postal Service to send a forwarding address to the sender whenever a letter is forwarded to a new address. Letters and forms sent to control subjects are presented in Figures 2.3-4 to 2.3-6; forms and letters sent to exposed subjects are presented in Figures 2.3-7 to 2.3-10.

Subjects who answered their letters were considered located. Subjects for whom letters were returned by the Postal Service as undeliverable continued to be traced. Subjects for whom no response was received two weeks after the mailing date of the first letter were sent another letter. Subjects

We need your help with an important health survey. In cooperation with the California Air Resources Board, we are examining possible health effects resulting from exposure to vinyl chloride gas. The need for this survey was recognized when elevated levels of vinyl chloride were detected around the area of the Saugus Elementary School. The school was located near a factory that uses vinyl chloride to make plastics. We are asking persons who attended schools in the Lancaster School District to help with the survey. Your name is included on a list of former students the Lancaster School District compiled for us.

In this survey we will contact a group of people who attended Saugus Elementary School (who may have been exposed to vinyl chloride) and a group of people who attended schools in the Lancaster School District (who were not exposed). We will determine where each person is living today. For those who have died we will determine the cause of death.

Though you were not exposed to vinyl chloride, your participation as a member of the comparison group is vitally important. Please fill out the enclosed "Attendance Verification" form verifying that you did attend a school in the Lancaster District, and return it to us. Also, if you know the address of brothers, sisters, or friends who attended Lancaster schools at about the same time as you, it would be extremely helpful to us if you would write this information on the "Friends and Relatives Who Attended Lancaster Schools" form.

You may, of course, elect not to participate. However, you and your former classmates, by cooperating with this research, are vitally important to its success.

If you have any questions about this study, at any time, you may call Mr. George Maldonado at (213) 553-2705.

Thank you.

Sincerely,

SCIENCE APPLICATIONS, INC.

Richard A. Ziskind, Ph.D.
Manager
Energy-Environment Division

Figure 2.3-4. Contact Letter Sent to Controls.

ATTENDANCE VERIFICATION

I [] did [] did not attend school in the Lancaster School District.

Is the above name and address information correct? []yes []no
If no, please provide correct information below. Please place in the return envelope provided and return to Science Applications, Inc.

Figure 2.3-5. Attendance Verification Form Sent to Controls.

FRIENDS AND RELATIVES WHO ATTENDED
LANCASTER SCHOOLS

If you know the address of friends or relatives who attended schools in the Lancaster School District between 1959 to 1970, please provide information below:

1. Name _____

   Presently alive? [] yes [] no
   If deceased: date of death_____ County/State of death _____

   Address_____

   _____

   Phone ( )_____

2. Name _____

   Presently alive? [] yes [] no
   If deceased: date of death_____ County/State of death _____

   Address_____

   _____

   Phone ( )_____

3. Name _____

   Presently alive? [] yes [] no
   If deceased: date of death_____ County/State of death _____

   Address_____

   _____

   Phone ( )_____

** Please place in the envelope provided and return to Science Applications, Inc., 1801 Ave. of the Stars, Suite 1205, Los Angeles, CA 90067

Figure 2.3-6. Form Used to Locate Friends and Relatives of Located Controls.

We need your help with an important health survey which is being conducted for the California Air Resources Board. We are examining possible health effects resulting from exposure to vinyl chloride gas.

The need for this survey was recognized when elevated levels of vinyl chloride (which may have health implications) were detected around the area of the Saugus Elementary School. The school was located near a factory that uses vinyl chloride to make plastics. We are asking persons who may have been exposed while attending this school to help with the survey. Your name is included on a list of former students the Saugus Union School District helped us compile.

In this survey we will contact a group of people who attended Saugus Elementary School (who may have been exposed to vinyl chloride) and a group of people who attended schools in the Lancaster School District (who were not exposed). We will determine where each person is living today. For those who have died, we will determine the cause of death.

If you participate in this study your name and address will be placed in a confidential file of former Saugus Elementary School Students, and you may be contacted in the future to obtain information pertinent to the study. If you agree, please sign the enclosed "Consent for Follow-up" form and the "Address Verification" form and return them to us in the enclosed, stamped envelope. Also, if you know the whereabouts of brothers, sisters, or friends, who attended Saugus Elementary School at about the same time as you, it would be extremely helpful to us if you would write this information on the "Friends and Relatives who attended Saugus Elementary School" form, so we can contact them and ask them to help with the survey.

You may, of course, elect not to participate. However, you and your former classmates, by cooperating with this research, are vitally important to its success. We believe that the information derived from this research could be of direct importance to you and your family.

If you have questions about this study, at any time, you may call Mr. George Maldonado at (213) 553-2705.

Thank you.

Sincerely,

SCIENCE APPLICATIONS, INC.

Richard A. Ziskind, Ph.D.
Manager
Energy-Environment Systems Division

Science Applications, Inc. 1900 Avenue of the Stars, Suite 900, Los Angeles, California 90067 (213) 553-2705
Other SAI Offices: Albuquerque, Atlanta, Chicago, Dayton, Denver, Huntsville, Los Angeles, Oak Ridge, San Diego, San Francisco, Tucson, and Washington, D.C.

Figure 2.3-7. Contact Letter Sent to Exposed Subjects.

ADDRESS VERIFICATION

Is the above information correct? [] yes [] no
If no, please provide correct information below. Please place in the return envelope provided and return to Science Applications, Inc.

Figure 2.3-8. Attendance Verification Form Sent to Exposed Group.

FRIENDS AND RELATIVES WHO ATTENDED
SAUGUS ELEMENTARY SCHOOL

If you know the address of friends or relatives who attended Saugus Elementary School anytime between 1959 to 1970, please provide information below:

1. Name _____

   Presently alive? [] yes [] no
   If deceased: date of death_____ County/State of death _____

   Address_____

   _____

   Phone ( )_____

2. Name _____

   Presently alive? [] yes [] no
   If deceased: date of death_____ County/State of death_____

   Address_____

   _____

   Phone ( )_____

3. Name _____

   Presently alive? [] yes [] no
   If deceased: date of death_____ County/State of death _____

   Address_____

   _____

   Phone ( )_____

** Please place in the envelope provided and return to Science Applications, Inc., 1801 Ave. of the Stars, Suite 1205, Los Angeles, CA 90067

Figure 2.3-9. Form Used to Locate Friends and Relatives of Located Exposed Subjects.

CONSENT FOR FOLLOW-UP

Science Applications, Inc., is investigating the possible health effects of exposure to vinyl chloride for the California State Air Resources Board. I agree to allow Science Applciations, Inc., to keep my name and address in a confidential file, and to contact me periodically in the future. I understand that any future contact will be for the purpose of gathering information pertinent to the study, and that I am not agreeing to any actual participation.

[SIGNATURE] [DATE]

Figure 2.3-10. Consent Form for Follow-Up.

who did not respond within two weeks after the mailing of the second letter were contacted by telephone whenever possible. Control subjects verified to be alive by phone contact were considered located. Exposed subjects known to be alive on or after the cut-off date for whom requests for a signed follow-up consent were sent to the correct address (verified by contact with subject, sibling or parent) were considered located. All subjects not located continued to be traced. In the next step of the tracing scheme, located subjects who had siblings not yet located were asked to provide information on their not-yet-located siblings. This was accomplished in several ways.

All subjects sent letters were asked to provide information on friends and relatives who attended Saugus Elementary or LSD schools, depending on their study grouping. Forms returned by located siblings were reviewed for information on their not-yet-located brothers and sisters. Information on this form, which is shown in Figures 2.3-6 and 2.3-7, was taken as evidence of vital status assuming that siblings would know and provide the vital status of siblings.

Located subjects having not-yet-located siblings, but who provided no information on the "Friends and Relatives" form, were contacted either by letter or by phone and asked to provide information on their brothers and sisters. Samples of the letters and forms sent to exposed and control siblings are presented in Figures 2.3-11 and 2.3-12, respectively. The script used to contact exposed and control siblings by phone is provided in Figures 2.3-13 and 2.3-14. Letter contact was used primarily in the earlier stages of tracing; we later found phone contact to be much more efficient, and letters were sent only when a telephone number could not be obtained. Controls found in this stage of the tracing scheme were considered located; exposed subjects found in this manner were sent requests for a signed follow-up consent and also considered located. Subjects not yet located continued to be traced.

The next step in the tracing scheme (Figure 2.3-1) was a search of local phone books for the telephone number of subjects, or their parents. (Parent's names were provided in both Saugus and Lancaster School records.)

We need your help with an important health survey. The California Air Resources Board and Science Applications, Inc., are studying possible health effects of exposure to vinyl chloride gas.

The need for this survey was recognized when elevated levels of vinyl chloride were detected around the area of the Saugus Elementary School. The school was located near a factory that uses vinyl chloride to make plastic. We are asking persons who attended this school during the 1950's and 60's to help with this survey. The Saugus Union School District has joined with us to compile a list of former students. According to their records, your brothers/sisters listed below, attended the Saugus Elementary School during this period of time. It is important that we contact them personally; therefore, we are depending on your help.

Please write current addresses and telephone numbers under their names and mail them back to us.

After talking with us, your brothers/sisters may, of course, decide not to participate. However, your help, and the help of your neighbors who lived in the Saugus area, is vitally important to the success of this research project. We believe that the information derived from this research could be of direct importance to your brothers/sisters and their families.

If you have any questions, please feel free to call us collect at (213) 553-2705, and ask for Mr. George Maldonado.

Thank you.

Sincerely,

SCIENCE APPLICATIONS, INC.

Richard A. Ziskind, Ph.D.
Manager
Energy-Environment Systems Division

Science Applications, Inc. 1900 Avenue of the Stars Suite 900 Los Angeles California 90067 (213) 553-2705
Other SAI Offices Albuquerque Atlanta Chicago Dayton Denver Huntsville Los Angeles Oak Ridge San Diego San Francisco Tucson and Washington D.C.

Figure 2.3-11. Letter to Siblings of Exposed Subjects.

Please provide information on the persons listed below:

1. Name _____

   Presently alive? [] yes [] no
   If deceased: date of death _____ County/State of death _____

   Address _____

   _____

   Phone ( ) _____

2. Name _____

   Presently alive? [] yes [] no
   If deceased: date of death _____ County/State of death _____

   Address _____

   _____

   Phone ( ) _____

3. Name _____

   Presently alive? [] yes [] no
   If deceased: date of death _____ County/State of death _____

   Address _____

   _____

   Phone ( ) _____

** Please place in the envelope provided and return to Science Applications, Inc., 1801 Ave. of the Stars, Suite 1205, Los Angeles, CA 90067

Figure 2.3-11 Ctd. Letter to Siblings of Exposed Subjects (Page 2).

We need your help with an important health survey. The California Air Resources Board and Science Applications, Inc., are studying possible health effects of exposure to vinyl chloride gas. We are asking people who attended elementary schools in the Lancaster or Saugus School Districts during the 1950's or 1960's to help with this research.

The need for this study was recognized when elevated levels of vinyl chloride were detected around the area of the Saugus Elementary School. The school was located near a factory that uses vinyl chloride to make plastic.

The Lancaster and Saugus Union School Districts have joined with us to compile a list of former students. According to their records, your brothers/sisters, listed on the attached form, attended Lancaster schools during this period of time. It is important that we contact them; therefore, we are depending on your help.

Please write current addresses and telephone numbers under their names and mail them back to us.

After talking with us, your brothers/sisters may, of course, decide not to participate. However, your help, and the help of your brothers/sisters is vitally important to the success of this research project. We believe that the information derived from this research could be of direct important to your brothers/sisters and their families.

If you have any questions, please feel free to call us collect at (213) 553-2705, and ask for Mr. George Maldonado.

Thank you.

Sincerely,

SCIENCE APPLICATIONS, INC.

Richard A. Ziskind, Ph.D.
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/m

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Figure 2.3-12. Letter to Siblings of Controls.

Please provide information on the persons listed below:

1. Name _____

   Presently alive? ☐ yes ☐ no
   If deceased: date of death_____ County/State of death _____

   Address_____

   _____

   Phone ( )_____

2. Name _____

   Presently alive? ☐ yes ☐ no
   If deceased: date of death_____ County/State of death _____

   Address_____

   _____

   Phone ( )_____

3. Name _____

   Presently alive? ☐ yes ☐ no
   If deceased: date of death_____ County/State of death _____

   Address_____

   _____

   Phone ( )_____

** Please place in the envelope provided and return to Science Applications, Inc., 1801 Ave. of the Stars, Suite 1205, Los Angeles, CA 90067

Figure 2.3-12 Ctd. Letter to Siblings of Controls (Page 2).

Hello. My name is _____. I'm a scientist with Science Applications - a research company in Los Angeles.

We are trying to contact your [brother/sister/son/daughter/children], [name(s)], to ask [him/her/them] to participate in an important health study we are conducting for the state of California, but we haven't been able to locate [him/her/them]. Could you give us [his/her/their] current address or phone number?

If Hesitant...

Or could you ask [him/her/them] to call us collect at (213) 553-2705 and talk to George Maldonado?

Let me tell you what this is all about - Science Applications and the state of California are studying the heath effects caused by vinyl chloride gas. It's important that we locate as many people as possible who attended Saugus Elementary School or schools in the Lancaster District during the 50's and 60's. Students in the Lancaster District were not exposed; Students who attended Saugus may have been exposed to vinyl chloride gas; The school districts have put together a list of students for us. Your [child's /children's name(s) [is/are] on that list.

What kind of participation?

At this point in the study we are simply trying to locate as many people as we can who attended these schools. We want to ask your [son/daughter/children] for names and addresses of friends or relatives who attended elementary school with [him/her/them.]

Figure 2.3-13. Telephone Contact Script for Parents and Siblings of Exposed Subjects.

Hello. My name is _____. I'm a scientist with Science Applications - a research company in Los Angeles.

We are trying to contact your [brother/sister/son/daughter/children], [name(s)], to ask [him/her/them] to participate in an important health study we are conducting for the state of California, but we haven't been able to locate [him/her/them]. Could you give us [his/her/their] current address or phone number?

If Hesitant...

Or could you ask [him/her/them] to call us collect at (213) 553-2705 and talk to George Maldonado?

Let me tell you what this is all about - Science Applications and the state of California are studying the heath effects caused by vinyl chloride gas. It's important that we locate as many people as possible who attended elementary schools in the Lancaster District or Saugus Elementary School duruing the 50's and 60's. Students in the Lancaster District were not exposed; Students who attended Saugus may have been exposed to vinyl chloride gas; The school districts have put together a list of students for us. Your [child's /children's name(s) [is/are] on that list.

What kind of participation?

At this point in the study we are simply trying to locate as many people as we can who attended these schools. We want to ask your [son/daughter/children] for names and addresses of friends or relatives who attended elementary school with [him/her/them.]

Figure 2.3-14. Telephone Contact Script for Parents and Siblings of Controls.

The Santa Clarita Valley (May 1982), Lancaster (August 1981), and Palmdale (May 1982) phone books were searched. All identified phone numbers were called and address and/or vital status information was requested for the subject being traced. A fair number of parents were located in this manner, some residing at the same address listed on the elementary school records. Again, control subjects found in this manner were considered located; exposed subjects were sent letters requesting follow-up consents and considered located. Copies of death certificates were requested for subjects reported to be deceased. Subjects not "located" in this step continued to be traced.

In the next step of the tracing scheme, 1981-1982 California State Property Tax Rolls were searched for the addresses of subjects, or their parents. Whenever possible, persons identified by this method were contacted by telephone, verified to be the correct subject/parent/relative, and asked to provide address and vital status information. When telephone numbers were not available, contact was made by letter. Copies of letters sent to parents are presented in Figures 2.3-15 and 2.3-16.

2.3.2 Additional Tracing Methods

Subjects not yet located at this point in the tracing scheme were funneled into four different tracing methods, in parallel:

(1) California Automated Mortality Linkage System (CAMLIS)
(2) Out-of-state DMV requests
(3) California marriage records
(4) Voter registration records

In a mortality study it is crucial to uncover as many deaths as possible. Up to this point in the tracing scheme we concentrated our efforts on tracing methods more likely to discover persons alive than persons deceased. For this reason we contacted Mr. Roger Smith of the State of California Department of Health Services, Vital Statistics Branch, and inquired about methods to match not-yet-located subjects against the California State mortality records. He suggested we use the California Automated Mortality Linkage System (CAMLIS) run by the Department of Epidemiology and International Health

We need your help with an important health survey. The California Air Resources Board and Science Applications, Inc., are studying possible health effects of exposure to vinyl chloride gas.

The need for this survey was recognized when elevated levels of vinyl chloride were detected around the area of the Saugus Elementary School. The school was located near a factory that uses vinyl chloride to make plastic. We are asking persons who attended this school during the 1950's and 60's to help with this survey. The Saugus Union School District has joined with us to compile a list of former students. According to their records, your children, listed below, attended the Saugus Elementary School during this period of time. It is important that we contact them personally; therefore, we are depending on your help.

Please write current addresses and telephone numbers under their names and mail them back to us.

After talking with us, your children may, of course, decide not to participate. However, your help, and the help of your neighbors who lived in the Saugus area, is vitally important to the success of this research project. We believe that the information derived from this research could be of direct importance to your children and their families.

If you have any questions, please feel free to call us collect at (213) 553-2705, and ask for Mr. George Maldonado.

Thank you.

Sincerely,

SCIENCE APPLICATIONS, INC.

Richard A. Ziskind, Ph.D.
Manager
Energy-Environment Systems Division

Science Applications, Inc. 1900 Avenue of the Stars Suite 900 Los Angeles California 90067 (213) 553-2705
Other SAI Offices: Albuquerque Atlanta Chicago Dayton Denver Huntsville Los Angeles Oak Ridge San Diego San Francisco Tucson and Washington DC

Figure 2.3-15. Letter to Parents of Exposed Subjects.

We need your help with an important health survey. The California Air Resources Board and Science Applications, Inc., are studying possible health effects of exposure to vinyl chloride gas. We are asking people who attended elementary schools in the Lancaster or Saugus School Districts during the 1950's or 1960's to help with this research.

The need for this study was recognized when elevated levels of vinyl chloride were detected around the area of the Saugus Elementary School. The school was located near a factory that uses vinyl chloride to make plastic.

