0490

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Agency for Toxic Substances
and Disease Registry
Atlanta GA 30333

JUL 16 1997

Elsie L. Munsell
Deputy Assistant Secretary of the Navy (Environment and Safety)
Office of the Assistant Secretary (Installations and Environment)
1000 Navy Pentagon
Washington, D.C. 20350-1000

Dear Ms. Munsell:

I am writing to express my concern regarding information discussed at a recent workgroup meeting held June 23 between representatives of the Agency for Toxic Substances and Disease Registry (ATSDR) and the Department of Defense (DOD), including representatives of the Naval Environmental Health Center (NEHC). The concerns revolve around an apparent reluctance to provide funding to support a study of childhood cancer associated with exposures to trichloroethylene (TCE) and tetrachloroethylene (PCE) at Marine Corps Base - Camp Lejeune, NC. It appears that some of this reluctance may be attributable to a lack of understanding regarding the need and requirement for the study.

ATSDR's investigation indicates that more than 6,000 children were probably exposed to TCE and PCE *in utero* between 1968 and 1985 in base housing at Camp Lejeune. Based on an epidemiologic study recently completed by the Massachusetts Department of Public Health in the town of Woburn, Massachusetts, there is evidence indicating that these children exposed to TCE and PCE may be at increased risk of adverse health effects.

The Woburn study observed an association between the mother's potential for exposure to TCE and PCE in drinking water and childhood leukemia, particularly when exposure occurred during pregnancy. To our knowledge, no other study has explicitly examined the potential association between these environmental contaminants and childhood leukemia. Although the solvent mixture was slightly different at Woburn than at Camp Lejeune, the levels of solvents found in the drinking water at Camp Lejeune were comparable to, or higher than, the solvents found in wells at Woburn.

Although a single epidemiologic study can rarely if every establish causality in absence of other evidence, the association observed at Woburn was unusually strong, specific to exposure during pregnancy, and consistent with a dose-response relationship between potential exposure and the cancer risk. In light of the findings of the Woburn study and in absence of evidence to the contrary, we feel that there is a substantial possibility that the children exposed to solvents *in utero* at Camp Lejeune are at increased risk of childhood cancer.

CLW

0000002815

Section 104(i)(7)(B) of the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) states in part "Whenever in the judgment of the Administrator of ATSDR it is appropriate on the basis of the results of such pilot study or other study or health assessment, the Administrator of ATSDR shall conduct such full scale epidemiological or other health studies as may be necessary to determine the health effects on the population exposed to hazardous substances from a release or threatened release." Based on the findings of the public health assessment and the study of pregnancy outcomes conducted on the base, ATSDR has determined that a health study of the association between exposure to TCE and PCE and childhood cancer is warranted. Under Section 107 and 120 of CERCLA, DOD is liable for the cost of this study.

I am enclosing a copy of the health study proposal developed by ATSDR to investigate the potential relationship between exposure to volatile organic compounds in drinking water and childhood leukemia at Camp Lejeune. I am also including a copy of the study conducted at Woburn.

ATSDR is currently negotiating the Fiscal Year 1998 Annual Plan of Work with Department of Defense representatives. The funding for conducting this study has been included into those negotiations. We would appreciate your assistance in ensuring that adequate funds are provided so that this important health study can be conducted.

Sincerely yours,

Joseph L. Hughart for

Mark M. Bashor, Ph.D.
Associate Administrator for
Federal Programs
Director, Office of Federal Programs

cc:
Andrea Lunsford, NEHC
Bill Judkins, NAVFAC
Kathleen Buchi, Ph.D., USACHPPM

CLW

0000002816

Proposed Budget and Timeline:

Fiscal Year 1998	
Phase I	
Location of Cohort	$ 40,000
Advertisements	$ 20,000
Toll-free Number	$ 430,000
Screening Phone Calls (12,000 calls)	$ 770,000
Participant tracing (5,000 records)	$ 240,000
Data entry and data management phase I and II	$ 100,000
Medical record review	
Fiscal Year 1999	
Phase II	
Verification of medical diagnosis (100 records)	$ 15,000
Phase III	
Interviews -- 200 (120 controls up to 80 cases)	$ 30,000
Data entry and data management	$ 10,000
Data analysis and reporting	$ 135,000
Total Fiscal Year 1998	$ 1,600,000
Total Fiscal Year 1999	$ 190,000
Total Fiscal Year 1998 and 1999	$ 1,790,000

