Protocol for the Cross-Sectional Exposure Assessment of Case-Children with Leukemia (Acute Lymphocytic and Acute Myelocytic Leukemias) and a Reference Population in Churchill County, Nevada

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PROJECT OVERVIEW

The Centers for Disease Control and Prevention's (CDC) National Center for Environmental Health (NCEH) was requested by an Expert Panel convened by the Nevada State Health Officer, Dr. Mary Guinan, to assess exposure to a variety of chemicals, radioactive elements, and infectious agents among children in Churchill County, Nevada diagnosed with leukemia (acute lymphocytic leukemia [ALL] and acute myelocytic leukemia [AML]). The exposures of case children will be compared to that of their immediate family members (parents and siblings only) and reference families. The reference families will consist of children without cancer diagnoses, and their parents. Siblings of reference children will not be included in the study. Reference – or "control" – children will be frequency-matched 4:1 with case-children on the basis of year of birth and sex. Strata for matching will encompass two-year periods. Exposure will be assessed by measuring for specific analytes within blood, urine, and household environmental samples, and with a questionnaire about pertinent risk factors.

A case is defined as a child age 0-19 years old, with a medically confirmed diagnosis of ALL or AML, who resided in Churchill County prior to diagnosis. Fourteen children who meet the case definition have been identified as of June 30, 2001. Fifty-six control children will be identified for participation in the study. Urine, blood, and buccal cell samples will be collected from case children and their families and from control children and their parents. Samples will be analyzed for specific chemicals, radioactive elements, and infectious agents. DNA will be extracted from blood and buccal cells and stored by CDC for future studies of candidate genes involved in metabolizing carcinogens and DNA repair from damage by environmental exposure. Based on consultations with experts, more complex genetic analysis may also be conducted with the stored DNA to identify new genes that are associated with childhood leukemia.

We will compare the results of laboratory testing of case-childrens' blood and urine samples to the results of tests of their family members' samples. We will also compare the results from case-families to those of control-families. This study is a cross-sectional exposure assessment of current exposures; it is very difficult to collect reliable information about exposures that happened in the past. Environmental samples will be collected from the current household of each participating case and control family to help interpret the results of the blood and urine tests. In addition to the case-family's current home, we will collect environmental samples from each house they previously occupied within Churchill County, Nevada during the defined time period for this study. We will also collect environmental samples from the previous residences of 1 out of every 4 control children in each frequency strata. The control family whose historic residences will be sampled will be randomly selected without prejudice to number of residences or duration of residence. We will collect indoor air, play yard soil, drinking water, and household dust from each past and current residential location. We will follow the same protocol for case-children regardless of whether they remain current residents of Churchill County, Nevada. The study time period for cases is defined as 1 year before birth of the case child to the month that he or she was diagnosed with leukemia. For controls, the time period begins 1 year before birth and ends on June 30, 2001.

Should additional cases of leukemia associated with the Fallon cluster be identified after data collection for the cross sectional study has been completed, questionnaire data and biologic specimens from the case children and their families will be collected. No control subjects will be matched or enrolled for newly identified cases. Biologic samples will be analyzed for the same analytes as other study participants, and results compared to those of other case families. However, results from new case families will not be included in the case control component of analysis. Questionnaire data collected from any additional cases will be analyzed statistically with the results of biologic samples, but again, will not be included in case control analyses. Additional case samples will be banked in the same manner that original case and control samples are stored.

Investigators/collaborators/funding sources:
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Agency Responsibilities

CDC will be responsible for:
- Designing the study, entering the data, analyzing the data, writing the report(s);
- Study logistics including: recruitment, administering the questionnaire and consent form, translating consent and questionnaire forms into Spanish, compiling the completed forms, maintaining the confidentiality of participating families, and collecting (or oversight of collecting) and shipping buccal cell, urine, and blood samples to CDC;
- Funding and conducting the laboratory tests to measure chemical, radioactive and viral/infectious exposure in biological specimens;
- Funding, collection (or oversight of collection), handling, and storage of biological specimens (blood, urine, and buccal cells) for future study;
- Developing informational materials, holding public meetings, and conducting other environmental exposure educational activities, as needed.
- Project oversight for CDC-hired contractors and Nevada State agency designees to conduct the environmental sampling and laboratory analysis, and recruitment process (e.g., random digit dialing) for study participants in accordance with study protocol.

NSHD will be responsible for:
- Identifying potential case family members for participation in the study;
- Oversight and cooperation with a CDC-hired contractor in the recruitment process;
- Community education about this study and dissemination of study results to participants;
- Oversight of environmental sampling, which includes collaboration with Nevada State Bureau of Health Protection Services (water) and the Department of Conservation and Natural Resources, Environmental Protection Division (soil and dust);
- Oversight of relationship with Fallon Community Hospital personnel.