The Lancaster and Saugus Union School Districts have joined with us to compile a list of former students. According to their records, your children, listed on the attached form, attended Lancaster schools during this period of time. It is important that we contact them; therefore, we are depending on your help.

Please write current addresses and telephone numbers under their names and mail them back to us.

After talking with us, your children may, of course, decide not to participate. However, your help, and the help of your children, is vitally important to the success of this research project. We believe that the information derived from this research could be of direct important to those persons who attended Saugus Elementary and their families.

If you have any questions, please feel free to call us collect at (213) 553-2705, and ask for Mr. George Maldonado.

Thank you.

Sincerely,

SCIENCE APPLICATIONS, INC.

Richard A. Ziskind, Ph.D.
Manager
Energy-Environment Systems Division

/m

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Figure 2.3-16. Letter to Parents of Controls.

at the University of California, San Francisco. As described in a CAMLIS brochure,

> The CAMLIS system has been specifically designed for the purpose of matching user files against State of California mortality files for the years 1966-81. In order to accomplish this objective, the system performs a two-stage match which incorporates the best features of match key and probabilistic matching procedures. Standard system output consists of printed listings of all definite matches in comparison-pair format, plus a supplementary punchcard file containing the User Record Identification Number, State File Number, Date of Death and Cause of Death for these matches. Data on borderline matches are also provided in a form convenient for purposes of review.

The CAMLIS System reportedly produces results superior to those attainable by manual review of death records. The names, birthdates, and dates last alive of all subjects not yet determined to be alive on or after 1 January 1980 were submitted to CAMLIS and matched against the California mortality files from 1966 to 1981. Deaths uncovered by the CAMLIS System were verified to be the correct person by obtaining copies of death certificates and checking full name, date of birth, parents' names and place of birth against the school records.

As a complement to the CAMLIS System we have asked the Veterans Administration to allow us access to the Veterans and Beneficiary Identification and Locator System (BIRLS). This is a data file which has been estimated to be 98-percent complete in listing veterans of the U.S. Armed Forces who have died. We hoped to use this data file to locate subjects who were veterans and who died outside of California. As of this writing the Veterans Administration has not yet responded to our request for access to this file.

As a "shot in the dark," names and birthdates of not yet located subjects were submitted to Arizona, Colorado, Nevada, Utah and Washington which were the states of residence for many of the located subjects who lived outside of California. As of this writing results have been received only for Colorado and Washington. A fair number of subjects were located by this method.

The maiden names of all female subjects, not yet located, were matched against the 1970-1979 California state marriage records to determine married name and husband's name; if these were found, DMV, phone book and property tax rolls were consulted again. Very few subjects were located as a result of this effort.

A small sample of non-located subjects was matched against the Los Angeles County Voter Registration records. It was determined that a search of these records would not be productive at this point in the tracing scheme.

Subjects not located at the end of the tracing scheme were classified as lost to follow-up.

2.4 VALIDATION PROTOCOL

A protocol was developed by SAI staff and consultant Gary H. Spivey to validate pilot study (Ziskind et al., 1981) questionnaire responses concerning reproductive outcomes and other selected outcomes.

2.4.1 Methods for Obtaining Validation Data

The questionnaire responses selected for validation included the following:

- Gravida/parity
- Difficulty conceiving
- Outcome of each pregnancy (i.e., live birth, still birth, miscarriage, abortion)
- Congenital defects in child
- Child still alive
- Major illnesses in child

Validation protocol procedures are diagrammed in Figure 2.4-1. Married female respondents were placed into two categories: those who reported an

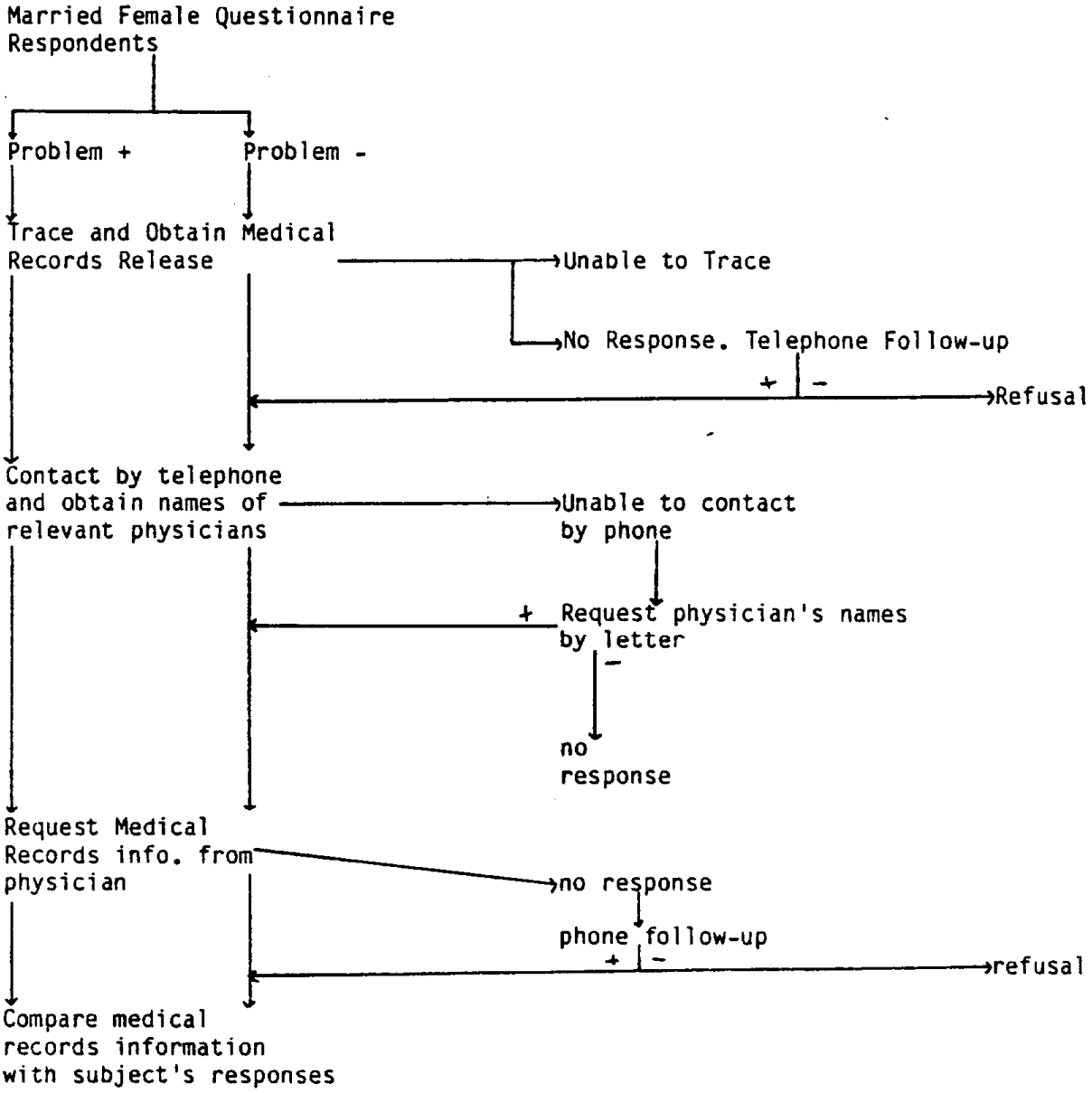

Figure 2.4-1. Validation Protocol Diagram.

abnormal reproductive outcome (i.e., congenital abnormality, miscarriage or stillbirth) and those who reported none of these problems. Subjects were randomly ordered in each category. Our goal was to validate the responses of 10 subjects in each category.

Most questionnaire respondents signed medical records release forms at the time of interview during the pilot study. Unfortunately, the medical records release forms had an expiration time of six months. Therefore, all validation subjects needed to be traced to the present and requested to sign new medical records release forms. Allowing for problems in tracing, refusal to sign release forms, problems in obtaining names of physicians, and problems in obtaining the cooperation of physicians, the first 15 names were selected from the random listing in each category. Part way through the validation procedure we realized that subjects who reported an abnormal reproductive outcome were much less willing to sign medical record release forms than subjects who did not report these problems. For this reason the next 10 random "problem positive" subjects were selected, traced and sent letters requesting their participation, for a total of 25 subjects selected in this group.

Most of the selected subjects were traced to the present and sent a letter explaining the validation protocol and requesting a signature on a Medical Records Release form (Figures 2.4-2, 2.4-3, 2.4-4). Those subjects who did not respond to the letter were contacted by telephone to verify that the letter and request for medical records release were received, to answer any questions and to persuade the subject to participate.

Those subjects who returned signed medical records release forms were contacted by telephone and asked to supply the names of obstetricians, gynecologists and family physicians who had treated them during the time they had been married. This information was recorded on a physician list form. The phone contact script and the physician list form are shown in Figures 2.4-5, and 2.4-6, respectively. A cover letter (Figure 2.4-7), questionnaire (Figure 2.4-8), and a stamped return envelope were sent to each of the named physicians. In addition, physicians of subjects who had reported an abnormal pregnancy outcome were also sent a Diagnosis Confirmation Request form (Figure 2.4-9). Typically, two to four physicians were named by each subject.

Some time ago you participated in the first phase of an important health survey conducted by Science Applications, Inc., for the U.S. Environmental Protection Agency. The study examined persons who may have been exposed to vinyl chloride while attending the Saugus Elementary School. This survey was initiated when elevated levels of vinyl chloride (which may have health implications) were detected in the area of the school. With the help of the Saugus Union School District we compiled a list of former students and asked them to help with the survey. Thank you for cooperating in the first phase of the study.

Science Applications, Inc., is now conducting the second phase of the study with support from the California State Air Resources Board. In this phase we will contact a group of people who attended Saugus Elementary School (who may have been exposed to vinyl chloride) and a group of people who attended Desert View School in the Lancaster School District (who were not exposed). We will determine where each person is living today. For those who have died we will determine the cause of death.

As you remember, you agreed to allow us to contact you periodically to inform you of our progress and to gather further information. No new health information is needed from you at this time. However, we need to examine the medical records for a sample of study participants to gain further information. Therefore, we would like you to sign the enclosed "Release Of Medical Records" form and return it to Science Applications, Inc., as soon as possible. Also, please fill out and return the enclosed "Address Verification" form verifying your address and phone number. We will use this information to update our files, allowing us to contact you in the future if necessary. If you know the address of brothers, sisters, or friends who attended Saugus Elementary School at about the same time as you, it would be extremely helpful to us if you would write this information on the "Friends and Relatives Who Attended Saugus Elementary School" form.

Science Applications, Inc. 1900 Avenue of the Stars Suite 900. Los Angeles California 90067 (213) 553-2705
Other SAI Offices Albuquerque Atlanta Chicago Dayton Denver Huntsville Los Angeles Oak Ridge San Diego San Francisco Tucson and Washington D.C.

Once again, thank you for your cooperation. The cooperation of you and your classmates is vitally important to the success of this study. We believe the information derived from this research may be of direct importance to you and your family.

If you have any questions about this study, at any time, you may contact Mr. George Maldonado at (213) 553-2705.

Thank you.

Sincerely,

SCIENCE APPLICATIONS, INC.

Richard A. Ziskind, Ph.D.
Manager
Energy-Environment Systems Division

Figure 2.4-2. Letter to Validation Protocol Participants Not Yet Contacted in This Phase of Study.

Recently you were kind enough to participate in a study of the possible effects of childhood exposure to vinyl chloride. Thank you for your cooperation.

As you remember, you agreed to allow us to contact you periodically to inform you of our progress and to gather further information. We need to examine the medical records for a sample of study participants to gather further data. You have been randomly chosen to participate in this phase of the study. Please sign the enclosed "Medical Records Release" form and return it to Science Applications, Inc., as soon as possible. We will be calling you in the near future to ask for names and phone numbers of physicians who have treated you during the time you have been married.

Once again, thank you for your cooperation. The cooperation of you and your classmates is vitally important to the success of this study. We believe the information derived from this research may be of direct importance to you and your family.

If you have any questions, you may contact Mr. George Maldonado at (213) 553-2705.

Thank you,

SCIENCE APPLICATIONS, INC.

Richard A. Ziskind, Ph.D.
Manager
Energy-Environment Division

/m

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Figure 2.4-3. Letter to Validation Protocol Participants Contacted Earlier in This Phase of Study.

RELEASE OF MEDICAL RECORDS

I have agreed to participate in a study being conducted by Science Applications, Inc., for the California Air Resources Board. This study is investigating possible health effects of exposure to vinyl chloride.

I authorize the release of my medical records to:

Program Physician
Vinyl Chloride Health Survey
Science Applications, Inc.
1900 Avenue of the Stars, #900
Los Angeles, California 90067

so that they may be reviewed for information pertinent to the study.

I understand that this information will be used for study purposes only and will not be released to any other party.

Signature _____ Date _____

Figure 2.4-4. Medical Records Release Form.

Hello. May I speak to [Mr. or] Mrs. [Subject's name]?

My name is ____ and I work for Science Applications, Inc.

As I'm sure you remember, Science Applications is studying the possible health effects of childhood exposure to vinyl chloride. We sent you a letter explaining the study, and you were kind enough to cooperate with us.

I am calling for a couple of reasons: First, I want to thank you for your cooperation; Second, as was explained in the letter we sent you, we need to examine the medical records for a small sample of people to gather further information. You [and your husband/wife] were randomly chosen to participate in this part of the study, and, as you remember, you signed a "Medical Records Release" form.

Before we can look at your records we need to know:

1. During the time you have been married, who has been your family physician(s)

   Name
   address
   City/State
   Phone
   Dates:

2. During the time you have been married, who has been you obstetrician/gynecologist(s)?

   Name
   Address
   City/State
   Phone
   Dates:

Figure 2.4-5. Validation Study Phone Contact Script.

ID#_____

Name of subject_____

1. Name of physician _____

Address
City/State/zip
Phone
Dates of Treatment: From _____ To _____

2.Name of physician _____

Address
City/State/zip
Phone
Dates of Treatment: From _____ To _____

3.Name of physician _____

Address
City/State/zip
Phone
Dates of Treatment: From _____ To _____

4.Name of physician _____

Address
City/State/zip
Phone
Dates of Treatment: From _____ To _____

5.Name of physician _____

Address
City/State/zip
Phone
Dates of Treatment: From _____ To _____

Figure 2.4-6. Physician List for Validation Study.

The patient named above has given us your name and permission to contact you about her medical history. A copy of her authorization is enclosed.

She is participating in an epidemiologic study of the health effects of childhood exposure to vinyl chloride, conducted by Science Applications, Inc., and funded by the California State Air Resources Board.

In order to classify this patient appropriately, we need to know if you have made certain diagnoses. We would appreciate your assistance in this research by filling out the attached form, which will be reviewed by the project physician.

We haven't received a response to our first request for medical records information. As I'm sure you understand, the scientific validity of epidemiologic studies such as this depends on the completeness and accuracy of the information obtained. Please take a few minutes and fill out the enclosed form.

We greatly appreciate the time and effort involved in complying with our request. Should you have any questions, please call George Maldonado at (213) 553-2705.

Sincerely,

SCIENCE APPLICATIONS, INC.

Richard A. Ziskind, Ph.D.
Principal Investigator

Encl

/m

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Figure 2.4-7. Letter to Physicians for Validation Study.

ID_____

Patient_____ Physician _____

1. To your knowledge, has this patient ever had difficulty conceiving?

[] No [] Yes --- Please Describe:_____

_____

_____

_____

2. Please record: Gravida_____ Parity _____

3. For each pregnancy you have information on, please record the following information:

	First Pregnancy	Second Pregnancy	Third Pregnancy
a. Duration (in weeks)			
b. Date of Delivery			
c. Did pregnancy end with live birth? If no, please record details Including explanation, if any, for this outcome.	[] yes [] no Describe:	[] yes [] no Describe:	[] yes [] no Describe:

Figure 2.4-8. Physician Questionnaire for Validation Study.

	First Pregnancy	Second Pregnancy	Third Pregnancy
d. Any congenital defects?	[] no [] yes Describe:	[] no [] yes Describe:	[] no [] yes Describe:

	First Pregnancy	Second Pregnancy	Third Pregnancy
FOR LIVE BIRTHS ONLY e. Child still alive?	[] yes [] don't know [] no Describe:	[] yes [] don't know [] no Describe:	[] yes [] don't know [] no Describe:

Figure 2.4-8. Physician Questionnaire for Validation Study (Ctd).

	First Pregnancy	Second Pregnancy	Third Pregnancy
FOR LIVE BIRTHS ONLY f. Any major illness in child?	[] no [] don't know [] yes Describe:	[] no [] don't know [] yes Describe:	[] no [] don't know [] yes Describe:

Figure 2.4-8. Physician Questionnaire for Validation Study (Ctd).

Physician _____ ID No. _____

Re: Your patient _____

Have you made the diagnosis of _____ in this patient?

YES ☐ → When did you make this diagnosis? _____

NO ☐ Please summarize the pertinent diagnostic information (e.g., history, laboratory, etc.)

_____

_____

_____

_____

_____

_____

_____

_____

_____

Thank you.

Do you know of another doctor who has made this diagnosis?

YES ☐ Can you give us the name and address?

NO ☐ _____

_____

Have you ever entertained this diagnosis in this patient?

YES ☐

NO ☐

Do you know of another diagnosis which the patient may have confused with this?

YES ☐ Specify: _____

_____

NO ☐

Figure 2.4-9. Diagnosis Confirmation Request Form.

Physicians who did not respond to our request for medical records information were contacted by phone. The procedure we found to work well was not to ask to speak to the physician, but to explain what was needed to the person who answered the telephone. In several cases information was obtained over the phone.