CLW

0000002817

Camp LeJeune - Childhood Leukemia Study Proposal

Purpose:

The purpose of the proposed study is to investigate the potential relationship between exposure to Volatile Organic Compounds (VOCs) in drinking water and childhood leukemia (CL) at the U.S. Marine Corps Base Camp LeJeune, Jacksonville, North Carolina. A secondary objective of the proposed study is to investigate the potential relationship between VOCs in drinking water and birth defects in this population.

Rationale:

CL is the most common cancer that occurs in childhood (*1*), and is of tremendous public health and public concern. There is limited evidence that exposure to VOCs such as trichloroethylene (TCE) in drinking water may be strongly associated with CL (*2*). ATSDR recently constructed a cohort of approximately 6,000 infants exposed to VOCs in drinking water during gestation and 6,000 births that were not exposed to VOCs for a study of pregnancy outcomes at Camp LeJeune. This existing database presents a unique opportunity to examine this potential association in a cohort of moderate size where exposure is relatively well-defined. Tracing the cohort will also allow us to identify any children that were diagnosed with birth defects, but because of the very small number of specific birth defects expected, this is only a secondary objective of the proposed study.

Study Overview:

Proposed is a nested case-control study of childhood leukemia (CL) and birth defects at Camp LeJeune. This study would occur in three phases. In phase I, an attempt would be made to locate as many of the children born to base residents between 1968 and 1985 as possible. During this phase, a brief screening interview would be conducted to identify potential cancer and

birth defect cases. In phase II, an attempt to verify reported CL and birth defect cases would be made by reviewing medical records of self-reported or parent-reported cases. In phase III, verified cases and a random sample of 100 non-cases would be interviewed in detail to obtain data on potential confounding factors. Additional information regarding proposed data collection methods follow.

Background:

The US Marine Corps Base at Camp LeJeune (MCB Camp LeJeune) is located in Jacksonville, on the eastern coast of North Carolina. Recently, ATSDR documented trichloroethylene (TCE), tetrachloroethylene (PCE), and 1,2-dichloroethylene (DCE) in water systems supplying two different family base housing areas at Camp LeJeune. The estimated number of infants born to residents living in each housing area receiving contaminated water, a list of contaminants, and contaminant levels are summarized in Table 1. Each of the affected housing areas received water containing a mixture of many contaminants, a phenomenon noted with almost every population exposed to contaminants released from hazardous waste sites.

The estimated number of infants in each housing area was determined by ATSDR during a detailed study of late pregnancy outcomes on the base, and a database now exists containing infant, mother and father's names, address at birth, and date of birth for all infants born to residents of base family housing between 1968 and 1985. This previous study identified residents of base family housing based on mother's residence at birth as reported on the birth certificate. For most births, this address was validated using base family housing records. The earliest births in the study occurred in 1968, the first year that birth certificates were computerized in North Carolina. The latest births studied occurred in 1985, the last year that contamination was detected

at the base. While the pregnancy study, now being completed, was useful in addressing questions related to some late pregnancy outcomes, questions persist about other health effects that may have occurred from this exposure including cancer and birth defects. The existence of this database presents a unique opportunity for continued research into the health effects of VOCs in drinking water, as well as to answer lingering questions about the health among residents at Camp LeJeune.

Childhood leukemia describes a disease process in which white blood cells accumulate, but fail to reach a state of functional maturity. This leaves the individual susceptible to infection, hemorrhage, and inadequate cellular nutrition (*3*). Leukemia has annual incidence of 7.1 per 100,000 among children 0-4 years old and declines to about 2.1 per 100,000 at ages 15—19 years (*4*). Five-year survival rates have increased substantially between 1974 and 1990. However, about one-third of children under 10 and about half of children over 10 still die from the leukemia within 5 years (*4*).