ATSDR will be responsible for:
- Identifying possible sources of contamination in Churchill County and conducting exposure pathway analyses

NDEP will be responsible for:

- Preparing and implementing an environmental sampling plan, with assistance from ATSDR, for collecting and shipping of environmental samples, and identifying laboratories that will analyze the samples.

USGS will be responsible for:

- Funding and sampling and analyzing water, and possibly soil, samples from the participating households;
- Data entry of the water test results into a database compatible with software used by CDC for database management;
- Maintaining the confidentiality of the participating families and residential locations;
- Sharing the water testing results with CDC and NSHD.

Churchill Community Hospital will be responsible for:

- Providing physical space for interviewing study participants and collecting biological specimens;
- Phlebotomy required for blood samples, in accordance with the clinical status of case-children;
- Interim cold storage (if needed), and oversight for shipping biological specimens according to CDC protocols;

U.S. Naval Air Station (Fallon) will be responsible for:

- Cooperation for environmental sampling at selected base housing sites;
- Collaboration in the recruitment process for control-families living in base housing.

INTRODUCTION

Leukemias are cancers of the blood-forming tissues. They may be subdivided according to the particular cell type involved, the major types being lymphocytic and myelocytic (granulocytic) leukemias. Leukemias are also classified by their behavior, as either "acute" or "chronic." Childhood leukemias are mostly acute, with the lymphocytic form predominating (Rudolph 1996). In the U.S., childhood leukemia rates are highest among Filipinos, followed by white Hispanics, non-Hispanic whites and blacks. Reliable rates could not be computed for children in the remaining racial/ethnic groups. The ratio of mortality-to-incidence rates is higher for adult leukemias than for childhood leukemias. Because treatment for childhood leukemias is quite successful, mortality from this cancer is comparatively low among children (Ries, et. al., 2001).

Several comprehensive reviews of risk factors for childhood cancers have been published in recent years and form the basis of the following discussion (Sandler and Ross, 1997; Pritchard-Jones, 1996; Zahm and Devesa, 1995; Ross et. al., 1994; Savitz and Chen, 1990; NJDHSS and ATSDR (Dover), 1998; Legakos et al., 1986; Massachusetts Department of Health (Woburn), 1997). Established causes of leukemia include ionizing radiation (such as occurs from x-irradiation), certain drugs used in the treatment of cancer, and some chemicals (most notably benzene) used largely in industrial settings. Ionizing radiation has been associated with all forms of leukemia except the chronic lymphocytic form. It is suspected that many childhood leukemias may result from parental exposures before the time of conception or during early fetal development (Savitz and Chen, 1990).

The following table presents the national ALL incidence rates reported by the Surveillance, Epidemiology, and End Results (SEER) registry and incidence rates of ALL within international settings, according to International Classification of Childhood Cancers (ICCC): (Ries, et al. 2001)

Age category	[1]National SEER data Incidence Rates of ALL: Dates, 1975-1998	ALL Survival Rates (SEER) (%)	[2]ICCC Incidence Rates of ALL: Dates, 1990-1999
0-4 yrs	6.1	87	5.5
5-9 yrs	3.0	87	Unavailable
10-14 yrs	1.7	76	Unavailable
15-19 yrs	1.2	58	1.1
0-19 yrs	1.9 – 3.3	Unavailable	2.7

[1] Reported as per 100,000 population and age-adjusted by 5-yr age groups, based on the 1970 standard US population of 0 to 19 year-olds.
[2] Reported as per 100,000 population (both sexes, all races) and age adjusted to the 1970 standard US population of 0 to 19 year-olds.

During the time period 1990 -1999, the background rate of ALL for persons under 20 years of age in Churchill County was 3.0 per 100,000 and 2.4 per 100,000 within the State of Nevada. During 1991 to 2000, the rate was 2.4 per 100,000 within the State of Nevada (Cancer Registry, State of Nevada). Based on these rates, 12 ALL cases in Churchill County from 1997 to 2000 indicate a statistically significant increase in the incidence of ALL for this area.

In July 2000, Dr. Randall Todd, State Epidemiologist, identified an increase in the incidence rate of ALL for Churchill County, Nevada. According to the Nevada State Cancer Registry, the first case of ALL diagnosed in Fallon, Nevada was in 1997, with 2 subsequent cases in 1999, and 9 additional cases diagnosed by July 2000. In September 2000, Dr. Todd began an investigation of the case-families by administering a questionnaire and collecting drinking water samples from case-family homes. The questionnaire covered residential history prior to conception, pregnancy history, water supply choices and use, chemical use inside the home, occupational history of parents, sources for radiation and electromagnetic (EMF) exposure, child activities, and smoking in the home. The investigation did not reveal any obvious risk factor or etiology. During on-going case-finding activities, a thirteenth case-child with ALL was detected, along with a case-child with acute myelocytic leukemia (AML), and finally a child diagnosed with aplastic anemia. The child with aplastic anemia is not being considered as a case in this study since this diagnosis is not a form of leukemia. In total, 14 cases of childhood leukemia were detected in Churchill County, Nevada between 1997-2001.