2.4.2 Validation Study Analytical Methods

For each valiation protocol subject, questionnaire responses were compared with physician's responses on the physician's questionnaire and, in a few cases, with medical records information obtained over the telephone. Subject and physician responses were compared for the following pieces of information:

- Pregnancy outcome: normal versus abnormal (miscarriage, stillbirth and therapeutic abortion)
- Miscarriage versus not miscarriage
- Congenital birth defect versus no birth defect
- Difficulty conceiving
- Gravida/parity
- Major illness in child
- Child still alive

Subject and physician responses were compared and categorized into 2 x 3 tables. The validity of the responses to the subject questionnaire for each of the above-listed outcomes was evaluated by calculating percentage sensitivity and percentage specificity. Percentage sensitivity is the percentage of abnormal outcomes (e.g., miscarriage, birth defect, etc.) which are correctly reported and verified by physician. This is calculated as follows:

		PHYSICIAN REPORTED OUTCOMES	
		Problem	No Problem
SUBJECT REPORTED OUTCOMES	problem	a	b
	no problem	c	d

$$\text{Pct sensitivity} = \frac{\text{No. of verified problem outcomes (a)}}{\text{Total number of reported problem outcomes (a+c)}} \times 100$$

Percentage specificity is the percentage of normal outcomes which were correctly reported and verified.

$$\text{Pct specificity} = \frac{\text{No. of verified normal outcomes (d)}}{\text{Total number of reported normal outcomes (b+d)}} \times 100$$

3.0
RESULTS

In this section we present the results of subject tracing, the mortality study, and the validation protocol.

3.1 RESULTS OF TRACING

The results of our tracing efforts were as follows:

Tracing Results	Exposed	Controls
Total persons	1,363	979
Traced	1,039 (76.2%)	764 (78.0%)
Lost to follow-up	324	215
Alive on or before 1 January 1980	1,023	749
Deaths before 1 January 1980	16	15

Table 3.1-1 shows frequency distributions of the year all exposed and control subjects were last known to be alive. The percentage of subjects traced is comparable for both exposed and control groups.

It is interesting to compare the point in time at which losses to follow-up occur in each group. A person-years and life table analysis in which the end-point of interest ("death") is defined as "losses to follow-up" is presented in Tables 3.1-2, 3.1-3 and Figure 3.1-1 for all exposed subjects and controls; in Tables 3.1-4, 3.1-5 and Figure 3.1-2 for males; and in Tables 3.1-6, 3.1-7 and Figure 3.1-3 for females.

In the person-years incidence tables, "deaths" = losses to follow-up. In the life tables:

X = year after the start of school attendance

NX = number of subjects not yet lost to follow-up at the beginning of the interval

DX = number of persons lost to follow-up during the interval

WX = number of deaths during the interval

Table 3.1-1

FREQUENCY DISTRIBUTION OF YEAR EXPOSED AND CONTROL GROUP WERE LAST KNOWN TO BE ALIVE

Year	Exposed Group No.	Exposed Group Pct.	Control Group No.	Control Group Pct.
1952	0	0	0	0
1953	0	0	0	0
1954	0	0	0	0
1955	0	0	0	0
1956	0	0	0	0
1957	0	0	0	0
1958	0	0	0	0
1959	18	1.32	0	0
1960	34	2.50	0	0
1961	31	2.28	13	1.33
1962	20	1.47	18	1.84
1963	46	3.38	36	3.68
1964	37	2.72	35	3.57
1965	38	2.79	35	3.57
1966	12	0.88	8	0.82
1967	10	0.73	3	0.31
1968	9	0.66	5	0.51
1969	5	0.37	7	0.72
1970	6	0.44	3	0.31
1971	2	0.15	1	0.10
1972	4	0.29	0	0
1973	6	0.44	5	0.51
1974	7	0.51	5	0.51
1975	9	0.66	6	0.61
1976	9	0.66	5	0.51
1977	4	0.29	10	1.02
1978	9	0.66	13	1.33
1979	24	1.76	22	2.25
1980	300	22.01	157	16.04
1981	333	24.43	254	25.94
1982	390	28.61	338	34.52
Totals	1,363	100.00	979	100.00

Table 3.1-2

PERSON-YEARS AND LIFE TABLE ANALYSIS OF LOSSES

TO FOLLOW-UP: EXPOSED GROUP

DEATHS ARE DEFINED AS LOST TO FOLLOW-UP IN THIS ANALYSIS
1363 RECORDS READ
BOTH SEXES

1. PERSON-YEARS INCIDENCE

DEATHS 324

PERSON-YEARS 21443.5833

DEATHS/PERSON-YEARS = .015109415

2. LIFE TABLE

X	NX	DX	WX	T	QX	PX	SX	RX
0	1363	45	0	0	.0330154072	.966984593	.966984593	.0330154072
1	1318	97	0	0	.0735963581	.926403642	.895818048	.104181952
2	1221	50	0	0	.0409500409	.959049959	.859134263	.140865737
3	1171	29	1	0	.0247757369	.975224263	.837848578	.162151422
4	1141	7	1	0	6.13765892E-03	.993862341	.832706149	.167293851
5	1133	15	1	0	.0132450331	.986754967	.821676929	.178323071
6	1117	14	0	0	.0125335721	.987466428	.811378382	.188621618
7	1103	5	0	0	4.53309157E-03	.995466908	.80770033	.19229967
8	1098	2	0	0	1.82149363E-03	.998178506	.806229109	.193770891
9	1096	0	1	0	0	1	.806229109	.193770891
10	1095	2	1	0	1.82731841E-03	.998172682	.804755871	.195244129
11	1092	3	1	0	2.74851122E-03	.997251489	.802543991	.197456009
12	1088	4	1	0	3.67816092E-03	.996321839	.799592105	.200407895
13	1083	3	1	0	2.77136259E-03	.997228637	.797376145	.202623855
14	1079	5	2	0	4.63821893E-03	.995361781	.79367774	.20632226
15	1072	11	3	32	.0104314841	.989568516	.785398503	.214601497
16	1026	7	2	169	7.44284955E-03	.992557151	.7795529	.2204471
17	848	12	1	94	.0149906309	.985009369	.767866911	.232133089
18	741	3	0	181	4.61183705E-03	.995388163	.764325634	.235674366
19	557	2	0	80	3.86847195E-03	.996131528	.761368861	.238631139
20	475	6	0	128	.0145985401	.98540146	.750253987	.249746013
21	341	2	0	339	.0116618076	.988338192	.74150467	.25849533

TOTAL 324 16 1023

Table 3.1-3

PERSON-YEARS AND LIFE TABLE ANALYSIS OF LOSSES

TO FOLLOW-UP: CONTROL GROUP

DEATHS ARE DEFINED AS LOST TO FOLLOW-UP IN THIS ANALYSIS
1025 RECORDS READ
BOTH SEXES

1. PERSON-YEARS INCIDENCE

DEATHS 215

PERSON-YEARS 15422.6667

DEATHS/PERSON-YEARS = .0139405204

2. LIFE TABLE

X	NX	DX	WX	T	QX	PX	SX	RX
0	979	30	0	0	.0306435138	.969356486	.969356486	.0306435139
1	949	51	0	0	.0537407798	.94625922	.917262512	.0827374875
2	898	29	0	0	.0322939866	.967706013	.887640449	.112359551
3	869	19	0	0	.0218642117	.978135788	.86823289	.13176711
4	850	14	0	0	.0164705882	.983529412	.853932584	.146067416
5	836	8	1	0	9.57510473E-03	.990424895	.84575609	.15424391
6	827	6	0	0	7.25513906E-03	.992744861	.839620012	.160379988
7	821	2	0	0	2.43605359E-03	.997563946	.837574652	.162425348
8	819	0	1	0	0	1	.837574652	.162425348
9	818	1	2	0	1.22399021E-03	.99877601	.836549469	.163450531
10	815	2	0	0	2.45398773E-03	.997546012	.834496587	.165503413
11	813	2	0	0	2.4600246E-03	.997539975	.832443705	.167556295
12	811	3	2	0	3.7037037E-03	.996296296	.82936058	.17063942
13	806	3	1	0	3.72439479E-03	.996275605	.826271714	.173728286
14	802	9	1	1	.0112359551	.988764045	.816987762	.183012238
15	791	6	2	9	7.63844685E-03	.992361553	.810747245	.189252755
16	774	7	2	171	.0101818182	.989818182	.802492364	.197507636
17	594	6	0	163	.0117073171	.988292683	.793097331	.206902669
18	425	8	0	93	.0211360634	.978863937	.776334376	.223665624
19	324	3	2	84	.0106761566	.989323844	.768046108	.231953892
20	235	5	0	84	.0259067358	.974093264	.748148541	.251851459
21	146	1	1	144	.0136054422	.986394558	.737969649	.262030351

TOTAL 215 15 74

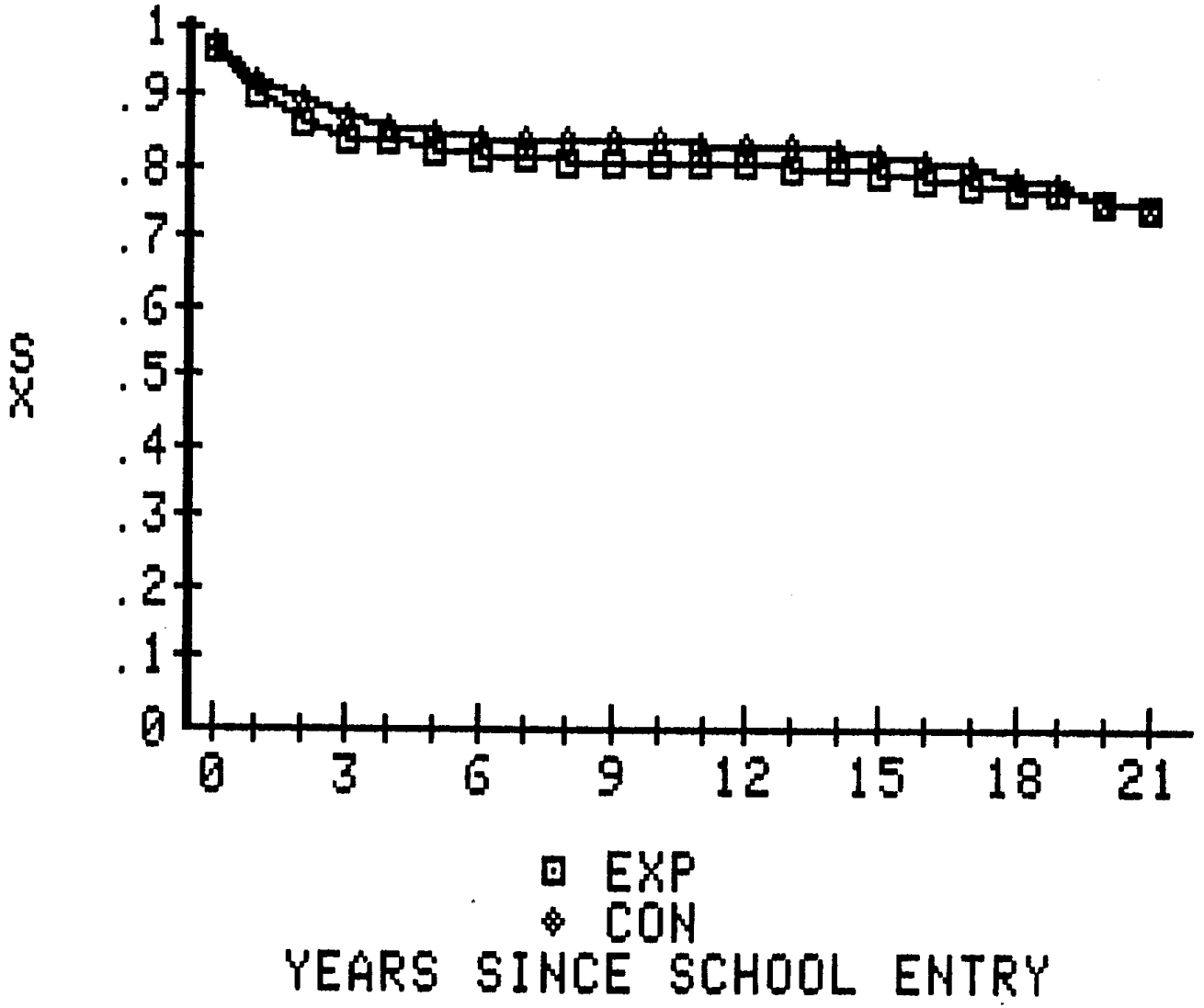

Figure 3.1-1. Cumulative Probability of Not Being Lost to Follow-Up: Exposed vs. Controls.

Table 3.1-4

PERSON-YEARS AND LIFE TABLE ANALYSIS OF LOSSES

TO FOLLOW-UP: EXPOSED MALES

DEATHS ARE DEFINED AS LOST TO FOLLOW-UP IN THIS ANALYSIS
1363 RECORDS READ
SEX = M

1. PERSON-YEARS TABLE

DEATHS 117

PERSON-YEARS 11225.4167

DEATHS/PERSON-YEARS = .0104227757

2. LIFE TABLE

X	NX	DX	WX	T	QX	PX	SX	RX
0	679	21	0	0	.0309278351	.969072165	.969072165	.030927835
1	658	35	0	0	.0531914894	.946808511	.917525773	.0824742268
2	623	17	0	0	.0272873194	.972712681	.892488954	.107511046
3	606	9	1	0	.014863749	.985136251	.879223223	.120776777
4	596	2	1	0	3.35852225E-03	.996641478	.876270332	.123729668
5	593	5	1	0	8.43881856E-03	.991561181	.868875646	.131124354
6	587	6	0	0	.0102214651	.989778535	.859994464	.140005536
7	581	2	0	0	3.44234079E-03	.996557659	.85703407	.14296593
8	579	0	0	0	0	1	.85703407	.14296593
9	579	0	1	0	0	1	.85703407	.14296593
10	578	1	0	0	1.73010381E-03	.998269896	.855551312	.144448688
11	577	0	0	0	0	1	.855551312	.144448688
12	577	1	1	0	1.73460538E-03	.998265395	.854067268	.145932732
13	575	1	1	0	1.74064404E-03	.998259356	.852580641	.147419359
14	573	3	2	0	5.24475524E-03	.994755245	.848109064	.151890936
15	568	4	3	11	7.13012478E-03	.992869875	.842061941	.157938059
16	550	2	1	99	4E-03	.996	.838693693	.161306307
17	448	5	1	57	.0119331742	.988066826	.828685415	.171314585
18	385	0	0	92	0	1	.828685415	.171314585
19	293	1	0	40	3.66300366E-03	.996336996	.825649937	.174350063
20	252	1	0	69	4.59770115E-03	.995402299	.821853846	.178146154
21	182	1	0	181	.0109289618	.989071038	.812871836	.187128164

TOTAL 117 13 549

Table 3.1-5

PERSON-YEARS AND LIFE TABLE ANALYSIS OF LOSSES TO FOLLOW-UP: CONTROL MALES

DEATHS ARE DEFINED AS LOST TO FOLLOW-UP IN THIS ANALYSIS
1025 RECORDS READ
SEX = M

1. PERSON-YEARS INCIDENCE

DEATHS 89

PERSON-YEARS 8450.58334

DEATHS/PERSON-YEARS = .010538173

2. LIFE TABLE

X	NX	DX	WX	T	QX	PX	SX	RX
0	515	13	0	0	.0252427184	.974757282	.974757282	.0252427184
1	502	18	0	0	.0358565737	.964143426	.939805825	.0601941745
2	484	10	0	0	.020661157	.979338843	.92038835	.0796116504
3	474	11	0	0	.0232067511	.976793249	.899029126	.100970874
4	463	5	0	0	.0107991361	.989200864	.889320388	.110679612
5	458	1	1	0	2.18579235E-03	.997814208	.887376519	.112623481
6	456	2	0	0	4.38596491E-03	.995614035	.883484516	.116515484
7	454	2	0	0	4.40528634E-03	.995594714	.879592514	.120407486
8	452	0	0	0	0	1	.879592514	.120407486
9	452	1	2	0	2.2172949E-03	.997782705	.877642198	.122357802
10	449	0	0	0	0	1	.877642198	.122357802
11	449	1	0	0	2.22717149E-03	.997772828	.875687538	.124312462
12	448	1	1	0	2.23463687E-03	.997765363	.873730695	.126269305
13	446	2	1	0	4.48933783E-03	.995510662	.869808222	.130191778
14	443	5	0	0	.0112866817	.988713318	.859990974	.140009026
15	438	4	1	5	9.1954023E-03	.990804598	.852083011	.147916989
16	428	2	2	85	5.20156047E-03	.99479844	.847650849	.152349151
17	339	4	0	102	.0138888889	.986111111	.835877921	.164122079
18	233	3	0	55	.0145985401	.98540146	.823675324	.176324676
19	175	2	2	44	.0131578947	.986842105	.81283749	.18716251
20	127	2	0	48	.0194174757	.980582524	.797054238	.202945762
21	77	0	0	77	0	1	.797054238	.202945762

TOTAL 89 10 416

CUMULATIVE PROBABILITY OF SURVIVAL = .797054238
STANDARD ERROR OF SX = .021865303
CUMULATIVE RISK = .202945762

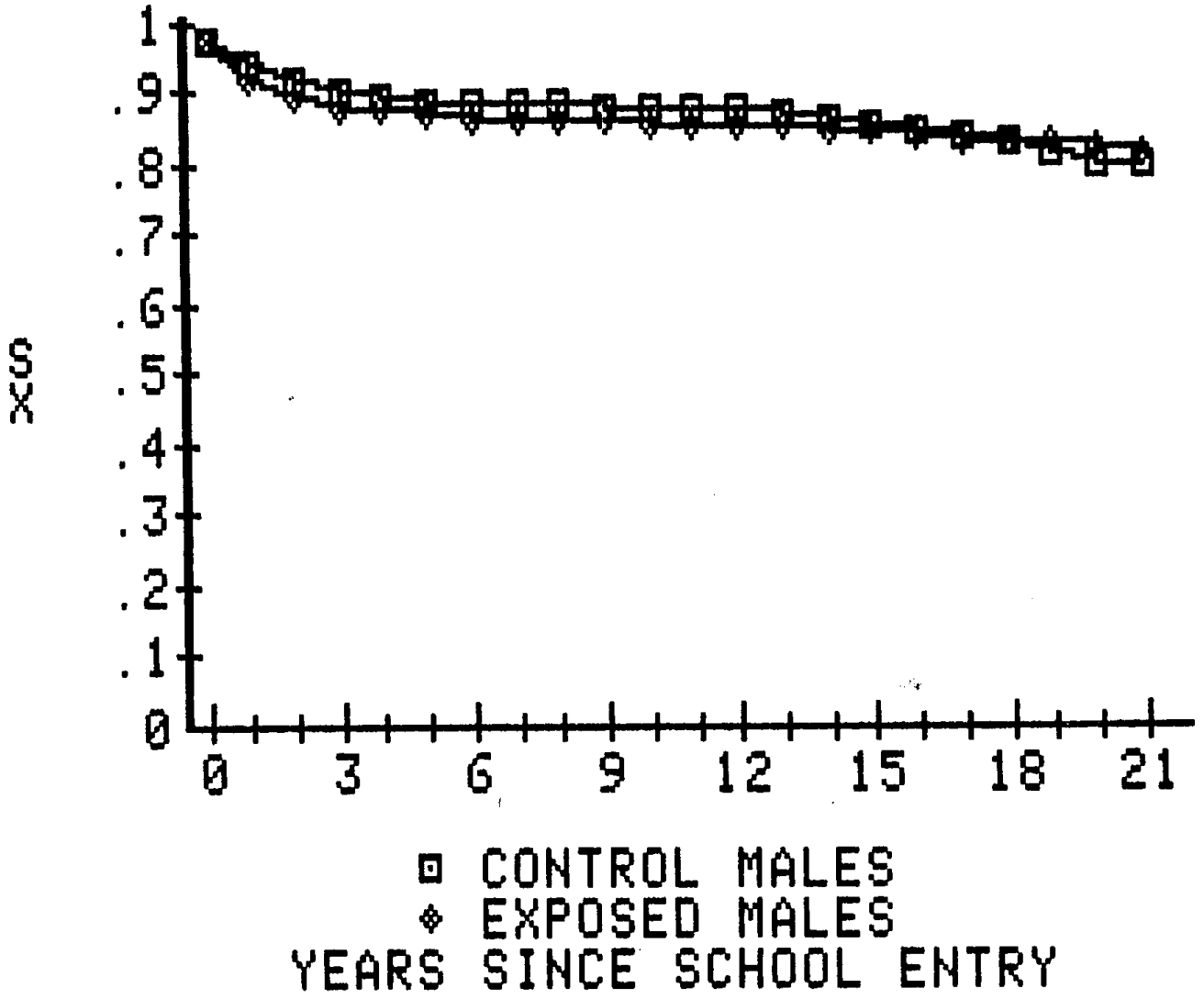

Figure 3.1-2. Cumulative Probability of Not Being Lost to Follow-Up: Exposed Males vs. Control Males.