There are few known risk factors for leukemias and those that have been identified appear to explain only a small fraction of leukemia incidence among adults or children (*1*). However, as Sandler (*5*) has argued, variation in leukemia incidence across gender and race in the United States, and between developing and undeveloped countries, supports at least some role for the environment in the etiology of leukemia (*5*). Some of the factors that may potentially increase the risk of CL are: electromagnetic fields, viruses, and consumption of n-Nitroso compounds (*5*).

PCE and TCE, which are metabolized to a common substance, trichloroethane (TCA), are both considered to be probable human carcinogens by the International Agency for Research on Cancer (IARC) on the basis of animal testing (*6-7*). However, IARC considers the human evidence to be too limited to draw definitive conclusions. Some studies of occupational exposure

CLW

to solvents, including PCE and TCE, have noted associations with leukemia and/or non-Hodgkin's lymphoma incidence (*8-9*) or mortality (*10-11*), but these studies did not include large enough groups of pregnant women to address the issue of cancer in offspring exposed *in utero*. A small study of the children of women who owned laundry or a dry-cleaning facility at the time of conception revealed a strong association (OR = 3.7) between occupation and incidence of any childhood cancer. However, because there were only 6 cases, this analysis was not broken out by cancer type (*12*).

Six studies, two in New Jersey and four in Massachusetts, have been conducted of PCE and/or TCE contaminated drinking water and leukemia or non-Hodgkins lymphoma (*2,13,14,15,16,17*). Three of the six studies are analyses of the same TCE-exposed community, and differed only in their details. Each of these six studies, summarized in Table 2, have noted associations between VOCs in drinking water and the incidence of leukemia, although in the New Jersey studies, excesses were limited to specific cell-types and were noted among females only.

Only the three studies in Woburn, Massachusetts focused specifically on leukemia in children. In 1979, two wells supplying water to east Woburn were found to contain approximately 267 ppb TCE and 21 ppb PCE. As summarized in Table 2, the most recent study in this series noted a very strong association between TCE exposure during gestation and CL (OR = 8.3 95% CI: 0.7-95). Moreover, the association was driven by cases which would have received the highest percentage of water from the contaminated wells (OR = 14.3 [0.9-225]). A weaker association was observed when exposure was examined from 2 years prior to conception through age of diagnosis (OR 2.4 95% CI: 0.5, 10.6). The major strengths of this study were good ascertainment of cases, a systematic model for defining exposure, and careful attention to the

CLW

timing of exposure. The major weakness of the study was the small sample size which was limited by the total number of cases in Woburn. Moreover, despite the efforts made to model exposure, the year when exposure first began was not known, and the concentrations of contaminants that would have been present in drinking water was modelled based on a minimal amount of data. In addition, because so little is known about the causes of CL, it is not known what potential confounders may have been overlooked. However, the likelihood that an unidentified confounder could create such a strong association is unlikely. Moreover, after 18 years of elevated CL incidence, CL rates reverted to expected in Woburn, approximately 8 years following the closure of the well. This would appear to be an appropriate lag time for CL. The previous investigations at Woburn (*13,14*) found approximately a 2-fold increase in risk, rather than an 8-fold to 14-fold increase, which probably reflects the less specific exposure window (i.e. from birth to diagnosis) in the earlier investigations.

Although it did not focus on CL, a study conducted by Cohn *et al.* (*16*) in New Jersey also noted that CL incidence, particularly acute lymphocytic leukemia (ALL) incidence, was elevated. However, the association between TCE and ALL was only observed in female children but not male children (*16*). Conversely, at Woburn, excesses in leukemia incidence were not limited to ALL and were greater in male children than female children *(2,13,14)*. Given the small numbers, it is difficult to evaluate how important these inconsistencies are.

There have also been suggestions that VOCs such as PCE and TCE may cause birth defects (*13,18,19,20*) although the associations noted were much weaker than for VOCs and CL. Moreover, public concern regarding the effects of these solvents on birth defects is very high.