In February, 2001 Dr. Mary Guinan, State Health Officer for Nevada, convened an Expert Panel to review the State of Nevada's investigation and other literature about ALL/AML among children. Following recommendations from this Expert Panel, the State of Nevada formally requested assistance from both CDC/NCEH and ATSDR on March 7, 2001 for further evaluation of risk factors or etiologic exposures linked to this childhood leukemia cluster in the Fallon area. ATSDR has been asked to evaluate historic contaminant releases in Churchill County, Nevada and provide an assessment of completed exposure pathways for the case-families. CDC/NCEH has been asked to design and conduct a cross-sectional exposure assessment of selective contaminants using environmental (household) and biologic specimens collected from case-families and a reference population. This protocol refers to the CDC/NCEH exposure study.

Justification for study:
State officials and an expert panel requested this study to further investigate the leukemia cluster in Churchill County, Nevada. It is necessary to study children since this cluster of leukemia is affecting children. An expert panel review of the ongoing state study recommended a cross-sectional exposure assessment be conducted, involving both case-families and reference-families. The cross-sectional design will allow us to compare the laboratory testing results from case-children's blood and urine to their family members' samples; and between case-families and control-families. It is very difficult to collect reliable information about exposures that happened in the past. Environmental samples will be collected from the current household of each participating case and control family to help interpret the results of the blood and urine tests. Environmental samples will also be collected from homes in Churchill County where the case child previously lived and compared to samples collected from their current home. Environmental samples will be collected from the historic residences of 1 out of every 4 control children and compared to historic residences of case children.

Intended/potential use of study findings:
- To help local health providers, public health officials, and the parents of the case-children understand the potential role of environmental exposures, infectious factors and genetics in manifesting this illness.
- To identify any environmental contamination that may be linked to this cluster so that it can be remediated to prevent further exposure to the residents of Churchill County, Nevada.
- To contribute to our scientific understanding of the health impacts of certain environmental exposures such that we can develop better prevention and control strategies in the future.
- To further our understanding of gene-environment interactions and the risk for manifesting leukemia in children.
- To better understand the potential role of infectious agents in the development of childhood leukemia.

Study design/locations:
We propose to conduct a cross-sectional exposure assessment of case and control children, and their families, in Churchill County, Nevada. This issue is of concern because of the elevated incidence of leukemia among children residing in this county. We will use questionnaire data and test biological and environmental samples to assess exposures. We will follow the same protocol for case-children regardless of whether they remain current residents of Churchill County, Nevada.

Objective:
- Assess for chemical, radioactive, and infectious exposures among the participating children and family members.
- Assess for genetic variation in genes involved in metabolizing toxic substances and DNA repair from damage by environmental exposure.

Hypotheses or questions:
- Do children who developed leukemia have a chemical, radioactive or infectious exposure that differs from their immediate family or from children or the families of children who do not have this condition (reference group)?

- Do children who developed leukemia have variant genes that code for the key enzymes involved in metabolizing toxic substances and DNA repair from damage by environmental exposures, as compared to their immediate family and reference children and their parents?
- Do household exposures from prior residences of case-children differ from their current household exposures or from exposures from prior and current residences of control children?

PROCEDURES/METHODS: STUDY POPULATION

The study population will be comprised of the children in Churchill County who meet the case definition and their families (parents and all siblings), and children who are enrolled as control subjects and their parents. Over 200 subjects will be enrolled in the study, 14 of whom will be case children and 56 of whom will be control children. We expect to enroll 28 case parents, all case siblings, and 112 control parents.

Case definition:
For the purposes of this study, a case is defined as a child aged 0 to 19 years of age at time of diagnosis, who has been medically diagnosed with childhood leukemia (ALL or AML) during the period from January 1, 1997 through June 30, 2001, and who resided in Churchill County prior to diagnosis.

Control definition:
Control-children will be 4:1 frequency-matched with case-children on the basis of stratified categories of year of birth (2-year strata) and sex (Table 1). Because control children will be recruited through random digit dialing of households in Churchill County, control-children will be residents of Churchill County at the time of enrollment. A child will be excluded from this control group if he/she is a sibling of a case-child or has ever been diagnosed with any form of cancer.

Geographic area and time period of study:
Churchill County, Nevada is the geographic area being studied. Case and control children will be required to have resided within this county. The study time period for both cases and controls differs for each participating child. For both cases and controls, the study period begins 1 year before birth. It ends at the month and year of diagnosis for case children, and at June 30, 2001, for control children.

Should additional cases of leukemia associated with the Fallon cluster be identified after data collection for the cross sectional study has been completed, questionnaire data and biologic specimens from the case children and their families will be collected. No control subjects will be matched or enrolled for newly identified cases. Biologic samples will be analyzed for the same analytes as other study participants, and results compared to those of other case families. However, results from new case families will not be included in the case control component of analysis. Questionnaire data collected from any additional cases will be analyzed statistically with the results of biologic samples, but again, will not be included in case control analyses. Additional case samples will be banked in the same manner that original case and control samples are stored.