Table 3.1-6

PERSON-YEARS AND LIFE TABLE ANALYSIS OF LOSSES TO FOLLOW-UP: EXPOSED FEMALES

DEATHS ARE DEFINED AS LOST TO FOLLOW-UP IN THIS ANALYSIS
1363 RECORDS READ
SEX = F

1. PERSON-YEARS TABLE

DEATHS 206

PERSON-YEARS 10193

DEATHS/PERSON-YEARS = .020209948

2. LIFE TABLE

X	NX	DX	WX	T	QX	PX	SX	RX
0	682	24	0	0	.0351906158	.964809384	.964809384	.0351906158
1	658	62	0	0	.094224924	.905775076	.873900293	.126099707
2	596	33	0	0	.0553691275	.944630872	.825513197	.174486803
3	563	20	0	0	.0355239787	.964476021	.796187683	.203812317
4	543	5	0	0	9.20810313E-03	.990791897	.788856305	.211143695
5	538	10	0	0	.0185873606	.981412639	.774193549	.225806451
6	528	8	0	0	.0151515152	.984848485	.762463343	.237536657
7	520	2	0	0	3.84615385E-03	.996153846	.759530792	.240469208
8	518	2	0	0	3.86100386E-03	.996138996	.756598241	.243401759
9	516	0	0	0	0	1	.756598241	.243401759
10	516	1	1	0	1.93986421E-03	.998060136	.755130543	.244869457
11	514	3	1	0	5.84225901E-03	.994157741	.750718875	.249281125
12	510	3	0	0	5.88235294E-03	.994117647	.746302881	.253697119
13	507	2	0	0	3.94477318E-03	.996055227	.743358886	.256641114
14	505	2	0	0	3.96039604E-03	.996039604	.74041489	.25958511
15	503	7	0	21	.014213198	.985786802	.729891227	.270108773
16	475	5	1	70	.0113765643	.988623436	.721587572	.278412428
17	399	7	0	36	.0183727034	.981627297	.708330058	.291669942
18	356	3	0	89	9.63081862E-03	.990369181	.701508259	.298491741
19	264	1	0	40	4.09836066E-03	.995901639	.698633226	.301366774
20	223	5	0	59	.0258397933	.974160207	.680580687	.319419313
21	159	1	0	158	.0125	.9875	.672073429	.327926571
TOTAL		206	3	473				

Table 3.1-7

PERSON-YEARS AND LIFE TABLE ANALYSIS OF LOSSES TO FOLLOW-UP: CONTROL FEMALES

DEATHS ARE DEFINED AS LOST TO FOLLOW-UP IN THIS ANALYSIS
1025 RECORDS READ
SEX = F

1. PERSON-YEARS INCIDENCE

DEATHS 125

PERSON-YEARS 6970.25

DEATHS/PERSON-YEARS = .0179333596

2. LIFE TABLE

X	NX	DX	WX	T	QX	PX	SX	RX
0	463	17	0	0	.0367170626	.963282937	.963282937	.0367170626
1	446	32	0	0	.0717488789	.928251121	.894168467	.105831533
2	414	19	0	0	.0458937198	.95410628	.85313175	.14686825
3	395	8	0	0	.0202531646	.979746836	.835853132	.164146868
4	387	9	0	0	.023255814	.976744186	.816414687	.183585313
5	378	7	0	0	.0185185185	.981481482	.801295897	.198704103
6	371	4	0	0	.0107816712	.989218329	.792656588	.207343412
7	367	0	0	0	0	1	.792656588	.207343412
8	367	0	1	0	0	1	.792656588	.207343412
9	366	0	0	0	0	1	.792656588	.207343412
10	366	2	0	0	5.46448088E-03	.994535519	.788325131	.211674869
11	364	1	0	0	2.74725275E-03	.997252747	.786159403	.213840597
12	363	2	1	0	5.51724138E-03	.994482759	.781821972	.218178028
13	360	1	0	0	2.77777778E-03	.997222222	.779650244	.220349756
14	359	4	1	1	.0111731844	.988826816	.770939068	.229060932
15	353	2	1	4	5.70613409E-03	.994293866	.766539986	.233460014
16	346	5	0	86	.0165016502	.98349835	.753890811	.246109189
17	255	2	0	61	8.90868597E-03	.991091314	.747174635	.252825365
18	192	5	0	38	.0289017341	.971098266	.725579992	.274420008
19	149	1	0	40	7.75193798E-03	.992248062	.719955341	.280044659
20	108	3	0	36	.0333333333	.966666667	.69595683	.30404317
21	69	1	1	67	.0285714286	.971428572	.676072349	.323927651

TOTAL 125 5 333

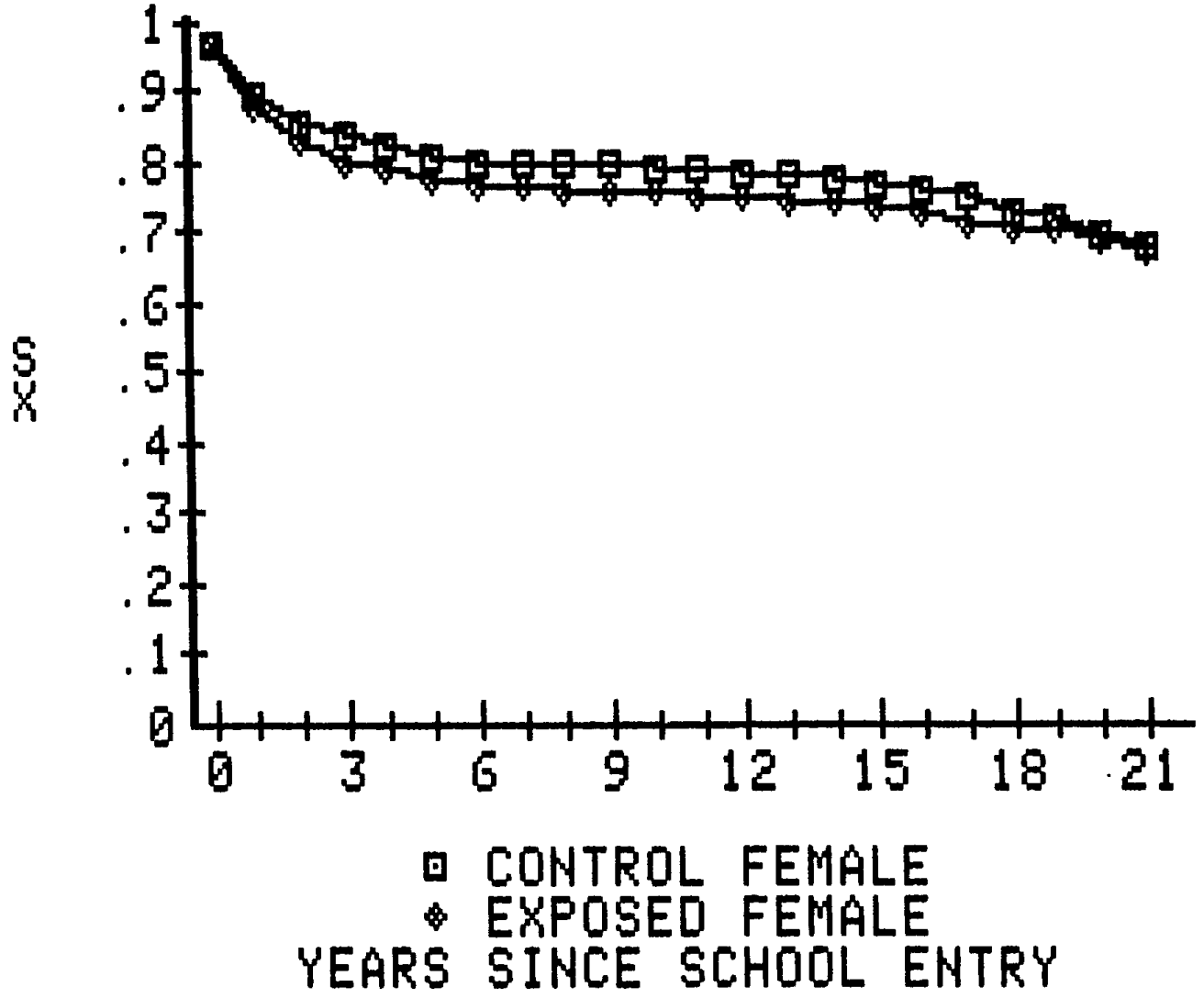

Figure 3.1-3. Cumulative Probability of Not Being Lost to Follow-Up: Exposed Females vs. Control Females.

T = number of subjects for whom tracing ended on 1 January 1980

QX = probability of being lost to follow-up during the interval

PX = probability of not being lost to follow-up during the interval

SX = cumulative probability of not being lost to follow-up from interval "0" to interval "X" (i.e., remaining in the study until 1 January 1980 or death)

RX = cumulative risk of being lost to follow-up from interval "0" to interval "X"

In summary, Figures 3.1-1, 3.1-2, 3.1-3 illustrate that losses to follow-up occurred at approximately the same intervals; Table 3.1-8 shows that the cumulative probability of not being lost to follow-up (SX) was not significantly different for the exposed and control group.

In a follow-up study it is desirable to keep losses to follow-up to a minimum. It is important to compare subjects traced sucessfully with those lost to follow-up; this comparison is made in Table 3.1-9 for the exposed group and control group. For both the exposed and control groups, subjects located were comparable to subjects lost to follow-up with respect to percent non-Spanish surname, median year of birth, and median year of entry into school; in both exposed and control groups a slightly higher percentage of males were located than females.

3.2 MORTALITY STUDY RESULTS

At the end of the tracing effort, we had confirmed a total of 31 deaths occurring before the 1 January 1980 cut-off date for analysis. Sixteen of these deaths occurred among members of the exposed cohort, and 15 occurred among the control cohort. These deaths are listed in Tables 3.2-1 and 3.2-2, for the exposed and control groups, respectively. We have secured copies of the death certificates for all of these deaths, save one, the death of a member of the control group that occurred during military service. The majority of deaths in both groups are due to homicide, suicide, and accidents (referred to hereafter as <u>trauma deaths</u>), contained in the International Classification of Diseases (ICD) rubrics 800-999. Of greater interest to the assessment of the effects of vinyl chloride exposure, however, are the <u>non-trauma</u> deaths,

Table 3.1-8

SUMMARY OF LOST-TO-FOLLOW-UP LIFE TABLE ANALYSIS

Lost to Follow-up	P(Survival) Exposed	P(Survival) Control	Z(diff)	p-value
Total	0.74	0.74	0.15	0.88
Males	0.81	0.80	0.56	0.58
Females	0.67	0.68	0.11	0.93

P(survival) = probability of remaining in the study until the end of tracing (1-1-80) or death

Table 3.1-9

COMPARISON OF SUBJECTS LOCATED AND NOT LOCATED, IN EXPOSED AND CONTROL GROUPS

Characteristic	Exposed Group				Control Group			
	Located		Not Located		Located		Not Located	
	No.	Pct.	No.	Pct.	No.	Pct.	No.	Pct.
All subjects	1039		324		764		215	
Males	562	54	117	36	426	56	89	41
Females	477	46	205	63	338	44	125	58
Unknown	0		2	1	0		1	0.5
Total	1039	100	324	100	764	100	215	100
Non-spanish surname	883	85	289	89	742	97	214	99.5
Spanish surname	156	15	35	11	22	3	1	0.5
Total	1039	100	324	100	764	100	215	100
Median year of birth	1953		1953		1953		1953	
Median year of entry into school	1960		1961		1961		1962	

Table 3.2-1

LIST OF DEATHS - EXPOSED GROUP

ID NO.	Sex	Age at Death	Year of Death	Cause	ICD Code	Revision No.
Non Trauma Deaths (N=6)						
0593	Male	23	1975	Malignant Melanoma	172.7	8th
0622	Female	15	1973	Rhabdomyosarcoma	171.9	8th
0881	Male	11	1963	Erythema Multiforme, etiology unknown	705.1	7th
1223	Male	13	1964	Malignant Lymphoma	200.2	7th
1235	Male	18	1971	Intracranial Abscess	322.0	8th
1293	Male	11	1968	Cystic Fibrosis	289.3	7th
Trauma Deaths (N=10)						
0026	Male	23	1973	Homicide	968.0	8th
0143	Male	19	1972	Motor Vehicle Accident	815.1	8th
0232	Male	23	1976	Motor Vehicle Accident	814.7	8th
0439	Male	25	1977	Homicide	966.0	8th
0701	Male	21	1973	Motor Vehicle Accident	815.2	8th
0767	Female	24	1975	Suicide	955.0	8th
1043	Female	18	1972	Motor Vehicle Accident	812.0	8th
1151	Male	28	1976	Motor Vehicle Accident	814.7	8th
1374	Male	23	1973	Motor Vehicle Accident	815.9	8th
1465	Male	22	1978	Motor Vehicle Accident	812.2	8th
Deaths Occurring after 1 January 1980 (N=2)						
0051	Male	25	1980	Motor Vehicle Accident	812.0	9th
1494	Female	28	1981	Motor Vehicle Accident	812.0	9th

Table 3.2-2

LIST OF DEATHS - CONTROL GROUP

ID No.	Sex	Age at Death	Year of Death	Cause	ICD Code	Revision No.
Non Trauma Deaths (N=3)						
2030	Male	21	1979	Idiopathic Thrombocytopenia	287.5	9th
2084	Female	17	1976	Astrocytoma	191.0	8th
2548	Female	23	1977	Cerebral Aneurysm	430.9	8th
Trauma Deaths (N=12)						
2096	Female	28	1979	Undetermined (body decomposed)	799.9	8th
2212	Female	20	1973	Motor Vehicle Accident	812.1	8th
2272	Female	13	1970	Motor Vehicle Accident	815.9	8th
2468	Male	27	1978	Suicide	955.0	8th
2671	Male	22	1976	Motor Vehicle Accident	816.1	8th
2759	Male	24	1977	Railway Accident	807.9	8th
2762	Male	20	1970	Motor Vehicle Accident	816.0	8th
3064	Male	27	1979	Cataclysm (Flood)	908.0	8th
3084	Male	20	1969	Deceased during military service (Vietnam)[a]		
3099	Male	18	1965	Firearm Accident	919.8	7th
3112	Male	24	1974	Suicide	955.0	8th
3143	Male	21	1971	Motor Vehicle Accident	812.0	8th
Deaths Occurring After 1 January 1980 (N=2)						
2250	Male	28	1980	Motor Vehicle Accident	812.0	9th
2365	Male	22	1980	Motor Vehicle Accident	812.2	9th

[a] Information from parents. Death certificate unavailable from California State Vital Statistics.

and so the observed deaths have been separated into these categories. For each death, we have included the ICD code (and revision number) of the death, as coded on the death certificate.

The tables also include mention of four deaths (two in each group) that we discovered during the course of the follow-up, but which had occurred after the cut-off date. These would be included in any future study of these groups, and have been used to update the cohort registry, so we include them here for completeness.

Tables 3.2-1 and 3.2-2 list many more males than females, especially among the trauma deaths, where males outnumbered females about three to one. This could be explained partly by the somewhat more complete follow-up for males than females (described in Section 3.1), but also by the fact that males in this age range have a much higher mortality rate than females. In 1970, for example, California males, between 20 and 30 years of age, had almost twice the mortality rate of females of the same age, and this difference was primarily due to trauma deaths (Schoen and Collins, 1973).

The non-trauma deaths represent truly a mixed bag. All are rare causes of death for this age group, a fact that will be discussed in Section 4.1. Four of the deaths are due to malignancies (malignant melanoma, rhabdomyosarcoma, lymphoma, and astrocytoma), three of them occurring in the exposed group.

Mortality analyses will be presented in the next three subsections. Section 3.2.1 describes the mortality rates from the cohort analysis; Section 3.2.2 describes the case/control-type analysis that examines duration of exposure for deceased and living exposed subjects; and Section 3.2.3 compares the distribution of trauma and non-trauma deaths in the study groups with the distribution of deaths in California during the same time period.