Methods:

As summarized above, the proposed study would be conducted in three phases. During phase 1, we will attempt to locate the members of the cohort identified in our birth database. Between 12 and 30 years have elapsed between birth and the time that we will attempt to locate this group. Tracing will present quite a challenge, because the current database does not contain social security number for the infants born at Camp LeJeune or for their parents. In addition, the database contains an age of each parent at the time of the infant's birth, but not exact birthdays for the parents. Therefore, we will attempt to reduce the number of individuals who must be traced by widely advertising our desire to locate individuals who were born, or whose children were born, at the USMC Camp LeJeune between 1968 and 1985 in publications targetting military personnel. A toll-free number will be established for respondents to provide their name and phone number and indicate their willingness to participate in a health study. A brief screening questionnaire would be used for the following purposes:

(1) to confirm the names of children born on base, their dates of birth, and dates and location of residences on base at the time of each birth;

(2) to determine the vital status of each child and the availability of his/her parents for interview;

(3) to determine whether or not each child had been diagnosed with cancer or birth defects before age 20 and ascertain, to the best of the respondent's knowledge the type of cancer and birth defect diagnosed;

(4) to invite callers to participate in the proposed ATSDR study as 'recruiters'. Recruiters would be asked to disseminate information about ATSDR and the health study to previous

base residents who may not have seen our advertisements. This would not violate confidentiality since ATSDR would not ask the caller for particular names, nor follow-up with them regarding their recruitment activities. However, it may greatly expand the audience that receives information regarding the proposed study.

If an 80 percent or greater response rate is not acheived through publicity, the remaining children or their parents will be traced through consultation with the Navy (which may have information as to each parent's most recent duty station) and by using services such as Equifax.

Conduct of phases II and III would be contingent on locating a large and representative proportion of the cohort in phase I, as well as the identification of sufficient numbers of cases to complete an acceptable study. We will assess the representativeness of the cohort that is located using demographic characteristics available from the late pregnancy outcome study including race, parity, military rank, and mother's education and age at birth.

In phase II, an attempt to verify reported CL cases would be made by reviewing medical records of self-reported or parent reported cases. Cancer cases for which the organ system was not specified would also be verified to determine the organ system affected. Relevant medical information such as histologic type would also be obtained at this time.

In phase III, the parents of verified cases and the parents of a random sample of non-cases, frequency matched at a rate of 5:1, would be interviewed more completely to assess information about exposure, such as significant time periods during pregnancy spent away from Camp LeJeune and bottled water use, and potential confounders such as parental occupation, smoking status, and service in Vietnam. Interviews would be conducted over the telephone. Odds ratios and 90% confidence intervals for exposure to VOCs in drinking water would be computed for all CL, and

when possible, for histologic subtypes. Because the number of expected cases in both the exposed and unexposed groups is small, standardized incidence rates would also be computed for the exposed cancer cases compared to an external comparison group, such as CL cases in the National Cancer Institute's Surveillance, Epidemiology, and End Results Program (SEER) registry. This latter comparison group, while possibly less comparable than the unexposed cohort born at Camp LeJeune, would provide greater power to detect a statistically significant difference between exposed and comparison groups, and would place CL rates in the exposed cohort within a national context.

Sample Size Calculations:

A sample size worksheet is included as Table 3. With a 5:1 matching scheme, the proposed internal comparison group analysis would have 80% power to detect a 5 fold or greater increase in rates of CL, using a one-tailed alpha of .05 (*21*). The proposed analysis using an external standard would have sufficient power to detect a 3 fold or greater increase in rates of CL, using a one-tailed alpha of .05 (*22*). Both power calculations are based upon the assumption that approximately 10,000 of the 12,000 infants (83%) whose parents lived in family base housing at Camp LeJeune when they were born between 1968 and 1985 would be located, and that half of these infants would have resided in exposed housing areas.

The magnitude of associations observed between TCE and PCE exposure and birth defects is much weaker than the magnitude of association observed between these VOCs and CL. Therefore, the power to detect such associations would be weaker. However, the added costs of investigating birth defects once the cohort has been reconstructed would be minimal, and of sufficient interest to be worthwhile.