Estimated number of households to be sampled:
It is estimated that environmental samples will be collected from approximately 88 residences in Churchill County. This figure includes current and past residences of all cases (n=22), current residences of all control subjects (n=56), and past residences of 1 out of every 4 control children enrolled in the study. Assuming that control families have proportionally similar numbers of historic homes as case families do, we estimate a total of 10 past residences for control subjects will be sampled.

Sampling, including sample size and statistical power:
The sample size for the study (n=>200) is sufficient to provide valuable data about possible chemical, radioactive, and infectious exposures in the study population. It is important to note, however, that the sample size was determined based on available resources, not on statistical power. If this study identifies pertinent trends in environmental exposure in the study

population, follow-up studies will be designed to target specific research questions. Statistical power for those studies will be determined by calculating statistical power.

Enrollment: (Figure 1)
Case children have been identified by the NSHD using the Nevada State Cancer Registry. NSHD has informed the case families about the upcoming CDC assessment and obtained their permission to release their contact information to CDC. CDC will contact case families to notify them about the study, inform them of the study process, and collect information that will be used to personalize a mailing packet that includes study consent forms and a questionnaire. In the cover letter accompanying the packet, cases will be asked (if they agree to participate in the study) to contact the CDC clinic offices in Fallon, Nevada to set up an appointment to give specimens of blood, urine, and buccal cells and to be interviewed. While on the telephone, cases will be asked for additional information, such as the number of adults and children living in their household that will be used to customize the interview questionnaire.

To identify eligible controls, households in Churchill County with local telephone exchanges will be contacted by telephone using a random digit dialing process. A standardized screening tool will be administered, in Spanish if necessary, to determine eligibility (Appendix C). If the household contacted has children who are eligible to be control subjects in the study and their parent or guardian agrees to receive study material including the consent forms, CDC study staff will use information collected on the call to customize the mailing packet and send to the eligible control. In the cover letter accompanying the packet, controls will be asked (if they agree to participate in the study) to contact the CDC clinic offices in Fallon, Nevada to set up an appointment to give specimens of blood, urine, and buccal cells and to be interviewed. While on the telephone, controls will be asked for additional personal information that will be used to customize the interview questionnaire.

Eligible control-children will meet the control definition (above) and match the requirements for the age and sex categories of the case-children. We will only enroll 1 child per control-household contacted to avoid clustering of exposure assessments within one household. Should more than one child per household be eligible to be a control, the youngest child will be selected. We will remove phone numbers of case-family households from the random digit dialing process to avoid enrolling a sibling as a control. In addition, we will remove phone numbers of the households already contacted during the recruitment process to avoid duplicate calls. This process will be repeated until we have enrolled 4 category-matched control-children per case-child.

PROCEDURES/METHODS: DESIGN

General approach:

In this study, we will assess exposure to a variety of chemicals, radioactive elements, and infectious agents among children diagnosed with leukemia, and compare this to their immediate family members (parents and siblings only) and to control children and their families (parents only). The reference group will consist of children without cancer diagnoses and their parents. Control-children will be frequency-matched 4:1 with case-children on the basis of age category (2-year intervals of year of birth) and sex. Exposure will be assessed by measuring for specific analytes within blood and urine (Table 2), and household samples, and with a questionnaire about pertinent risk factors.

How study design addresses hypotheses and meets objectives:

Study Description

This is a cross-sectional exposure assessment. We will measure chemical and radioactive substances and infectious agents in blood and urine specimens in over 200 case and control subjects. We will compare the results of the tests from case-children's blood and urine to that of their family members, and between case-families and reference-families. Environmental samples will be collected from the current household of each participating family to help interpret the results of the blood and urine tests. In addition to case-families' current homes, we will collect environmental samples from each house they occupied previously within Churchill County, Nevada during a defined time period for this study. For cases, this time period is defined as beginning 1 year before birth and ending with the month and year that he or she was diagnosed with leukemia. Environmental samples will also be collected from 1 out of 4 control family's historic residences. For controls, the time period begins 1 year before birth and ends June 30, 2001. We will collect environmental samples from approximately 88 homes in Churchill County, Nevada. This figure was calculated based on the number of current and historic case homes (n=22), the number of current control homes (n=56), and the number of historic control homes of 1 out of 4 controls. Assuming that controls have proportionally the same number of past residences as cases, we estimate 10 past residences in Churchill County for controls. Samples of household dust, indoor air, tap water, and play yard soil will be collected from each housing location. We anticipate collecting samples during August-September, 2001.

Consent

CDC staff will obtain consent from adult cases and controls and from the parents of case or control children younger than 18 years of age (Appendix A). We will obtain assent from children aged 7-17 years old. Consent forms will be mailed to adult case and control subjects, translated to Spanish as necessary, and to the parents of case and control subjects under the age of 18 years old. Study participants will return their signed consent forms to CDC at the time of their visit to the CDC clinic offices in Fallon, which have been lent to CDC by the Churchill Community Hospital. CDC staff will administer the assent form to children aged 7-17 years old at the time of their clinic visit.