3.2.1 Cohort Analysis

The overall average mortality rates for the exposed and control cohorts are presented in Table 3.2-3. Rates are presented for deaths of all causes and the subset of deaths from non-trauma causes. Among the exposed cohort, 16 deaths were observed in a total of 21,443.58 person-years of follow-up, which translates to a total mortality rate of 75 deaths per 100,000 person-years. The corresponding rate for the control cohort is 97 deaths per 100,000 person-years. The rate ratio (RR) for these rates is 0.77. In contrast, the rate for the non-trauma deaths is higher among the exposed cohort than the control (RR = 1.44). The RRs are not statistically significant, however, because the numbers of deaths are small.

The observed RRs could be confounded by the difference in the proportion of Spanish surname subjects. Therefore, we examined the rates among non-Spanish surname subjects only in both groups, in Table 3.2-4. (The number of Spanish surname subjects was too small, particularly in the control group, to allow an analysis of Spanish surname subjects.) Table 3.2-4 shows the same pattern as Table 3.2-3, with the all causes rate being slightly lower among the exposed group, but the RR for non-trauma deaths elevated (RR = 2.05). Again, the elevation is not statistically significant.

Since males and females in the young adult ages have different mortality rates in the general population, we have also stratified the comparison by sex (Tables 3.2-5 and 3.2-6). As expected, the male rates are much higher than the female rates. Table 3.2-5 again shows the same pattern as before, with the all causes RR being slightly less than unity, and the non-trauma RR elevated (RR = 3.76).

Among females (Table 3.2-6), both the all causes RR and the non-trauma RR are less than 1.0. However, these comparisons are based upon extremely small numbers, and the rates can be considered highly unstable.

Because the male subgroups contained the majority of the observed deaths, we present one further comparison (Table 3.2-7): rates among non-Spanish surname males. The restriction of the cohorts to the non-Spanish surname subgroup does not alter the trend observed for males, or both sexes combined.

Table 3.2-3

MORTALITY RATES, ALL SUBJECTS

	Exposed Group	Control Group
Number of Subjects	1363	979
Person-Years of Follow-up	21443.58	15422.67
Average Person-Years of Follow-up per Subject	15.7	15.8
Deaths (All Causes)	16	15
Mortality Rate (All Causes	$74.6/10^5$ p-y	$97.3/10^5$ p-y
Rate Ratio (Exposed/Control)	RR (all causes) = 0.77 (p = 0.46)	
Non-Trauma Deaths	6	3
Mortality Rate (Non-Trauma)	$28.0/10^5$ p-y	$19.5/10^5$ p-y
Rate Ratio (Exposed/Control)	RR (Non-Trauma) = 1.44 (p = 0.56)	

Table 3.2-4

MORTALITY RATES, NON-SPANISH SURNAME SUBJECTS

	Exposed Group	Control Group
Number of Subjects	1172	956
Person-Years of Follow-up	18280.75	15020.67
Average Person-Years of Follow-up per Subject	15.6	15.7
Deaths (All Causes)	14	14
Mortality Rate (All Causes)	$76.6/10^5$ p-y	$93.2/10^5$ p-y
Rate Ratio (Exposed/Control)	RR(All Causes) = 0.82 (p = 0.60)	
Non-Trauma Deaths	5	2
Mortality Rate (Non-Trauma)	$27.4/10^5$ p-y	$13.3/10^5$ p-y
Rate Ratio (Exposed/Control)	RR(Non-Trauma) = 2.05 (p = 0.44)	

Table 3.2-5

MORTALITY RATES, MALES

	Exposed Group	Control Group
Number of Subjects	679	516
Total Person-Years of Follow-up	11225.42	9450.58
Average Person-Years of Follow-up per Subject	16.5	16.4
Deaths (All Causes)	13	10
Mortality Rate (All Causes)	$115.8/10^5$ p-y	118.3/10 p-y
Rate Ratio (Exposed/Controls)	RR (All Causes) = 0.98 (p = 0.96)	
Non-Trauma Deaths	5	1
Mortality Rate (Non-Trauma)	$44.5/10^5$ p-y	$11.8/10^5$ p-y
Rate Ratio (Exposed/Control)	RR (Non-Trauma) = 3.76 (p = 0.22)	

Table 3.2-6

MORTALITY RATES, FEMALES

	Exposed Group	Control Group
Number of Subjects	682	462
Total Person-Years of Follow-Up	10193.00	6970.25
Average Person Years of Follow-Up per Subject	14.9	15.1
Deaths (All Causes)	3	5
Mortality Rate (All Causes)	$29.4/10^5$ p-y	$71.7/10^5$ p-y
Rate Ratio (Exposed/Controls)	RR(All Causes) = 0.41 (p = 0.76)	
Non-Trauma Deaths	1	2
Mortality Rate (Non-Trauma)	$9.8/10^5$ p-y	$28.7/10^5$ p-y
Rate Ratio (Exposed/Controls)	RR(Non-Trauma) = 0.34 (p = 0.52)	

Table 3.2-7

MORTALITY RATES, NON-SPANISH SURNAME MALES

	Exposed Group	Control Group
Number of Subjects	582	506
Person-Years of Follow-up	9558.58	8275.17
Average Person-Years of Follow-Up per Subject	16.4	16.4
Deaths (All Causes)	11	9
Mortality Rate (All Causes)	$115.1/10^5$ p-y	$108.8/10^5$ p-y
Rate Ratio (Exposed/Control)	RR (All Causes) = 1.06 (p = 0.90)	
Deaths (Non-Trauma)	4	0
Mortality Rate (Non-Trauma)	$41.8/10^5$ p-y	-
Rate Ratio (Exposed/Control)	RR (Non-Trauma) = undefined (p = 0.13)	

The all causes rates are fairly similar between the exposed and control groups, while the non-trauma rate is higher among the exposed.

The results of the life table analyses are summarized in Table 3.2-8. The complete life tables have been included in Appendix A. The life table provides the year-by-year risk (probability) that the subjects who were alive at the beginning of the year died during that year. Subjects lost to follow-up during the year are assumed to have left at the midpoint of the year. The table also calculates the cumulative risk for the entire length of the follow-up, as opposed to the rates examined previously, which can be thought of as yearly mortality rates averaged over the entire study period. The cumulative risks have been listed in Table 3.2-8, along with the risk ratios (RR) for the exposed group relative to the controls.

The RRs in Table 3.2-8 are similar to the previously presented RRs based on person-year rates. Again, because of the small numbers of deaths observed during the follow-up period, the RRs are not significant. However, for the total groups and for males, the risk for all causes is greater for the control cohort, and the risk for non-trauma is greater for the exposed.

3.2.2 Retrospective Analysis

In order to examine the small number of deaths in the exposed group accumulated up to this point in the follow-up, we compared the months of exposure of the deceased to those of living exposed cohort members. The rationale here is that persons with greater vinyl chloride exposure might be at higher risk. As described in Section 2.1.5, three comparison subjects were matched to each deceased subject, by sex, year of birth, type of surname, and length of follow-up. The results are presented in Table 3.2-9. The odds ratios (OR) for all deaths and for the non-trauma deaths are slightly above 1, both for the crude (unadjusted) OR and the adjusted Mantel-Haenszel OR, indicating somewhat greater exposure among deceased exposed subjects than living exposed subjects. The difference, however, is not statistically significant.

Table 3.2-8

CUMULATIVE RISKS FROM LIFE TABLE ANALYSIS[a]

	Exposed Group	Control Group
TOTAL COHORT		
Cumulative Risk (All Causes)	0.0152	0.0355
Risk Ratio (All Causes)	RR=0.43 (p=0.18)	
Cumulative Risk (Non-Trauma)	0.0055	0.0039
Risk Ratio (Non-Trauma)	RR=1.41 (p=0.69)	
NON-SPANISH SURNAME		
Cumulative Risk (All Causes)	0.0157	0.0347
Risk Ratio (All Causes)	RR=0.45 (p=0.22)	
Cumulative Risk (Non-Trauma)	0.0055	0.0026
Risk Ratio (Non-Trauma)	RR=2.13 (p=0.32)	
MALES		
Cumulative Risk (All Causes)	0.0233	0.0314
Risk Ratio (All Causes)	RR=0.74 (p=0.53)	
Cumulative Risk (Non-Trauma)	0.0087	0.0026
Risk Ratio (Non-Trauma)	RR=3.35 (p=0.19)	
FEMALES		
Cumulative Risk (All Causes)	0.0062	0.0394
Risk Ratio (All Causes)	RR=0.16 (p=0.25)	
Cumulative Risk (Non-Trauma)	0.0019	0.0056
Risk Ratio (Non-Trauma)	RR=0.34 (p=0.41)	
MALES, NON-SPANISH SURNAME		
Cumulative Risk (All Causes)	0.0233	0.0293
Risk Ratio (All Causes)	RR=0.80 (p=0.65)	
Cumulative Risk (Non-Trauma)	0.0083	0.0000
Risk Ratio (Non-Trauma)	RR=undefined (p=0.05)	

[a] Cumulative risk from 21-year follow-up life table.

Table 3.2-9

RETROSPECTIVE ANALYSIS, DECEASED EXPOSED SUBJECTS
AND MATCHED LIVING EXPOSED SUBJECTS

A. All Deaths: (All Causes)

	Deaths	Controls
>20 Months Exposure	9	20
<20 Months Exposure	7	28
	16	48

Crude Odds Ratio = 1.80 (p=0.31)
Mantel-Haenszel Summary Odds Ratio = 1.88 (p=0.30)
(Adjusted for age, sex, type of surname, length of follow-up)

B. Deaths Due to Non-Trauma Causes:

	Non-Trauma Deaths	Controls
> 20 Months Exposure	3	8
< 20 Months Exposure	3	10
	6	18

Crude odds Ratio = 1.25
Mantel-Haenszel Summary Odds Ratio = 1.50
(Adjusted for age, sex, type of surname, length of follow-up)
(Chi-square test not reliable because of small cell sizes)

3.2.3 Mortality Odds Ratio

As noted in Section 3.2, a large proportion of the observed deaths in both groups were due to trauma causes. In order to compare the observed proportion of trauma and non-trauma deaths in the study groups, we compared them with the numbers of trauma and non-trauma deaths that occurred in California among the same sex and age groups and in the same ICD revision period. The results can be analyzed in the standard case/control study format (Miettinen and Wang, 1981), and are presented in Table 3.2-10. Both the crude and adjusted OR for the exposed group are elevated, indicating that more non-trauma deaths occurred in the exposed group than would be expected, based upon California deaths. In contrast, the distribution of deaths in the control group is not weighted toward the non-trauma deaths, and in fact, the control group deaths have somewhat fewer non-trauma deaths than expected (OR < 1). Again, the numbers of deaths are too small to permit a valid chi-square test for statistical significance (Mantel and Fleiss, 1980).

3.3 RESULTS OF QUESTIONNAIRE RESPONSE VALIDATION

The results of the random selection and tracing of validation protocol subjects are tabulated in Table 3.3-1. Our goal was to validate the responses of 10 married, female subjects (or spouses of male subjects) who reported a stillbirth, miscarriage or congenital defect in a child (problem +) and 10 who did not report these problems (problem -). More "problem +" subjects were randomly selected than "problem -" subjects because we experienced more difficulty tracing and obtaining medical records release forms for them. Several subjects who signed release forms could not be re-contacted to obtain names of physicians. For two of the subjects, medical records information could not be obtained. The only relevant physician for one subject refused to provide information; the other subject provided insufficient information to locate the only relevant physician. The responses of 9 "problem +" and 7 "problem -" subjects were tested.

Table 3.3-2 summarizes the questionnaire responses of the validation protocol subjects. Subjects' responses were categorized into 2 x 3 tables, and percentage sensitivity and percentage specificity were calculated for the following outcomes:

Table 3.2-10

COMPARISON OF OBSERVED MORTALITY TO STATE OF CALIFORNIA DEATHS

A. Exposed Group Deaths:	Exposed Group Deaths	California Deaths
Non-Trauma Deaths	6	16,374
Trauma Deaths	10	54,024
	16	70,398

Crude Odds Ratio = 1.98
Mantel-Haenszel Summary Odds Ratio = 1.88
(Adjusted for sex, age, ICD coding period)

B. Control Group Deaths:	Control Group Deaths	California Deaths
Non-Trauma	3	20,137
Trauma	12	65,846
	15	85,983

Crude Odds Ratio = 0.82
Mantel-Haenszel Summary Odds Ratio = 0.79
(Adjusted for age, sex, ICD coding period)

Table 3.3-1

VALIDATION PROTOCOL SUBJECT SELECTION AND TRACING

	Number of Subjects	
	Problem +	Problem -
Married, female subjects randomly selected	25	15
Subjects traced	20	14
Subjects who signed medical records release	11	10
Subjects who provided names of physicians	9	9
Subjects for whom sufficient medical records information was received	9	7

Table 3.3-2

SUMMMARY OF VALIDATION PROTOCOL SUBJECTS' QUESTIONNAIRE RESPONSES

Questionnaire Responses	Problem +	Problem -	Total
Pregnancies	25	16	41
Live births	20	15	35
Total abnormal pregnancy outcomes	5	1	6
Miscarriages	3	0	3
Therapeutic abortions	2	1	3
Stillbirths	0	0	0
Birth defects	8	0	8
Major illnesses in child	4	2	6
Difficulty conceiving	1	2	3
Number of subjects whose responses were tested	9	7	16

- Normal versus abnormal pregnancy outcome (stillbirth, miscarriage, and therapeutic abortion)
- Miscarriage versus other pregnancy outcomes (normal birth or therapeutic abortion)
- Birth defect versus no birth defect
- Major illness in child
- Child still alive at time of interview
- Difficulty conceiving
- Gravida/parity (subject's response vs. physician information, as of the date of interview)

Physician responses categorized as "unknown" are those for which all of a subject's physicians reported that they could not provide information to that particular question. The results for pregnancy outcomes, miscarriages, birth defects and gravida/parity are very encouraging. Agreement between subjects' and physicians' responses for these outcomes is 100 percent, with the exception of one unknown for gravida/parity.

As seen in Table 3.3-3, validation of "difficulty conceiving" was much less favorable. Difficulty conceiving was classified as "yes" if the subject reported not being able to become pregnant, or trying for more than six months to become pregnant. One reason for the zero sensitivity and 75- to 86-percent specificity may be that a time period was not specified on the physician questionnaire.

Validation of "major illness in child" and "child alive at date of interview," (Table 3.3-4 and 3.3-5, respectively) though showing good agreement between the responses of subjects and their physicians, should be interpreted cautiously. For a large percentage of responses, physicians could not provide information, probably because we requested names of obstetricians/gynecologists and family physicians who had treated the mother; we did not specifically ask for names of physicians who have cared for the children. We consider the lack of validation of these responses to be due to a flaw in our validation protocol. With the exception of this flaw, the validation protocol

Table 3.3-3

VALIDATION PROTOCOL RESULTS: DIFFICULTY CONCEIVING

"Problem +" Subjects (N=9)

		PHYSICIAN			
		Yes	No	Unknown	
SUBJECT	Yes	0	1	0	% Sensitivity = 0/1 = 0%
	No	1	6	1	% Specificity = 6/7 = 86% Unknown = 1

"Problem -" Subjects (N=7)

		PHYSICIAN			
		Yes	No	Unknown	
SUBJECT	Yes	0	2	0	% Sensitivity = 0/0
	No	0	5	0	% Specificity = 6/8 = 75% Unknown = 0

All Validation Subjects (N=16)

		PHYSICIAN			
		Yes	No	Unknown	
SUBJECT	Yes	0	3	0	% Sensitivity = 0/1 = 0%
	No	1	11	1	% Specificity = 11/14 = 79% Unknown = 1

Table 3.3-4

VALIDATION PROTOCOL RESULTS: MAJOR ILLNESS IN CHILD

"Problem +" Subjects (N=9)

		PHYSICIAN			
		Yes	No	Unknown	
SUBJECT	Yes	2	0	2	% Sensitivity = 2/2 = 100%
	No	0	5	11	% Specificity = 5/5 = 100% Unknown = 13

"Problem - " Subjects (N=7)

		PHYSICIAN			
		Yes	No	Unknown	
SUBJECT	Yes	0	1	1	% Sensitivity = 0/0
	No	0	10	3	% Specificity = 10/11 = 91% Unknown = 4

All Validation Subjects (N=16)

		PHYSICIAN			
		Yes	No	Unknown	
SUBJECT	Yes	2	1	3	% Sensitivity = 2/2 = 100%
	No	0	15	14	% Specificity = 15/16 = 94% Unknown = 17

Table 3.3-5

VALIDATION PROTOCOL RESULTS: CHILD ALIVE AT DATE OF INTERVIEW

"Problem +" Subjects (N=9)

		PHYSICIAN			
		Yes	No	Unknown	
SUBJECT	Yes	10	0	10	% Sensitivity = 10/10 = 100%
	No	0	0	0	% Specificity = 0/0 Unknown = 10

"Problem -" Subjects (N=7)

		PHYSICIAN			
		Yes	No	Unknown	
SUBJECTS	Yes	10	0	5	% Sensitivity = 10/10 = 100%
	No	0	0	0	% Specificity = 0/0 Unknown = 5

All Validation Subjects (N=16)

		PHYSICIAN			
		Yes	No	Unknown	
SUBJECT	Yes	20	0	15	% Sensitivity = 20/20 = 100%
	No	0	0	0	% Specificity = 0/0 Unknown = 15

we designed worked well. In future validation studies we will make no changes in forms, telephone scripts or physician's questionnaires. Since we experienced difficulty in influencing subjects to re-sign medical records release forms, we recommend that these forms (without expiration times) be signed at the time of interview if future interviews are done. Physicians' names and addresses should also be collected at this time for outcomes to be validated.

4.0
DISCUSSION

4.1 FOLLOW-UP SUCCESS

Under the circumstances, we feel that the follow-up effort was quite successful. We were presented with the problem of tracing cohorts constructed from elementary school records, filled out (sometimes only haphazardly) by school office staff 18 to 24 years ago. The cohort members were, at the time, only about 5 to 12 years of age. Since then, they have grown up, moved, some have changed their names--all making our tracing effort more difficult.