CLW

Strengths and Limitations:

There are several important strengths of the proposed study. The first is the existence of a database from which can be reconstructed a cohort that was very likely to have been exposed *in utero* to a variety of VOCs in drinking water. Using this database, a representative sample of the exposed population should be identifiable. Moreover, since advertisements will be based on whether individuals were born in base housing, and will not specify which housing areas were exposed, it is hoped that differential participation by exposure will be minimized. In addition, the existing database already contains valuable information about residential history from housing records which can be compared with parental reports of residence. Realistically, 6,000 infants with similar in utero exposures is about as large a population as one would be able to locate in most situations where drinking water contamination has occurred substantially above current drinking water standards. Hence, it could help us to answer questions about CL in this population, and also about the risks of CL in the many smaller populations of individuals where exposure to VOCs through maternal consumption of drinking water may have occurred in utero.

The major limitation of the proposed study is the low study power, such that only very strong associations between exposure and CL will be detected. However, the study power is great enough to detect statistically significant results of the magnitude of those observed at Woburn. Moreover, even findings that are not statistically significant can provide information on the most likely range of values for the association between the exposure and outcome.

References:

1. Groves FD, Linet MS, Devessa SS. Patterns of occurrence of leukaemias. Eur J Cancer 1995; 31A:941-949.

2. Massachusetts Department of Public Health. Woburn childhood leukemia follow-up study. 1996: 112 pp.

3. Miller KB, Rosenthal DS, Weinstein HJ. Leukemia. In: Cancer Manual. 7th ed. Boston: American Cancer Society, 1986: 318-33.

4. Table XXVII-9. Childhood Cancer. SEER Incidence, U.S. Mortality and 5-year Relative Survival Rates in: Ries LAG, Miller BA, Hankey BF, Kosary CL, Harras A, Edwards BK (eds). SEER Cancer Statistics Review, 1978-1991: Tables and Graphs, National Cancer Institute, NIH Pub. No. 94-2789. Bethesda, MD, 1994.

5. Sandler DP. Recent studies in leukemia epidemiology. Current Opinion in Oncology 1995; 7:12-18.

6. ATSDR. Toxicological profile for tetrachloroethylene.

7. Agency for Toxic Substances and Disease Registry. Toxicological profile for trichloroethylene. Update. Atlanta: US Department of Health and Human Services, Public Health Service, 1993, Report No.: TP-92/19.

8. Antilla A, PUkkala E, Sallmen M, Herberg S, Hemminki K. Cancer incidence among Finnish workers exposed to halogenated hydrocarbons. JOEM 1995; 37:797-806.

9. Blair A, Linos A, Stewart PA, et al. Evaluation of risks for non-Hodgkin's lymphoma by occupation and industry exposures from a case-control study. Am J Ind Med 1993; 23:301-312.

10. Olsen GW, Hearn S, Cook RR, Currier MF. Mortality experience of a cohort of Louisiana chemical workers. J Occup Med 1989; 31:32-34.

11. Spirtas R, Stewart PA, Lee JS, et al. Retrospective cohort mortality study of workers at an aircraft maintenance facility. I. Epidemiological results. Brit J Ind Med 1991; 48:515-530.

12. Olsen JH, de Nully Brown P, Schulgen G, Jensen OM. Parental employment at time of conception and the risk of cancer in offspring. Eur J Cancer 1991; 27:958-965.

13. Lagakos, SW, Wessen BJ, Zelen M. An analsyis of contaminated well water and health effects in Woburn, Massachusetts. JASA 1986; 395:583-96.

14. Cutler JJ, Parker GS, Rosen Sh, Prenney B, Healey R, Caldwell GG. Childhood leukemia in Woburn, Massachusetts. Public Health Reports 1986;101:201-5.

~~15. Aschengrau A, Ozonoff D, Paulu C, et al. Cancer risk and tetrachloroethylene-contaminated drinking water in Massachusetts. Arch Environ Health 1993; 48:284-292.15.~~

16. Cohn P, Klotz J, Bove F, Berkowitz M, Fagliano J. Drinking water contamination and the incidence of leukemia and non-Hodgkin's lymphoma. Environ Health Perspect 1994; 102:556-561.