Questionnaire Administration

The study questionnaire (Appendix B) will be administered in two parts. Study subjects will receive a mailed questionnaire and a face-to-face interview regarding potential risk or etiologic factors for developing leukemia. The mailed and interview questionnaires will cover the same time frame(s) as described above and will address water consumption patterns, child activities, pertinent medical and pregnancy histories, and possible chemical exposures from recreational activities, hobbies, or parental occupations. The mailed questionnaire will accompany the

consent forms, and should be returned to CDC when the study subject visits the CDC field clinic offices. The second questionnaire, the interview, will be administered as part of the study subject's visit to the clinic offices the CDC study team will be occupying while in the field. If it is more convenient for the family to be interviewed and give samples at home, members of the CDC team will visit the family at their home. Mailed and interview questionnaires will be translated into Spanish as necessary. A Spanish-speaking member of the CDC study team will administer the questionnaire to Spanish speaking subjects.

Biological Specimen Collection
After receiving consent/assent from case or control families, CDC and other trained laboratory personnel will obtain a urine, blood, and buccal cell sample from each participant using standardized collection, storage, and transport protocols. CDC laboratory staff and trained contractors and volunteers from the Churchill Community Hospital will obtain 32.5 ml (2 ½ tablespoons) of voided urine from each participant in this study, with the help of a participating parent as needed. Water and fruit juice will be provided to participants to assist in the production of urine, as needed. A trained phlebotomist will obtain 21 ml (1½ tablespoons) of whole venous blood from case-children, case-family participants, and control children and their parents. We will work with the case childrens' physicians to ensure clinical appropriateness in taking a 21 ml blood sample, on the day of the child's visit to the CDC clinic offices. Trained CDC scientists will implement and/or supervise standard CDC protocols for specimen collection, handling, storage, and shipment to the NCEH Laboratory in Atlanta, Georgia. CDC will analyze the biological specimens at the NCEH Laboratory (NCEH/EHLS) in Atlanta, Georgia. Blood and buccal cells for DNA extraction will be handled separately using standardized protocols.

Blood and urine will be analyzed for the substances listed in Table 2. DNA extracted from blood and buccal cells will be stored by CDC without personal identifiers. The stored DNA will be used for future studies of candidate genes involved in metabolizing carcinogens and DNA repair from damage by environmental exposure. More complex genetic analysis may also be conducted with the stored DNA, after consultations with experts, to identify new gene variants that are associated with childhood leukemia.

Chain of Custody of Samples
CDC's Environmental Health Laboratory has a detailed chain of custody protocol for tracking biologic samples. The laboratory meets or exceeds the requirements of CLIA 88 (Clinical Laboratory Improvements Amendments of 1998) for specimen/sample chain of custody. This method will be used while collecting samples in the field through analysis at the laboratory in Atlanta, Georgia. The US Environmental Protection Agency (EPA) website provides a detailed description of their chain of custody protocol. The U.S. Geological Survey (USGS) employs this methodology for tracking samples as they move from persons and locations. The Natural Resources Division of Environmental Protection (NDEP) will also utilize the EPA protocol for tracking environmental samples from collection in the field to analysis in the EPA laboratory.

Environmental Sample Collection
Samples of household tap water will be collected by USGS. They will collect and analyze these samples according to their standard protocols. Samples of dust, soil and indoor air will be collected by NDEP. The NDEP, with assistance from ATSDR, will prepare and implement an environmental sampling plan. The analysis of dust, soil, and air samples will be conducted by the US EPA Region IX laboratory. Some samples may be sent to alternate laboratories based on the analyses required and the technical limitations of the EPA laboratory.

Audience and stakeholder participation:
Participating stakeholders in this study include the families participating in this study, residents of Churchill County, the Mayor of the City of Fallon, military personnel and their families living at the Naval Air Station in Fallon, the Fallon Paiute-Shoshone Tribe, the Nevada State Health Division (NSHD), Bureau of Health Protection Services, the State of Nevada Department of Conservation and Natural Resources, Division of Environmental Protection (NDEP), the U.S. Geological Survey (USGS), Water Resources Division (Carson City), the U.S. Environmental Protection Agency (EPA; Region IX), Senator Harry Reid, Representative Jim Gibbons, and State Assemblywoman Marcia DeBraga. In addition, we are working closely with the Agency for Toxic Substances and Disease Registry (ATSDR).

Cost benefit/prevention effectiveness:
Few studies have been conducted to assess chemical, radioactive, and infectious exposures for etiologic linkage to developing leukemia. The State of Nevada, with the support of key members of the US Congress and the US Senate, has formally requested that CDC conduct an exposure assessment study that includes a referent population. Information learned from this study would help local health providers, public health officials, and the parents of the case-children understand the potential role of environmental and infectious exposures, and genetics in manifesting this illness. If identified, environmental contamination or exposures could be remediated, possibly preventing further exposure to the residents of Churchill County, Nevada. Findings in this study may help us improve prevention and control strategies in the future.