A summary of the follow-up success is presented in Table 4.1-1. Approximately 77 percent of the subjects were followed up, either to 1 January 1980, or until their deaths. As we expected, the percentage of males traced exceeded that for females by about 10 percent. This difference in tracing success was probably due to the fact that women usually change their names when they marry, but could also be caused by other biases in our tracing methods. Males may be more likely to have driver's licenses, own property, or be registered to vote; hence males may have been easier to find.

We expected at the outset that Spanish-surnamed subjects would be more difficult to locate than non-Spanish, because they would be more mobile. It appeared that, among the Saugus group, many of the Spanish-surnamed children belonged to families who were farm workers, since many of them gave the name of a farm or ranch as an address. Surprisingly, as Table 4.1-1 shows, Spanish-surname subjects in both groups proved easier to locate.

Figures 3.1-1 to 3.1-3 illustrated the loss to follow-up over time. The pattern of loss as it accumulated since the time the subjects were first enrolled has remained almost identical between the exposed and control groups.

In order to evaluate the success of the follow-up further, we calculated the number of person-years of observation that would have been theoretically possible, if the follow-up had been perfect. To derive this figure, we used the same computer program used to calculate observed person-years of fol-

Table 4.1-1

ASSESSMENT OF FOLLOW-UP

Characteristic	Exposed Group	Control Group
Number of Subjects	1363	979
Pct. of Subjects Followed-up	76	78
Pct. Males Followed-up	83	83
Pct. Females Followed-up	70	73
Pct. Spanish Surname Followed-up	82	96
Pct. Non-Spanish Surname Followed-up	75	78
No. of Person-Years of Follow-up Possible	25913.75	18011.67
No. of Person-Years of Follow-up Achieved	21418.42	15420.83
Pct. Person-Years Achieved	83	86

low-up, but assumed that each subject, once enrolled in the school, was followed until 1 January 1980 (or the date of his or her known death), with no loss to follow-up. This total possible follow-up would have generated about 25,900 person-years of observation in the exposed group, and 18,000 person-years in the control group*. The actual person-years of observation that we achieved was 21,418 (83 percent) for the exposed group, and 15,420 (86 percent) for the controls.

4.2 MORTALITY STUDY

The analysis of the mortality study was hampered by the small rates in both groups with which to work. Nevertheless, the overall trends can be summarized:

- The mortality rates for all causes of death have not been elevated among the exposed group (compared to the controls), but in fact are somewhat lower. On the other hand, the mortality rates from non-trauma causes (which are more likely to be associated with an environmental exposure) are elevated among the exposed cohort as a whole. This increase is due to the higher rate for male exposed members, since female exposed members do not, as yet, show any increase. Also, the rate for trauma deaths was lower in the exposed group than in the control group.

- The proportion of deaths among the exposed due to non-trauma causes exceeds that of the controls, or the proportion expected based upon California deaths.

- Lastly, the deceased members of the exposed group appear to have had more exposure than their living counterparts in the cohort.

The census tract data presented in Table 2.1-2 shows that the exposed and control groups have similar demographic characteristics. However, it appears that the control group is in a slightly higher socioeconomic status category than the exposed group. Based on this data we might expect the exposed group to have a slightly higher overall mortality rate than the controls. It is interesting that it was, in fact, slightly lower. It may be

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* Actually, this figure is slightly inflated, because it assumes that all of the persons who were actually lost to follow-up would have survived until the study's end.

that mortality is too insensitive a measure to detect a difference in health status between the two groups, and that morbidity would be better. Also, the latency may not be long enough (median 20 years) for an increase in mortality, especially cancer mortality, to become manifest.

In Section 3.2, we described the deaths observed in the exposed and control groups up to this point in the follow-up. In the age group that the cohorts are passing through, a large proportion of the deaths would be expected to be due to accidents, or other forms of trauma. However, when examining the list of causes of death in Tables 3.2-1 and 3.2-2, we note that many of the observed non-trauma deaths were due to rare causes. We noted in the pilot study report (Ziskind et al., 1981), that the three exposed group deaths that had been discovered at that time were from extremely rare causes. Some of these causes are rare not only in terms of the total number that occur every year, but also in their occurrence among a young adult age group. Some of these deaths represent the only California instance of the specific cause, for the subject's 5-year age group and year of death.

In order to explore the rarity of these deaths, we have calculated a rough estimate of the number of deaths from the observed causes that might have been expected among the study groups. An estimated California mortality rate for these causes was calculated by averaging the total number of deaths (for males and females separately, aged 5 through 34) occurring in 1968-72, divided by the California population (males and females, aged 5-34) in 1970*. This produced sex-specific mortality rates for 5 to 34 year olds. This age range was chosen in order to span the approximate age of the cohort, from entry into kindergarten to the present. The year 1970 was chosen, first, because of the availability of decennial census data for the denominator, and also because 1970 represents the midpoint between the median entry year (1960) and the end of follow-up (1980). Multiplying these rates for males and females by the number of person-years of observation produces an estimate of the number of deaths that might be expected from these causes.

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* Some conversions had to be made between the 7th and 8th Revision ICD codes.

The rates and expected numbers for the exposed and control groups are provided in Tables 4.2-1 and 4.2-2, respectively. For the non-trauma causes of death, all of the estimated California rates are on the order of 1 death per 100,000 population per year, or less. However, it bears noting that rare deaths have been observed in both the exposed and control groups. Moreover, the observed deaths do not fall into any obvious pattern, as for example if all had occurred in a particular organ system. Vinyl chloride exposure has been associated with increased cancer incidence at several sites, and three deaths from malignancies (rare for this age group) have occurred among the exposed, with one occurring among the controls.

In contrast to the disparity between the expected and observed non-trauma deaths, the expected trauma deaths (derived the same way) are much closer to the observed. In the exposed group, we would have expected about 17 trauma deaths, and observed 10. In the control group, we would expect about 13, and observed 12. About 25 total deaths were expected in the exposed group whereas 16 were observed, and 18 were expected in the control group while 15 were observed.

The expected rates are admittedly crudely derived, and are not intended to provide precise numbers of expected events, as in a formal Standard Mortality Ratio (SMR) analysis. However, we present them in order to demonstrate (1) the unusualness of some of the observed deaths, and (2) that our overall mortality assessment is not too far afield from what might be expected.

We have presented the mortality rates and the RRs based upon the number of deaths up to 1 January 1980. The lack of statistical significance in the analysis has led us to investigate the power of the mortality study, based upon the number of subjects and the length of follow-up. The number of subjects in our sample size is essentially fixed, and defined by the dates of their school attendance. In Table 4.1-1 we presented the number of person-years of follow-up we achieved up to 1 January 1980. If we assume that the overall mortality rate is approximately 80 per 100,000 person-years (the average observed rate for both groups), and that we want to detect a doubling of this rate in the exposed group (RR = 2.0) with 80-percent power at the 0.05 level, we can use the sample size and power formulae given by Walter (1977)

Table 4.2-1

EXPECTED NUMBERS OF DEATHS DUE TO OBSERVED CAUSES,
BASED UPON CALIFORNIA MORTALITY RATES, EXPOSED SUBJECTS

Cause of Death (ICD, Revision)	Sex	Estimated Yearly State Mortality Rate	Person-Years of Observation	Expected Deaths	Observed Deaths
Malignant Melanoma (172,8th)	M	0.7/100,000	11225.42	0.08	1
Malignant Lymphoma (200.2, 7th)	M	0.3/100,000	11225.42	0.03	1
Cystic Fibrosis (289.3, 7th)	M	0.4/100,000	11225.42	0.04	1
Intracranial Abscess (322, 7th)	M	0.1/100,000	11225.42	<0.01	1
Erythema Multiforme (705.1, 7th)	M	0.004/100,000	11225.42	<0.01	1
Rhabdomyosarcoma (171,8th)	F	0.3/100,000	10193.00	0.03	1
Trauma (800-999, 8th)	M	115.8/100,000	11225.42	13.0	8
	F	40.7/100,000	10193.00	4.1	2
All Causes	M	156.3/100,000	11225.42	17.5	13
	F	74.2/100,000	10193.00	7.6	3
				25.1	16

Table 4.2-2

EXPECTED NUMBERS OF DEATHS DUE TO OBSERVED CAUSES,
BASED UPON CALIFORNIA MORTALITY RATES, CONTROL SUBJECTS

Cause of Death (ICD, Revision)	Sex	Estimated Yearly State Mortality Rate	Person-Years of Observation	Expected Deaths	Observed Deaths
Thrombocytopenia (287.5, 9th	M	0.04/100,000	8450.58	<0.01	1
Astrocytoma (193, 7th)	F	1.0/100,000	6970.25	0.07	1
Cerebral Aneurysm (430.9 8th)	F	0.9/100,000	6970.25	0.06	1
Trauma (800-999, 8th)	M	115.8/100,000	8450.58	9.8	9
	F	40.7/100,000	6970.25	2.8	3
All Causes	M	156.3/100,000	8450.58	13.2	10
	F	74.2/100,000	6970.25	5.2	5
				18.4	15

and Rothman and Boice (1979) to calculate the number of person-years of follow-up needed. To detect a RR of 2.0 with 80-percent probability, we would need approximately 29,000 person-years of observation as an average per group. This translates into about 25 person-years of follow-up per person.

We actually achieved about 16 person-years per person. This actual follow-up would have detected a RR of 2.0 with only about 60-percent power. The total amount of person-time that would have been theoretically possible up to this point in the study (if our follow-up efforts had been perfect) was 18.8 person years per person. Therefore, even with perfect follow-up, insufficient time has elapsed for detection of an RR of 2.0 with 80-percent power.

4.3 VALIDATION PROTOCOL

In the EPA-sponsored phase of this study 159 married females subjects who had been pregnant at least once and 87 male subjects' wives who had been pregnant at least once were interviewed. These 246 women form the pool from which our validation subjects were selected. Of these, 180 were classified as "problem-", and 66 as "problem+". Thus, we validated the responses of 14-percent (9/66) of the "problem+" subjects and 4-percent (7/180) of the "problem-" subjects.

The percentage of subjects whose responses were validated is, admittedly, small. Also, of the 34 subjects who were requested to sign medical records release forms, the responses of only 16 were validated. A large portion of the "refusals" occurred in the "problem +" group. However, of those validated, the agreement between subjects' and physicians' responses was good for pregnancy outcome, miscarriage, birth defects, and gravida/parity.

In the pilot study 450 subjects, or 33 percent of the expected cohort, were interviewed. No control subjects were interviewed. The small percentage of exposed subjects interviewed, and the lack of data for a control group, hamper our ability to make meaningful comparisons of reported pregnancy outcomes. However, an internal comparison of exposed females and non-exposed wives of male subjects suggest that the risk of fetal death (miscarriage, stillbirth) and major illnesses in children may be elevated in exposed females (Ziskind et al., 1981). This validation protocol revealed no evidence that the fetal deaths were incorrectly reported.

5.0
CONCLUSIONS AND RECOMMENDATIONS

5.1 CONCLUSIONS

In this program we have accomplished the following aims:

(1) Establishing a cohort registry and follow-up mechanism, including

- Developing a data base management system on a microcomputer, and the software needed for updating tracing information and generating contact letters, mailing labels, DMV driver's information requests forms, etc.;
- Selecting a non-exposed control cohort, and incorporating them into the data base;
- Acquiring and using tracing resources, such as property tax rolls, voter registration lists, marriage records, and telephone books; and
- Tracing the exposed and control cohort, numbering 2,342 subjects, and achieving a total follow-up of 77 percent.

(2) Performing an analysis of the mortality observed in the two cohorts up to 1980. The mortality rates up to this point are small, but there is some evidence of an increased proportion of non-trauma deaths among the exposed group, and an increased rate among males. There is also evidence of a decreased rate of trauma deaths among the exposed group.

(3) Setting up a mechanism and designing the forms for validating pregnancy outcomes reported by questionnaire during the pilot phase of this study, which interviewed a portion of the exposed females. We have identified problems in gaining cooperation with subjects and physicians, and determining the proper physicians to use for validation. The validation we performed on a sample of the responses indicated that the questionnaire is capable of recording valid reproductive information. We have identified areas where it can be improved, however.

5.2 RECOMMENDATIONS

5.2.1 Cohort Follow-up

As discussed in Section 4.2, the length of the observation period for the VC-exposed cohort is insufficient to detect subtle or low-level effects. This problem has been recognized from the outset, and the establishment of a cohort registry was deemed necessary to facilitate the follow-up of this exposed group into the future. We strongly recommend including the control group in the prospective follow-up as well, since it is required to make valid comparisons, and has been entered into its own comparable registry system. We make the following additional recommendations:

(1) Annually exercizing the cohort registries

- Updating address and name changes; and
- Tracing and relocating subjects who are lost between the annual updates.

(2) Annually updating the mortality assessment

- Acquiring death certificate copies for known deaths occurring during the year; and
- For lost-to-follow-up subjects, searching for their deaths through the CAMLIS system. Other mortality resources include the newly formed National Death Index, which operates nationwide, and the Veterans Administration BIRLS file, which can give information on the payment of veterans' death benefits.

(3) Intensive tracing of subjects who have been identified as lost-to-follow-up (23 percent of the total), in order to increase the proportion of the cohort for which vital status has been determined. These efforts can include:

- Repeat mailings, and continuation of the contacting procedures for those few subjects who we had located, but who were not yet contacted by the end of the study period;
- Repeat DMV requests, to get updated addresses for subjects who had been located through the DMV, but whose addresses were out of date;

- Out-of-state DMV requests, which proved unexpectedly fruitful, based upon our tests in a few neighboring states;
- Re-examining school records to identify schools of transfer, contacting long-term residents of the neighborhoods to ask the whereabouts of the family; and
- Manually reviewing mortality files for deaths that may have occurred before 1966, when the CAMLIS system's records begin.

5.2.2 Study of Reproductive and Other Morbidity Outcomes

The validation study suggests that the questionnaire accurately collects pregnancy outcome data. It supports the findings of the pilot phase, which had indicated increased adverse reproductive outcomes among the small portion (33 percent) of the exposed group that had been interviewed. In order to follow up on these very preliminary findings, we recommend a study in the exposed and control groups of reproductive outcomes, and other morbidity outcomes, with the following suggestions:

(1) Re-using the reproductive history portion of the questionnaire. We can, nevertheless, make some revisions based upon our previous experience using this instrument in the field.

(2) Revising our procedure for obtaining physician names, and medical record release forms, and revising the wording of those forms.

(3) Analyzing the data in the manner of the pilot study, in order to compare the reproductive outcomes among the exposed subjects to those of the controls.

6.0

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APPENDIX A

LIFE TABLE ANALYSES

Table A1-1

LIFE TABLE ANALYSIS OF EXPOSED COHORT, ALL DEATHS

1. PERSON-YEARS TABLE

DEATHS 16

PERSON-YEARS 21443.5833

DEATHS/PERSON-YEARS = 7.46143951E-04

2. LIFE TABLE

X	NX	DX	WX	T	QX	PX	SX	RX
0	1363	0	45	0	0	1	1	0
1	1318	0	97	0	0	1	1	0
2	1221	0	50	0	0	1	1	0
3	1171	1	29	0	8.64677908E-04	.999135322	.999135322	8.6467783E-04
4	1141	1	7	0	8.79120879E-04	.999120879	.998256962	1.74303842E-03
5	1133	1	15	0	8.88494003E-04	.999111506	.997370016	2.6299837E-03
6	1117	0	14	0	0	1	.997370016	2.6299837E-03
7	1103	0	5	0	0	1	.997370016	2.6299837E-03
8	1098	0	2	0	0	1	.997370016	2.6299837E-03
9	1096	1	0	0	9.12408759E-04	.999087591	.996460007	3.53999296E-03
10	1095	1	2	0	9.14076783E-04	.999085923	.995549166	4.45083389E-03
11	1092	1	3	0	9.17010546E-04	.99908299	.994636237	5.36376284E-03
12	1088	1	4	0	9.20810313E-04	.99907919	.993720366	6.27963408E-03
13	1083	1	3	0	9.24641702E-04	.999075358	.992801531	7.19846948E-03
14	1079	2	5	0	1.85787274E-03	.998142127	.990957031	9.04296851E-03
15	1072	3	11	32	2.85578296E-03	.997144217	.988127073	.0118729267
16	1026	2	7	169	2.13219616E-03	.997867804	.986020193	.0139798075
17	848	1	12	94	1.25786164E-03	.998742138	.984779916	.0152200845
18	741	0	3	181	0	1	.984779916	.0152200845
19	557	0	2	80	0	1	.984779916	.0152200845
20	475	0	6	128	0	1	.984779916	.0152200845
21	341	0	2	339	0	1	.984779916	.0152200845
TOTAL		16	324	1023				

CUMULATIVE PROBABILITY OF SURVIVAL = .984779916
STANDARD ERROR OF SX = 3.79430066E-03
CUMULATIVE RISK = .015220084

Table A1-2

LIFE TABLE ANALYSIS OF CONTROL COHORT, ALL DEATHS

1. PERSON-YEARS TABLE

DEATHS 15

PERSON-YEARS 15422.6667

DEATHS/PERSON-YEARS = 9.72594449E-04

2. LIFE TABLE

X	NX	DX	WX	T	QX	PX	SX	RX
0	979	0	30	0	0	1	1	0
1	949	0	51	0	0	1	1	0
2	898	0	29	0	0	1	1	0
3	869	0	19	0	0	1	1	0
4	850	0	14	0	0	1	1	0
5	836	1	8	0	1.20192308E-03	.998798077	.998798077	1.20192301E-03
6	827	0	6	0	0	1	.998798077	1.20192301E-03
7	821	0	2	0	0	1	.998798077	1.20192301E-03
8	819	1	0	0	1.22100122E-03	.998778999	.997578543	2.42145662E-03
9	818	2	1	0	2.44648318E-03	.997553517	.995137984	4.8620156E-03
10	815	0	2	0	0	1	.995137984	4.8620156E-03
11	813	0	2	0	0	1	.995137984	4.8620156E-03
12	811	2	3	0	2.4706609E-03	.997529339	.992679336	7.32066413E-03
13	806	1	3	0	1.24300808E-03	.998756992	.991445428	8.55457247E-03
14	802	1	9	1	1.25470514E-03	.998745295	.990201456	9.79854423E-03
15	791	2	6	9	2.55264837E-03	.997447352	.98767382	.0123261802
16	774	2	7	171	2.91970803E-03	.997080292	.984790101	.0152098993
17	594	0	6	163	0	1	.984790101	.0152098993
18	425	0	8	93	0	1	.984790101	.0152098993
19	324	2	3	84	7.13012478E-03	.992869875	.977768424	.0222315756
20	235	0	5	84	0	1	.977768424	.0222315756
21	146	1	1	144	.0136054422	.986394558	.964465453	.0355345472