17. Fagliano J, Berry M, Bove F, Burke T. Drinking water contamination and the incidence of leukemia: an ecologic study. Am J Public Health 1990; 80:1209-1212.

18. Bove FJ, Fulcomer MC, Klotz JB, Esmart J, Dufficy EM, Savrin JE. Public drinking water contamination and birth outcomes. Am J Epid 1995; 141:850-62.

19. Goldberg SJ, Lebowitz MD, Graver EJ, Hicks S. An association of human congenital cardiac malformations and drinking water contaminants. J Am Coll Cardiol 1990;16:155-64.

20. Dawson BV, Johnson PD, Goldberg SJ, Ulreich JB. Cardiac teratogenesis of halogenated hydrocarbon-contaminated drinking water. J Am Coll Cardiol 1993; 21:1466-72.

21. Fleiss JL, Statistical Methods for Rates and Proportions, 2nd, Ed., John Wiley and Sons, New York:1981;38-45.

22. Breslow, NE, Day NE. Statistical Methods in Cancer Research. Volume II-The Design and Analysis of Cohort Studies, IARC Scientific Publications No. 82. International Agency for Research on Cancer, Lyon: 1987;p.277.

Table 1. Summary of exposure groups and the estimated concentrations of volatile organic compounds in drinking water.

Exposure Group	Exposed Housing Area	Number of Infants	Contaminants detected	Estimated contaminant levels (in ppb)	Period of Exposure
PCE exposed	Tarawa Terrace	6,362	Tetrachloroethylene Trichloroethylene 1,2-Dichloroethylene	215 8 12	1958-Feb 1985
TCE exposed	Hospital Point	32	Trichloroethylene Dichloroethylene Benzene Methylene chloride Vinyl chloride	900-1400 321-407 35* 54 3†	? - Feb 1985 (Activities began in 1940s)
Unexposed***	Midway Park, Berkeley Manor, Rifle Range, Courthouse Bay, Watkin's Village, Paradise Point	5,898			

* Estimated assuming a dilution factor of 20 from sampling data for well 602.

† Detection limit was 10 ppb.

*** Infants were excluded from this group if gestation occurred in their housing area during a 12 day exposure period in 1985

Table 2. Review of studies of TCE and PCE [illegible]

Study Location and Maximum VOC Concentrations Observed in Drinking Water *(Reference)*	Study design and sample size	Odds ratio [95% Confidence Interval] (# of cases) or other results
Woburn, Massachusetts *(2)* Trichloroethylene 237 ppb Tetrachloroethylene 21 ppb	Matched case-control study. 19 incident childhood leukemia cases born 1969-1989 and diagnosed while residing in Woburn. 37 controls selected from school records for the Woburn school district, and on age, race, sex and residence in Woburn on date of diagnosis. Exposure was based on a model for distribution of different water wells to different areas of Woburn, and the duration of residence during different critical periods.	Exposure during pregnancy None 1.0 (9) Any 8.3 [0.7, 95] (10) Least 3.5 [0.2, 58] (3) Most 14.3 [0.9,225] (7)
Woburn, Massachusetts *(13)* Trichloroethylene 237 ppb Tetrachloroethylene 21 ppb	Cumulative and ever-never exposure to contaminated wells was assessed 20 incident childhood leukemia cases diagnosed between 1969 and 1983, and compared to the rate expected based on exposure rates in 164 healthy controls. Exposure was based on a model for distribution of different water wells to different areas of Woburn, and the duration of residence in Woburn throughout the child's life.	Ratio of observed ever exposed/ expected ever exposed: 1.8 (p = .02) Ratio of observed cumulative exposure score/ expected cumulative score:2.0 (p = .03)
Woburn, Massachusetts *(14)* Trichloroethylene 237 ppb Tetrachloroethylene 21 ppb	Incidence of childhood leukemia between 1969 and 1978 in Woburn was compared to the expected incidence based on the Third National Cancer Survey. The geographic location of cancers was also assessed.	Incidence in Woburn 2.3 times expected (p=.007) (12 cases) Incidence in East Woburn 7.5 times expected (p = .0002)
Barnstable County, Massachusetts *(15)* Tetrachloroethylene 7750 ppb	34 incident leukemia (all ages) cases and 737 controls during 1983-1986 were studied. Exposure dose was modelled based on information regarding PVC piping use in the water system. Information on demographic characteristics, residential history, smoking, medical and occupational history, bottled water consumption, and bathing habits was also collected.	Exposure category Any 2.0 [0.7-5.5] (7) Above 90th percentile 5.8 [1.4-25] (2)
New Jersey *(16)* Trichloroethylene > 5 ppb Tetrachloroethylene > 5 ppb	Registry-based study of leukemia and non-Hodgkins lymphoma of all ages in 75 municipalities. Mean VOC concentrations were estimated for each distribution system based on water samples taken in 1984 and 1985. Cancer incidence between 1979-1987 were compared in municipalities that had different levels of VOCs in public drinking water supplies.	TCE and childhood ALL in females < 1 ppb 1.0 > 5 ppb 3.3 [1.3, 8.3] (6) TCE not associated with ALL in males PCE not associated with ALL in either sex
New Jersey *(17)* TCE 46 ppb PCE 16 ppb	Ecologic study based on leukemia incidence data for all ages from cancer registry for the years 1979-1984. Observed rates were compared with expected in exposure categories defined by mean chemical-specific concentration of VOCs.	TCE in females 1.7 [not reported] PCE in females 1.7 [not reported] No association between exposure and leakemia in males.