Study time line:

Task	**Completion date**
Institutional Review Board (IRB) approval	2nd quarter 2001
Training	2nd quarter 2001
Subject recruitment and biological/environmental sample collection	3rd quarter 2001
Biological/environmental sample analyses	3rd/4th quarter 2001
Data analysis and final report preparation	1st/2nd quarter 2002
Presentation of study results to study participants	3rd quarter 2002

Expedited protocol review request:
Yes

PROCEDURES/METHODS: DATA COLLECTION PROCEDURES

The data collection component of this study has 3 components: biological data, environmental data, and questionnaire data. The questionnaire has two parts, one of which will be mailed, and one that will be administered during a face-to-face interview.

Mail Packet

The Mail Packet will be sent to the parent(s) or guardian(s) of eligible case or control children, or to adult case or control subjects who are over 18 years of age, who have agreed verbally during an initial phone conversation to receive study materials and consent forms. The packet includes the study consent forms, primary demographic information about the participating child and his/her family, a questionnaire about the hobbies of the participating case or control subject and the people living with the participating child, and forms requesting the participating child's immunization, school attendance, and travel histories. The hobby questionnaire will collect information about the types of hobbies engaged in by the participating child or his family members and types of exposures associated with those hobbies. The participating child's immunization history, including types and dates immunizations were given, will be collected on the immunization form. The school attendance form will collect the names of all schools the participating child attended, including day care and pre-schools, and the dates they were attended. The travel history form will include information about out-of-state domestic and international travel. The mail packet also includes a form to list information about parent or guardian's current occupations, current and past military service, and a form to list past and current residences of the participating child. All case and control subjects will receive the form to list past residences in Churchill County. However, only 1 out of every 4 controls will be selected to have samples taken from their previous residences in Churchill County. The forms are only to be completed and returned if the study subject or parent/guardian signs the consent forms. A calendar will be developed for each study subject highlighting relevant time frames. The calendar will help interviewees visualize the important time frames. The first page of the mailing packet will ask for personal identification information and will be separated from the rest of the packet upon receipt by CDC. The personal identification information will be stored by CDC in a locked file away from the rest of the data collection forms. A study ID number will be assigned each case and control subject/family and will be pre-printed on each page of the forms in the mailing packet.

Person-to-person interview

In the letter that case and control subjects receive with the mailed packet, case and control subjects will be asked to contact the CDC clinic offices in Fallon, Nevada to make an appointment if they decide to participate in the study. During the appointment, study subjects will give blood and urine and will be interviewed. The interview is the first face-to-face contact the CDC will have with families participating in the study. The interview will be administered to an eligible member of the participating child's family (e.g., mother, father, maternal or paternal grandparent, step-parent). The interview consists of five parts: Study Subject Information, Child and Family Medical History, Maternal Pregnancy History, Child Nutrition, and Secondary Demographics. Information obtained from cases and controls at the time they call to make an appointment for their clinic visit will be used to customize the interview questionnaires to each interviewee. Personal identifiers will be collected on the first page of the interview, which will be separated from the body of the interview prior to submission for data entry. This page will be kept by CDC in a locked file away from the completed data collection forms. Data about past residences collected during the interview will be used to contact the current residents of those homes to inform them about the study and request permission to collect environmental samples from their residences.

Relevant Time Frames:

Cases:

- From one year before birth to month and year of diagnosis for parent/guardian hobby history, child's residential history, child medical history, military service history.
- From one year before birth to birth for case child pregnancy history.
- From one month before interview to interview for child nutrition.
- Through lifetime of parents and grandparents of participating child for family medical history.
- Current day information about parent/guardian occupations and primary and secondary demographics.

Controls:

- From one year before birth to June 30, 2001 for parent/guardian hobby history, child's residential history, child medical history, and military service history
- From one year before birth to birth for control child pregnancy history
- From one month before interview to interview for child nutrition.
- Through lifetime of parents and grandparents of participating child for family medical history.
- Current day occupational information and primary and secondary demographics.

PROCEDURES/METHODS: VARIABLES/INTERVENTIONS

Variables:

The mailing and interview questionnaires will collect information on school attendance, immunizations, travel history, water consumption patterns, child activities, pertinent medical and pregnancy histories, and possible chemicals, radioactive substances, or infectious exposures from recreational activities, hobbies, or current parental occupations. Urine samples will be analyzed for selected pesticides and heavy metals; blood samples will be analyzed for volatile organic compounds and selected heavy metals (Table 2). DNA will be harvested from blood and buccal cells and stored for future studies that will be determined based on the assessment of environmental exposures. We will analyze for most/all of the substances listed in Table 2 within the appropriate environmental sample (household dust, drinking water, and play yard soil). Analytes to be tested for were determined by consultation with experts in the analysis of biological and environmental samples. The analytes tested for in environmental samples reflect those to be tested for in the biological samples. Indoor air will be tested for radon and VOCs. Water samples collected from all case and control homes, past and present, will be tested for primary and secondary contaminants listed by EPA, arising from the National Primary Drinking Water Regulations.