TOTAL 15 215 749

CUMULATIVE PROBABILITY OF SURVIVAL = .964465453
STANDARD ERROR OF SX = .0147195954

Table A2-1

LIFE TABLE ANALYSIS OF EXPOSED COHORT, NON TRAUMA DEATHS

1. PERSON-YEARS TABLE

DEATHS 6

PERSON-YEARS 21443.5833

DEATHS/PERSON--YEARS = 2.79803982E-04

2. LIFE TABLE

X	NX	DX	WX	T	QX	PX	SX	RX
0	1363	0	45	0	0	1	1	0
1	1318	0	97	0	0	1	1	0
2	1221	0	50	0	0	1	1	0
3	1171	1	29	0	8.64677908E-04	.999135322	.999135322	8.6467783E-04
4	1141	1	7	0	8.79120879E-04	.999120879	.998256962	1.74303842E-03
5	1133	1	15	0	8.88494003E-04	.999111506	.997370016	2.6299837E-03
6	1117	0	14	0	0	1	.997370016	2.6299837E-03
7	1103	0	5	0	0	1	.997370016	2.6299837E-03
8	1098	0	2	0	0	1	.997370016	2.6299837E-03
9	1096	1	0	0	9.12408759E-04	.999087591	.996460007	3.53999296E-03
10	1095	1	2	0	9.14076783E-04	.999085923	.995549166	4.45083389E-03
11	1092	0	4	0	0	1	.995549166	4.45083389E-03
12	1088	0	5	0	0	1	.995549166	4.45083389E-03
13	1083	0	4	0	0	1	.995549166	4.45083389E-03
14	1079	0	7	0	0	1	.995549166	4.45083389E-03
15	1072	0	14	32	0	1	.995549166	4.45083389E-03
16	1026	1	8	169	1.06666667E-03	.998933333	.994487247	5.5127528E-03
17	848	0	13	94	0	1	.994487247	5.5127528E-03
18	741	0	3	181	0	1	.994487247	5.5127528E-03
19	557	0	2	80	0	1	.994487247	5.5127528E-03
20	475	0	6	128	0	1	.994487247	5.5127528E-03
21	341	0	2	339	0	1	.994487247	5.5127528E-03
TOTAL		6	334	1023				

CUMULATIVE PROBABILITY OF SURVIVAL = .994487247
STANDARD ERROR OF SX = 2.25038107E-03

Table A2-2

LIFE TABLE ANALYSIS OF CONTROL COHORT, NON TRAUMA DEATHS

1. PERSON-YEARS TABLE

DEATHS 3

PERSON-YEARS 15422.6667

DEATHS/PERSON-YEARS = 1.9451889E-04

2. LIFE TABLE

X	NX	DX	WX	T	QX	PX	SX	RX
0	979	0	30	0	0	1	1	0
1	949	0	51	0	0	1	1	0
2	898	0	29	0	0	1	1	0
3	869	0	19	0	0	1	1	0
4	850	0	14	0	0	1	1	0
5	836	0	9	0	0	1	1	0
6	827	0	6	0	0	1	1	0
7	821	0	2	0	0	1	1	0
8	819	0	1	0	0	1	1	0
9	818	0	3	0	0	1	1	0
10	815	0	2	0	0	1	1	0
11	813	0	2	0	0	1	1	0
12	811	1	4	0	1.23609394E-03	.998763906	.998763906	1.23609393E-03
13	806	0	4	0	0	1	.998763906	1.23609393E-03
14	802	1	9	1	1.25470514E-03	.998745295	.997510752	2.48924829E-03
15	791	0	8	9	0	1	.997510752	2.48924829E-03
16	774	1	8	171	1.46092038E-03	.99853908	.996053468	3.94653203E-03
17	594	0	6	163	0	1	.996053468	3.94653203E-03
18	425	0	8	93	0	1	.996053468	3.94653203E-03
19	324	0	5	84	0	1	.996053468	3.94653203E-03
20	235	0	5	84	0	1	.996053468	3.94653203E-03
21	146	0	2	144	0	1	.996053468	3.94653203E-03

TOTAL 3 227 749

CUMULATIVE PROBABILITY OF SURVIVAL = .996053468
STANDARD ERROR OF SX = 2.28083041E-03

Table A3-1

LIFE TABLE ANALYSIS OF EXPOSED COHORT, NON-SPANISH SURNAME, ALL DEATHS

1. PERSON-YEARS TABLE

DEATHS 14

PERSON-YEARS 18280.75

DEATHS/PERSON-YEARS = 7.65832912E-04

2. LIFE TABLE

X	NX	DX	WX	T	QX	PX	SX	RX
0	1172	0	43	0	0	1	1	0
1	1129	0	86	0	0	1	1	0
2	1043	0	46	0	0	1	1	0
3	997	0	26	0	0	1	1	0
4	971	1	6	0	1.03305785E-03	.998966942	.998966942	1.03305792E-03
5	964	1	12	0	1.04384134E-03	.998956159	.997924179	2.07582093E-03
6	951	0	10	0	0	1	.997924179	2.07582093E-03
7	941	0	4	0	0	1	.997924179	2.07582093E-03
8	937	0	1	0	0	1	.997924179	2.07582093E-03
9	936	1	0	0	1.06837607E-03	.998931624	.996858021	3.14197922E-03
10	935	1	2	0	1.07066381E-03	.998929336	.995790721	4.20927908E-03
11	932	1	3	0	1.07469103E-03	.998925309	.994720554	5.27944649E-03
12	928	0	4	0	0	1	.994720554	5.27944649E-03
13	924	1	2	0	1.08342362E-03	.998916576	.99364285	6.35715015E-03
14	921	2	4	0	2.17627856E-03	.997823721	.991480406	8.51959363E-03
15	915	3	11	26	3.3463469E-03	.996653653	.988162569	.0118374312
16	875	2	7	144	2.50156348E-03	.997498437	.985690617	.0143093825
17	722	1	11	81	1.47928994E-03	.99852071	.984232495	.0157675047
18	629	0	3	155	0	1	.984232495	.0157675047
19	471	0	2	67	0	1	.984232495	.0157675047
20	402	0	4	114	0	1	.984232495	.0157675047
21	284	0	2	282	0	1	.984232495	.0157675047
TOTAL		14	289	869				

CUMULATIVE PROBABILITY OF SURVIVAL = .984232495
STANDARD ERROR OF SX = 4.20202788E-03

1. PERSON-YEARS TABLE

DEATHS 14

PERSON-YEARS 15020.6667

DEATHS/PERSON-YEARS = 9.32049176E-04

2. LIFE TABLE

X	NX	DX	WX	T	QX	PX	SX	RX
0	956	0	30	0	0	1	1	0
1	926	0	51	0	0	1	1	0
2	875	0	29	0	0	1	1	0
3	846	0	19	0	0	1	1	0
4	827	0	14	0	0	1	1	0
5	813	1	8	0	1.23609394E-03	.998763906	.998763906	1.23609393E-03
6	804	0	6	0	0	1	.998763906	1.23609393E-03
7	798	0	2	0	0	1	.998763906	1.23609393E-03
8	796	1	0	0	1.25628141E-03	.998743718	.997509178	2.49082246E-03
9	795	2	1	0	2.51730648E-03	.997482694	.994998141	5.00185881E-03
10	792	0	2	0	0	1	.994998141	5.00185881E-03
11	790	0	1	0	0	1	.994998141	5.00185881E-03
12	789	2	3	0	2.53968254E-03	.997460318	.992471162	7.528838E-03
13	784	1	3	0	1.27795527E-03	.998722045	.991202828	8.79717176E-03
14	780	1	9	1	1.29032258E-03	.998709677	.989923857	.0100761431
15	769	2	6	9	2.62639527E-03	.997373605	.987323926	.0126760744
16	752	1	7	161	1.49700599E-03	.998502994	.985845896	.0141541043
17	583	0	6	161	0	1	.985845896	.0141541043
18	416	0	8	90	0	1	.985845896	.0141541043
19	318	2	3	81	7.24637681E-03	.992753623	.978702085	.0212979151
20	232	0	5	82	0	1	.978702085	.0212979151
21	145	1	1	143	.0136986301	.98630137	.965295207	.034704793

TOTAL 14 214 728

CUMULATIVE PROBABILITY OF SURVIVAL = .965295207
STANDARD ERROR OF SX = .0148049298

Table A4-1

LIFE TABLE ANALYSIS OF EXPOSED COHORT, NON-SPANISH SURNAME, NON TRAUMA DEATHS

1. [illegible]-YEARS TABLE

DEATHS	5
PERSON-YEARS	18280.75

DEATHS/PERSON-YEARS = 2.735117546-04

2. LIFE TABLE

X	NX	DX	WX	T	BX	PX	SX	RX
0	1172	0	43	0	0	1	1	0
1	1129	0	86	0	0	1	1	0
2	1043	0	46	0	0	1	1	0
3	997	0	26	0	0	1	1	0
4	971	1	6	0	1.033057856-03	.9989669942	1	1.033057926-03
5	964	1	12	0	1.043841346-03	.9989959159	1	2.075820936-03
6	951	0	10	0	0	1	1	2.075820936-03
7	941	0	4	0	0	1	1	2.075820936-03
8	937	0	1	0	0	1	1	2.075820936-03
9	936	1	0	0	1.068376076-03	.9988931624	1	3.141977226-03
10	935	1	2	0	1.070663816-03	.9986629336	1	4.209279086-03
11	932	0	4	0	0	1	1	4.209279086-03
12	928	0	4	0	0	1	1	4.209279086-03
13	924	0	3	0	0	1	1	4.209279086-03
14	921	0	6	0	0	1	1	4.209279086-03
15	915	0	14	26	0	1	1	4.209279086-03
16	875	1	8	144	1.251554466-03	.9987484436	1	5.455575196-03
17	722	0	12	81	0	1	1	5.455575196-03
18	629	0	3	155	0	1	1	5.455575196-03
19	471	0	2	67	0	1	1	5.455575196-03
20	402	0	4	114	0	1	1	5.455575196-03
21	284	0	2	282	0	1	1	5.455575196-03
TOTAL		5	298	869				

CUMULATIVE PROBABILITY OF SURVIVAL = .9945444425
STANDARD ERROR OF SX = 2.439702786-03
[illegible]

Table A4-2

LIFE TABLE ANALYSIS OF CONTROL COHORT, NON-SPANISH SURNAME, NON-TRAUMA DEATHS

1. PERSON-YEARS TABLE

DEATHS 2

PERSON-YEARS 15020.6667

DEATHS/PERSON-YEARS = 1.33149882E-04

2. LIFE TABLE

X	NX	DX	WX	T	CX	PX	SX	RX
0	956	0	30	0	0	1	1	0
1	926	0	51	0	0	1	1	0
2	875	0	29	0	0	1	1	0
3	846	0	19	0	0	1	1	0
4	827	0	14	0	0	1	1	0
5	813	0	9	0	0	1	1	0
6	804	0	6	0	0	1	1	0
7	798	0	2	0	0	1	1	0
8	796	0	1	0	0	1	1	0
9	795	0	3	0	0	1	1	0
10	792	0	2	0	0	1	1	0
11	790	0	1	0	0	1	1	0
12	789	1	4	0	1.27064803E-03	.998729352	.998729352	1.27064809E-03
13	784	0	4	0	0	1	.998729352	1.27064809E-03
14	780	1	9	1	1.29032258E-03	.998709677	.997440669	2.55933101E-03
15	769	0	8	9	0	1	.997440669	2.55933101E-03
16	752	0	8	161	0	1	.997440669	2.55933101E-03
17	583	0	6	161	0	1	.997440669	2.55933101E-03
18	416	0	8	90	0	1	.997440669	2.55933101E-03
19	318	0	5	81	0	1	.997440669	2.55933101E-03
20	232	0	5	82	0	1	.997440669	2.55933101E-03
21	145	0	2	143	0	1	.997440669	2.55933101E-03
TOTAL		2	226	728				

CUMULATIVE PROBABILITY OF SURVIVAL = .997440669
STANDARD ERROR OF SX = 1.80745606E-03
CUMULATIVE RISK = 2.55933101E-03

Table A5-1

LIFE TABLE ANALYSIS OF EXPOSED COHORT, MALES, ALL DEATHS

1. PERSON-YEARS TABLE

DEATHS 13

PERSON-YEARS 11225.4167

DEATHS/PERSON-YEARS = 1.15808619E-03

2. LIFE TABLE

X	NX	DX	WX	T	QX	PX	SX	RX
0	679	0	21	0	0	1	1	0
1	658	0	35	0	0	1	1	0
2	623	0	17	0	0	1	1	0
3	606	1	9	0	1.66251039E-03	.99833749	.99833749	1.66251045E-03
4	596	1	2	0	1.68067227E-03	.998319328	.996659612	3.34038841E-03
5	593	1	5	0	1.6934801E-03	.99830652	.994971788	5.02821174E-03
6	587	0	6	0	0	1	.994971788	5.02821174E-03
7	581	0	2	0	0	1	.994971788	5.02821174E-03
8	579	0	0	0	0	1	.994971788	5.02821174E-03
9	579	1	0	0	1.72711572E-03	.998272884	.993253357	6.74664322E-03
10	578	0	1	0	0	1	.993253357	6.74664322E-03
11	577	0	0	0	0	1	.993253357	6.74664322E-03
12	577	1	1	0	1.73460538E-03	.998265395	.991530454	8.46954575E-03
13	575	1	1	0	1.74064404E-03	.998259356	.989804553	.0101954474
14	573	2	3	0	3.49956255E-03	.996500437	.98634067	.0136593303
15	568	3	4	11	5.35236396E-03	.994647636	.981061416	.0189385845
16	550	1	2	99	2.002002E-03	.997997998	.979097329	.0209026714
17	448	1	5	57	2.39808154E-03	.997601918	.976749373	.0232506266
18	385	0	0	92	0	1	.976749373	.0232506266
19	293	0	1	40	0	1	.976749373	.0232506266
20	252	0	1	69	0	1	.976749373	.0232506266
21	182	0	1	181	0	1	.976749373	.0232506266

TOTAL 13 117 549

CUMULATIVE PROBABILITY OF SURVIVAL = .976749373
STANDARD ERROR OF SX = 6.40752756E-03

Table A5-2

LIFE TABLE ANALYSIS OF CONTROL GROUP, MALES, ALL DEATHS

1. PERSON-YEARS INCIDENCE

DEATHS 10

PERSON-YEARS 8450.58334

DEATHS/PERSON-YEARS = 1.18335026E-03

2. LIFE TABLE

X	NX	DX	WX	T	QX	PX	SX	RX
0	515	0	13	0	0	1	1	0
1	502	0	18	0	0	1	1	0
2	484	0	10	0	0	1	1	0
3	474	0	11	0	0	1	1	0
4	463	0	5	0	0	1	1	0
5	458	1	1	0	2.18579235E-03	.997814208	.997814208	2.18579243E-03
6	456	0	2	0	0	1	.997814208	2.18579243E-03
7	454	0	2	0	0	1	.997814208	2.18579243E-03
8	452	0	0	0	0	1	.997814208	2.18579243E-03
9	452	2	1	0	4.42967885E-03	.9955703211	.993394211	6.60578906E-03
10	449	0	0	0	0	1	.993394211	6.60578906E-03
11	449	0	1	0	0	1	.993394211	6.60578906E-03
12	448	1	1	0	2.23463687E-03	.9977653663	.991174336	8.82566441E-03
13	446	1	2	0	2.24719101E-03	.9977528089	.988946978	.0110530225
14	443	0	5	0	0	1	.988946978	.0110530225
15	438	1	4	5	2.30680508E-03	.9976931949	.98666567	.0133343302
16	428	2	2	85	5.20156047E-03	.99479844	.9815333469	.0184665313
17	339	0	4	102	0	1	.9815333469	.0184665313
18	233	0	3	55	0	1	.9815333469	.0184665313
19	175	2	2	44	.0131578947	.9868421053	.9686185555	.0313814455
20	127	0	2	48	0	1	.9686185555	.0313814455
21	77	0	0	77	0	1	.9686185555	.0313814455
TOTAL		10	89	416				

CUMULATIVE PROBABILITY OF SURVIVAL = .9686185555

STANDARD ERROR OF SX = .0111015968

Table A6-1

LIFE TABLE ANALYSIS OF EXPOSED COHORT, MALES, NON TRAUMA DEATHS

1. PERSON-YEARS TABLE

DEATHS 5

PERSON-YEARS 11225.4167

DEATHS/PERSON-YEARS = 4.45417765E-04

2. LIFE TABLE

X	NX	DX	WX	T	QX	PX	SX	RX
0	679	0	21	0	0	1	1	0
1	658	0	35	0	0	1	1	0
2	623	0	17	0	0	1	1	0
3	606	1	9	0	1.66251039E-03	.99833749	.99833749	1.66251045E-03
4	596	1	2	0	1.68067227E-03	.998319328	.996659612	3.34038841E-03
5	593	1	5	0	1.6934801E-03	.99830652	.994971788	5.02821174E-03
6	587	0	6	0	0	1	.994971788	5.02821174E-03
7	581	0	2	0	0	1	.994971788	5.02821174E-03
8	579	0	0	0	0	1	.994971788	5.02821174E-03
9	579	1	0	0	1.72711572E-03	.998272884	.993253357	6.74664322E-03
10	578	0	1	0	0	1	.993253357	6.74664322E-03
11	577	0	0	0	0	1	.993253357	6.74664322E-03
12	577	0	2	0	0	1	.993253357	6.74664322E-03
13	575	0	2	0	0	1	.993253357	6.74664322E-03
14	573	0	5	0	0	1	.993253357	6.74664322E-03
15	568	0	7	11	0	1	.993253357	6.74664322E-03
16	550	1	2	99	2.002002E-03	.997997998	.991264862	8.73513846E-03
17	448	0	6	57	0	1	.991264862	8.73513846E-03
18	385	0	0	92	0	1	.991264862	8.73513846E-03
19	293	0	1	40	0	1	.991264862	8.73513846E-03
20	252	0	1	69	0	1	.991264862	8.73513846E-03
21	182	0	1	181	0	1	.991264862	8.73513846E-03
TOTAL		5	125	549				