ALL= acute lymphocytic leukemia

Table 3. Sample Size Worksheet

Target: Identify 10,000/12,000 (83%) births. 5,000 will be unexposed.

Age	Baseline Incidence rate	Person-years*	Expected Unexposed cases	Expected Exposed cases (If no elevation in risk)
0-4 years	7.1/100,000	25,000	1.8	1.8
5-9 years	3.9/100,000	25,000	1.0	1.0
10-14 years	2.3/100,000	24,510	0.6	0.6
15-19 years	2.1/100,000	11,550	0.2	0.2
All ages:			3.6	3.6

Power Calculation Using Internal Comparison Group

Odds Ratio	Expected Exposed Cases	Power to detect when one-tailed alpha = .05
2.0	2(3.6) = 7.2	.12
3.0	3(3.6) = 10.8	.57
5.0	5(3.6) = 18	.79

Power Calculation Using External Comparison Group

Odds Ratio	Expected Exposed Cases (When risk does not differ from baseline)	Power to detect when one-tailed alpha = .05
2.0	3	.39
3.0	3	.79
5.0	3	.99
2.0	4	.41
3.0	4	.84
5.0	4	1.0

* Person-years declines because some cohort members will be younger than 19.

Medical Records Review:

In FY 1998, ATSDR plans to review between 400 and 600 prenatal care medical records for mothers included in the Camp LeJeune Pregnancy Outcome Study. In FYs 1995-1997 ATSDR conducted a study of birth outcomes in the infants of mothers exposed to VOCs during pregnancy. Results contained in the Interim Report from this study indicated an association between PCE exposure and small for gestational age in two potentially susceptible subgroups: mothers with previous fetal losses and mothers 35 years of age and older. As concluded in the Interim Report, these results merit further scrutiny.

Reviewing prenatal care records would be useful to improve upon the information available to us from the birth certifiicate. One critical source of information available on the medical record is an expanded maternal pregnancy history. Each birth certificate contained information on previous fetal deaths for all gestational ages combined. However, fetal deaths occurring at early gestational ages (miscarriages) have a different etiology than fetal deaths occurring at late gestational ages (stillbirths). It is also not clear whether fetal deaths at these different gestational ages were reported more or less completely. Unlike the birth certificate, the medical record indicates whether the fetal losses were stillbirths or miscarriages. Information regarding maternal medical conditions such as diabetes and hypertension, maternal height, and maternal weight gain would also greatly enrich the existing data for both the older mothers and the mothers with histories of fetal death. Given the adverse findings for women in these clinically susceptible subgroups, the modest cost involved in abstracting medical records from a sample of women would be quite valuable.