Training for all study personnel:

CDC study team members will be conducting the structured interviews after being trained on how to administer the interview questionnaire consistently and without bias. Each study interviewer will successfully administer a mock interview under the supervision of a CDC scientist. Biological samples will be collected and processed by staff from CDC's environmental laboratory, who will train locally contracted phlebotomists and volunteers from the Churchill County Community Hospital to assist them. Environmental sample collection will be conducted using protocols developed and implemented by participating agencies (USGS, NSHD, NDEP, ATSDR; Region IX, and EPA; Region IX. Training of team members who will participate in collecting soil, dust, and air samples will be conducted when the teams meet in Fallon, Nevada.

PROCEDURES/METHODS: DATA HANDLING AND ANALYSIS

Data analysis plan:

CDC scientists will be responsible for collecting all data from the collaborating agencies, and reviewing all data for quality, accuracy, and completeness. CDC will describe characteristics of the case-children, the case-families, and the control-families (e.g., socio-economic status, age, sex, parents' education level and occupation). Cross-sectional indices of environmental exposure for individuals will be constructed based on a comparison of biological measurements and measurements taken from an individual's current home. We will then compare the exposure indices between case-families and control-families, and between case-children and their immediate family members. Multiple logistic regression techniques will be employed to model significant risk factors and confounders of exposure in this community. Tables and figures describing the characteristics of the study group, the environmental exposure indices, risk factors, confounders, and exposure models will supplement the descriptive analyses. Conditional multiple regression will be used to examine the impact of any environmental contaminants measured in previous family homes among case-families and between case and control families.

Data Analysis:

Biological Specimen Analysis

Urine and blood samples will be analyzed by NCEH's Environmental Health Laboratory for the analytes listed in Table 2 using standardized analysis protocols for each analyte.

DNA will be extracted from buccal cells at CDC's environmental laboratory and from an aliquot of blood in the field. DNA samples will be aliquoted and shipped using a detailed protocol developed by NCEH/Genetics office and NCEH/EHLS. Serum from at least 7 ml of whole blood collected, and any urine specimens in excess of 20 ml, will be sent to the CDC and ATSDR Specimen Packaging, Inventory and Repository (CASPIR) for storage in the event that further tests are indicated by the exposure pathway analysis being concurrently conducted by ATSDR. Any biological samples sent to CASPIR receive an additional unique number, via bar coding. No personal identifiers will be used to label the specimens.

DNA will be stored at CDC until we evaluate the results of the exposure assessment. The advice of experts will be obtained to determine the best approach for the genetic analysis of the specimens collected. The approach may include examining genotypes of study participants for genes relevant to detoxification pathways of suspected chemical or radioactive exposures, or in DNA repair from damage by such exposure; and identification of genomic regions of interest through family studies and sib-pair analysis that may lead to hypotheses about new gene variants associated with ALL/AML.

Questionnaire Analysis

CDC will contract with a data management company to merge datasets of questionnaire, biological, and environmental data. This company will be responsible for entering questionnaire data, merging datasets from other study agencies, and analyzing the data for associations.

Environmental Sample Analysis
Water samples collected by USGS will be analyzed at the USGS laboratory. Soil, dust, and air samples collected by NDEP will be analyzed at the EPA, Region IX laboratory. Some samples may be sent to other state or federal laboratories, depending on the analyses needed and the technical limitations of the EPA Region IX laboratory. Analytes to be tested for in environmental samples will closely mirror those to be tested for in biologic samples. Examples include arsenic, chromium, and volatile organic compounds. These datasets will be forwarded to CDC for analysis.

Data entry, editing and management, including handling data collection forms, different versions of data and data storage and disposition:
CDC will coordinate all data entry, editing, and management.

Quality control/assurance:
We will adhere to standard laboratory quality assurance and quality control procedures for all biological and environmental sampling, handling, shipping, and analysis.

Intermediate reviews and analyses:
The biological and environmental sampling results will be reviewed as available to identify potential threats to public health. All biological results will be reviewed at CDC prior to release to NSHD and study participants (parent/guardian). Review of the environmental sampling results will be coordinated with CDC prior to release to the study participants (parent/guardian). Any potential public health threats identified by intermediate reviews will be reviewed in conjunction with the Nevada State health officials for possible immediate remedial action.