CUMULATIVE PROBABILITY OF SURVIVAL = .991264862
STANDARD ERROR OF SX = 3.89944491E-03
CUMULATIVE RISK = 8.73513944E-03

Table A6-2

LIFE TABLE ANALYSIS OF CONTROL COHORT, MALES, NON TRAUMA DEATHS

1. PERSON-YEARS INCIDENCE

DEATHS 1

PERSON-YEARS 8450.58334

DEATHS/PERSON-YEARS = 1.18335026E-04

2. LIFE TABLE

X	NX	DX	WX	I	BX	PX	SX	RX
0	515	0	13	0	0	1	1	0
1	502	0	18	0	0	1	1	0
2	484	0	10	0	0	1	1	0
3	474	0	11	0	0	1	1	0
4	463	0	5	0	0	1	1	0
5	458	0	2	0	0	1	1	0
6	456	0	2	0	0	1	1	0
7	454	0	2	0	0	1	1	0
8	452	0	0	0	0	1	1	0
9	452	0	3	0	0	1	1	0
10	449	0	0	0	0	1	1	0
11	449	0	1	0	0	1	1	0
12	448	0	2	0	0	1	1	0
13	446	0	3	0	0	1	1	0
14	443	0	5	0	0	1	1	0
15	438	0	5	5	0	1	1	0
16	428	1	3	85	2.60416667E-03	.997395833	.997395833	2.60416674E-03
17	339	0	4	102	0	1	.997395833	2.60416674E-03
18	233	0	3	55	0	1	.997395833	2.60416674E-03
19	175	0	4	44	0	1	.997395833	2.60416674E-03
20	127	0	2	48	0	1	.997395833	2.60416674E-03
21	77	0	0	77	0	1	.997395833	2.60416674E-03
TOTAL		1	98	416				

CUMULATIVE PROBABILITY OF SURVIVAL = .997395833
STANDARD ERROR OF SX = 2.60077361E-03
CUMULATIVE RISK = 2.60416674E-03

Table A7-1

LIFE TABLE ANALYSIS OF EXPOSED COHORT, MALES, NON-SPANISH SURNAME, ALL DEATHS

1. [illegible] TABLE

DEATHS 11

PERSON-YEARS 9558.58334

DEATHS/PERSON-YEARS = 1.150798 15E-03

2. LIFE TABLE

X	NX	DX	WX	T	QX	PX	SX	EX
0	582	0	20	0	0	1	1	0
1	562	0	29	0	0	1	1	0
2	533	0	16	0	0	1	1	0
3	517	0	9	0	0	1	1	0
4	508	1	2	0	1.97238659E-03	.998027613	.998027613	1.97238661E-03
5	505	1	4	0	1.98807157E-03	.998011929	.996043463	3.95653678E-03
6	500	0	5	0	0	1	.996043463	3.95653678E-03
7	495	0	2	0	0	1	.996043463	3.95653678E-03
8	493	0	0	0	0	1	.996043463	3.95653678E-03
9	493	1	0	0	2.02839757E-03	.997971602	.994023091	5.97690884E-03
10	492	0	1	0	0	1	.994023091	5.97690884E-03
11	491	0	0	0	0	1	.994023091	5.97690884E-03
12	491	0	1	0	0	1	.994023091	5.97690884E-03
13	490	1	0	0	2.04081633E-03	.997959184	.991994473	8.00552732E-03
14	489	2	3	0	4.10256410E-03	.995897436	.987924752	.012075248 4
15	484	3	4	8	6.27615063E-03	.993723849	.981724387	.018275613
16	469	1	2	84	2.34741784E-03	.997652582	.97941987	.020580130 4
17	382	1	5	47	2.80898876E-03	.997191011	.976666869	.023331309 9
18	329	0	0	81	0	1	.976666869	.023331309 9
19	248	0	1	36	0	1	.976666869	.023331309 9
20	212	0	0	63	0	1	.976666869	.023331309 9
21	149	0	1	148	0	1	.976666869	.023331309 9
TOTAL		11	105	466				

CUMULATIVE PROBABILITY OF SURVIVAL = .976666869

STANDARD ERROR OF SX = 6.99213068E-03

Table A7-2

LIFE TABLE ANALYSIS OF CONTROL COHORT, MALES, NON-SPANISH SURNAME, ALL DEATHS

1. PERSON-YEARS INCIDENCE

DEATHS 9

PERSON-YEARS 8275.16667

DEATHS/PERSON-YEARS = 1.08759139E-03

2. LIFE TABLE

X	NX	DX	WX	T	QX	PX	SX	RX
0	505	0	13	0	0	1	1	0
1	492	0	18	0	0	1	1	0
2	474	0	10	0	0	1	1	0
3	464	0	11	0	0	1	1	0
4	453	0	5	0	0	1	1	0
5	448	1	1	0	2.23463687E-03	.997765363	.997765363	2.23463681E-03
6	446	0	2	0	0	1	.997765363	2.23463681E-03
7	444	0	2	0	0	1	.997765363	2.23463681E-03
8	442	0	0	0	0	1	.997765363	2.23463681E-03
9	442	2	1	0	4.53001133E-03	.995469989	.993245475	6.75452501E-03
10	439	0	0	0	0	1	.993245475	6.75452501E-03
11	439	0	1	0	0	1	.993245475	6.75452501E-03
12	438	1	1	0	2.28571429E-03	.997714286	.9909752	9.02480027E-03
13	436	1	2	0	2.29885057E-03	.997701149	.988697096	.0113029042
14	433	0	5	0	0	1	.988697096	.0113029042
15	428	1	4	5	2.36127509E-03	.997638725	.98636251	.0136374899
16	418	1	2	81	2.6560425E-03	.997343957	.983742689	.0162573108
17	334	0	4	101	0	1	.983742689	.0162573108
18	229	0	3	52	0	1	.983742689	.0162573108
19	174	2	2	44	.0132450331	.986754967	.970712985	.0292870153
20	126	0	2	48	0	1	.970712985	.0292870153
21	76	0	0	76	0	1	.970712985	.0292870153
TOTAL		9	89	407				

CUMULATIVE PROBABILITY OF SURVIVAL = .970712985
STANDARD ERROR OF SX = .0109566079
CUMULATIVE RISK = [illegible]

Table A8-1

LIFE TABLE ANALYSIS OF EXPOSED COHORT, MALES, NON-SPANISH SURNAME, NON TRAUMA DEATHS

1. PERSON-YEARS TABLE

DEATHS 4

PERSON-YEARS 9558.58334

DEATHS/PERSON-YEARS = 4.184720554E-04

2. LIFE TABLE

X	NX	DX	WX	1	OX	PX	SX	RX
0	582	0	20	0	0	1	1	0
1	562	0	29	0	0	1	1	0
2	533	0	16	0	0	1	1	0
3	517	0	9	0	0	1	1	0
4	508	1	2	0	1.972386591E-03	.998027613	.998027613	1.972386611E-03
5	505	1	4	0	1.988071571E-03	.998011929	.996043463	3.956536576E-03
6	500	0	5	0	0	1	.996043463	3.956536576E-03
7	495	0	2	0	0	1	.996043463	3.956536576E-03
8	493	0	0	0	0	1	.996043463	3.956536576E-03
9	493	1	0	0	2.028397571E-03	.997971602	.994023091	5.976909884E-03
10	492	0	1	0	0	1	.994023091	5.976909884E-03
11	491	0	0	0	0	1	.994023091	5.976909884E-03
12	491	0	1	0	0	1	.994023091	5.976909884E-03
13	490	0	1	0	0	1	.994023091	5.976909884E-03
14	489	0	5	0	0	1	.994023091	5.976909884E-03
15	484	0	7	8	0	1	.994023091	5.976909884E-03
16	469	1	2	84	2.347417841E-03	.997652582	.991689704	8.310296341E-03
17	382	0	6	47	0	1	.991689704	8.310296341E-03
18	329	0	0	81	0	1	.991689704	8.310296341E-03
19	248	0	1	35	0	1	.991689704	8.310296341E-03
20	212	0	0	63	0	1	.991689704	8.310296341E-03
21	149	0	1	148	0	1	.991689704	8.310296341E-03
TOTAL		4	112	466				

CUMULATIVE PROBABILITY OF SURVIVAL = .991689704

STANDARD ERROR OF SX = 4.149056526E-03

CUMULATIVE RATE = 8.310296341E-03

Table A8-2

LIFE TABLE ANALYSIS OF CONTROL COHORT, MALES, NON-SPANISH SURNAME, NON TRAUMA DEATHS

1. [illegible] INCIDENCE

[illegible] 0

PERSON-YEARS 8275.16667

DEATHS/PERSON-YEARS = 0

X	PX	SX	EX
0	1	1	0
1	1	1	0
2	1	1	0
3	1	1	0
4	1	1	0
5	1	1	0
6	1	1	0
7	1	1	0
8	1	1	0
9	1	1	0
10	1	1	0
11	1	1	0
12	1	1	0
13	1	1	0
14	1	1	0
15	1	1	0
16	1	1	0
17	1	1	0
18	1	1	0
19	1	1	0
20	1	1	0
21	1	1	0

2. LIFE TABLE

X	NX	DX	WX	T	QX
0	505	0	13	0	0
1	492	0	18	0	0
2	474	0	10	0	0
3	464	0	11	0	0
4	453	0	5	0	0
5	448	0	2	0	0
6	446	0	2	0	0
7	444	0	2	0	0
8	442	0	0	0	0
9	442	0	3	0	0
10	439	0	0	0	0
11	439	0	1	0	0
12	438	0	2	0	0
13	436	0	3	0	0
14	433	0	5	0	0
15	428	0	5	5	0
16	418	0	3	81	0
17	334	0	4	101	0
18	229	0	3	52	0
19	174	0	4	44	0
20	126	0	2	48	0
21	76	0	0	76	0
TOTAL		0	98	407	

CUMULATIVE PROBABILITY OF SURVIVAL = 1

STANDARD ERROR OF SX = 0

[illegible]

Table A9-1

LIFE TABLE ANALYSIS OF EXPOSED COHORT, FEMALES, ALL DEATHS

1. PERSON-YEARS TABLE

DEATHS 3

PERSON-YEARS 10193

DEATHS/PERSON-YEARS = 2.94319631E-04

2. LIFE TABLE

X	NX	DX	WX	T	QX	PX	SX	RX
0	682	0	24	0	0	1	1	0
1	658	0	62	0	0	1	1	0
2	596	0	33	0	0	1	1	0
3	563	0	20	0	0	1	1	0
4	543	0	5	0	0	1	1	0
5	538	0	10	0	0	1	1	0
6	528	0	8	0	0	1	1	0
7	520	0	2	0	0	1	1	0
8	518	0	2	0	0	1	1	0
9	516	0	0	0	0	1	1	0
10	516	1	1	0	1.93986421E-03	.998060136	.998060136	1.93986413E-03
11	514	1	3	0	1.95121951E-03	.99804878	.996112701	3.88729852E-03
12	510	0	3	0	0	1	.996112701	3.88729852E-03
13	507	0	2	0	0	1	.996112701	3.88729852E-03
14	505	0	2	0	0	1	.996112701	3.88729852E-03
15	503	0	7	21	0	1	.996112701	3.88729852E-03
16	475	1	5	70	2.28571429E-03	.997714286	.993835873	6.1641275E-03
17	399	0	7	36	0	1	.993835873	6.1641275E-03
18	356	0	3	89	0	1	.993835873	6.1641275E-03
19	264	0	1	40	0	1	.993835873	6.1641275E-03
20	223	0	5	59	0	1	.993835873	6.1641275E-03
21	159	0	1	158	0	1	.993835873	6.1641275E-03
TOTAL		3	206	473				

CUMULATIVE PROBABILITY OF SURVIVAL = .993835873
STANDARD ERROR OF SX = 3.55864677E-03

1. PERSON-YEARS INCIDENCE

DEATHS 5

PERSON-YEARS 6970.25

DEATHS/PERSON-YEARS = 7.17334385E-04

2. LIFE TABLE

X	NX	DX	WX	T	QX	PX	SX	RX
0	463	0	17	0	0	1	1	0
1	446	0	32	0	0	1	1	0
2	414	0	19	0	0	1	1	0
3	395	0	8	0	0	1	1	0
4	387	0	9	0	0	1	1	0
5	378	0	7	0	0	1	1	0
6	371	0	4	0	0	1	1	0
7	367	0	0	0	0	1	1	0
8	367	1	0	0	2.72479564E-03	.997275204	.997275204	2.7247956E-03
9	366	0	0	0	0	1	.997275204	2.7247956E-03
10	366	0	2	0	0	1	.997275204	2.7247956E-03
11	364	0	1	0	0	1	.997275204	2.7247956E-03
12	363	1	2	0	2.76243094E-03	.997237569	.9945203	5.4796997E-03
13	360	0	1	0	0	1	.9945203	5.4796997E-03
14	359	1	4	1	2.80504909E-03	.997194951	.991730622	8.26937798E-03
15	353	1	2	4	2.85714286E-03	.997142857	.988897106	.0111028941
16	346	0	5	86	0	1	.988897106	.0111028941
17	255	0	2	61	0	1	.988897106	.0111028941
18	192	0	5	38	0	1	.988897106	.0111028941
19	149	0	1	40	0	1	.988897106	.0111028941
20	108	0	3	36	0	1	.988897106	.0111028941
21	69	1	1	67	.0285714286	.971428572	.960642903	.0393570971
TOTAL		5	125	333				

CUMULATIVE PROBABILITY OF SURVIVAL = .960642903
STANDARD ERROR OF SX = .0283594766

1. PERSON-YEARS TABLE

DEATHS 1

PERSON-YEARS 10193

DEATHS/PERSON-YEARS = 9.81065437E-05

2. LIFE TABLE

X	NX	DX	WX	T	QX	PX	SX	RX
0	682	0	24	0	0	1	1	0
1	658	0	62	0	0	1	1	0
2	596	0	33	0	0	1	1	0
3	563	0	20	0	0	1	1	0
4	543	0	5	0	0	1	1	0
5	538	0	10	0	0	1	1	0
6	528	0	8	0	0	1	1	0
7	520	0	2	0	0	1	1	0
8	518	0	2	0	0	1	1	0
9	516	0	0	0	0	1	1	0
10	516	1	1	0	1.93986421E-03	.998060136	.998060136	1.93986413E-03
11	514	0	4	0	0	1	.998060136	1.93986413E-03
12	510	0	3	0	0	1	.998060136	1.93986413E-03
13	507	0	2	0	0	1	.998060136	1.93986413E-03
14	505	0	2	0	0	1	.998060136	1.93986413E-03
15	503	0	7	21	0	1	.998060136	1.93986413E-03
16	475	0	6	70	0	1	.998060136	1.93986413E-03
17	399	0	7	36	0	1	.998060136	1.93986413E-03
18	356	0	3	89	0	1	.998060136	1.93986413E-03
19	264	0	1	40	0	1	.998060136	1.93986413E-03
20	223	0	5	59	0	1	.998060136	1.93986413E-03
21	159	0	1	158	0	1	.998060136	1.93986413E-03

TOTAL 1 208 473

CUMULATIVE PROBABILITY OF SURVIVAL = .998060136
STANDARD ERROR OF SX = 1.93798176E-03

Table A10-2

1. PERSON-YEARS INCIDENCE

DEATHS 2

PERSON-YEARS 6970.25

DEATHS/PERSON-YEARS = 2.86933754E-04

2. LIFE TABLE

X	NX	DX	WX	T	QX	PX	SX	RX
0	463	0	17	0	0	1	1	0
1	446	0	32	0	0	1	1	0
2	414	0	19	0	0	1	1	0
3	395	0	8	0	0	1	1	0
4	387	0	9	0	0	1	1	0
5	378	0	7	0	0	1	1	0
6	371	0	4	0	0	1	1	0
7	367	0	0	0	0	1	1	0
8	367	0	1	0	0	1	1	0
9	366	0	0	0	0	1	1	0
10	366	0	2	0	0	1	1	0
11	364	0	1	0	0	1	1	0
12	363	1	2	0	2.76243094E-03	.997237569	.997237569	2.76243105E-03
13	360	0	1	0	0	1	.997237569	2.76243105E-03
14	359	1	4	1	2.80504909E-03	.997194951	.994440269	5.55973128E-03
15	353	0	3	4	0	1	.994440269	5.55973128E-03
16	346	0	5	86	0	1	.994440269	5.55973128E-03
17	255	0	2	61	0	1	.994440269	5.55973128E-03
18	192	0	5	38	0	1	.994440269	5.55973128E-03
19	149	0	1	40	0	1	.994440269	5.55973128E-03
20	108	0	3	36	0	1	.994440269	5.55973128E-03
21	69	0	2	67	0	1	.994440269	5.55973128E-03
TOTAL		2	128	333				

CUMULATIVE PROBABILITY OF SURVIVAL = .994440269
STANDARD ERROR OF SX = 3.92049127E-03

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Although a considerable body of occupational and laboratory toxicology data have demonstrated the carcinogenic action of vinyl chloride monomer, there appears to be little epidemiological literature which examines significant exposure to children. This study expanded a pilot study which identified a cohort of 1,363 children who attended an elementary school adjacent to a vinyl chloride monomer processing plant in Saugus, California in the 1950's and 1960's. The current study identified a non-exposed control group (N=979), set up a computer data base management system to facilitate subject tracing, performed an analysis of the mortality experience of the two groups up to 1980, and developed a protocol to validate pregnancy outcome data. Vital status was determined for 76.2 percent of the exposed group and 78.0 percent of the control group. Although the mortality rates up to this point are small, there is some evidence of an increased portion of non-trauma deaths among the exposed group, and increased rate among males. There is also evidence of a decreased rate of trauma deaths among the exposed cohort. Reproductive outcome responses were validated for 16 of the 246 married females (pregnant at least once) who had been interviewed. The validation protocol results suggest that the questionnaire is a good instrument capable of recording valid reproductive information.

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