Bias in data collection, measurement and analysis:
- Trained CDC scientists and representatives will administer the questionnaire using uniform techniques, which will reduce the likelihood for interviewer bias.
- Because the environmental sample collection team members are the same people who are on the study development team and who have written the collection protocols, it is not possible to blind them to case/control status as they have all received the line listing of cases.
- The biological and environmental samples will be blinded to those conducting the laboratory analyses, which will reduce the likelihood for measurement bias.
- Larger-sized families have a greater chance to be selected as control-families (more likely to have a child that is eligible), which is a selection bias among controls. We will only select one control-child per eligible household to avoid clustering exposure information.

Limitations of study:
- This study targets case-children who resided in Churchill County, Nevada at or before the time of diagnosis. Thus, case-family results from this study may not be representative of exposures occurring within Churchill County and should not be generalized.
- Collection of environmental samples provides a “snapshot” of the potential chemical and radioactive exposures to which a child/person may have been exposed. There will be no information on chemical or radioactive degradation or longevity in the children’s environment. Thus, this study will not tell us about long-term or cumulative exposure in this county.
- Given the small number of cases, it is not likely that we will be able to detect statistically significant differences in the common gene variants that code for the enzymes that metabolize toxic substances or repair DNA damaged by environmental exposures.

PROCEDURES/METHODS: HANDLING OF UNEXPECTED OR ADVERSE EVENTS

Response to new or unexpected findings and to changes in the study environment:
Medically significant exposure to chemicals, radioactive elements, or infectious agents, or vital genetic information detected as a result of urine, blood, or buccal cell sample analysis, would constitute unexpected findings in this study. In the rare event that such unexpected findings are found, CDC will report these findings immediately to the NHSD. NSHD and CDC will then immediately notify the affected study participant and, if appropriate, recommend that his or her family see their physician. State environmental and public health officials will be contacted if any potential public health threat is identified by intermediate review of environmental sample results. Collaborative review of any such findings would allow the state to assess the need for, and urgency of, remedial actions.

Emergency care:
In the highly unlikely event any subjects require emergency care in relation to the biological measurements indicative of chemical or radioactive exposure in this study, a designated official from NHSD will advise the family to obtain emergency medical care immediately.

PROCEDURES/METHODS: DISSEMINATING, NOTIFICATION, AND REPORTING OF RESULTS

Notifying participants of their individual results/study findings:

CDC will work with NSHD to inform study participants about their biological and environmental test results. Only the results of tests conducted on samples collected from study participants' current homes will be reported to the study subjects. Results of tests on past residences will be given to the current homeowners. At the same time, educational materials will be provided to help the study participants understand what the findings mean. CDC and ATSDR will develop the educational materials and conduct public meetings in conjunction with the NSHD, as necessary. Genetic research results will be provided to study participants if they are individually relevant. CDC will confidentially contact individuals, provide pre-disclosure counseling, and disclosure, if the parent and child wish to receive this information.

Anticipated products or interventions resulting from the study and their use:

The State of Nevada is already aware of the significant arsenic contamination of groundwater used for human consumption in Churchill County. We anticipate that the State of Nevada will proceed with their phased plans to reduce arsenic in Churchill County's drinking water supplies below the maximum contaminant level (MCL) mandated by EPA.

USGS will use drinking water data collected in this study, along with groundwater data obtained from a separate USGS study to characterize the aquifers in Churchill County. USGS will prepare a report of their groundwater characterization according to agency standards at USGS.

Disseminating results to the public:

We intend to publish the information we learn from analyzing these data in a report to parents of participating children and in a peer-reviewed journal to make it easily accessible to all parties interested in possible linkages between environmental or infectious exposures and childhood cancer. The information will also be presented at professional conferences.

PROTECTION OF HUMAN RESEARCH PARTICIPANTS

Risks:
This is a minimal risk study. The collection of blood, buccal cells, and urine specimens pose no significant risk to the study participants. Any future genetic research will be conducted to look for common variants of genes that code for enzymes involved in detoxification or DNA repair from damage by environmental exposure. Genetic research results will be provided to study participants if they are individually relevant.

Anticipated benefits:
All study participants will benefit from learning the results of their urine, blood, and household testing. The scientific community and the general public also benefit from a further understanding of the role of environmental exposure and genetics on the likelihood of developing ALL/AML.

Vulnerable populations:
Children aged 2 -18 years old will comprise a third of the study population for this investigation.

Implementation/documentation of informed consent and parental permission:
The appropriate informed consent document in Appendix A will be mailed to the recruited study participants. Families of case or control children under the age of 18 will receive the consent form for families (Appendices A4 and A5). Recruited children 18 years of age or older will read and sign their own informed consent document (Appendices A1, A2) as well as the consent form for families so that their parents and siblings may participate. At the time of the interview and specimen collection, recruited case and control children aged 7-17 will be asked to assent to participation in the study (Appendices A3, A1, A2). The Adolescent Assent forms are essentially the same as the Adult Case/Reference forms. On each consent form, study participants and their families will be invited to call the on-site project coordinator at the study center in Fallon if they have any questions at all about the study or the consent process.

Protection of privacy and confidentiality:
Confidentiality of participating children, adults, and families will be maintained to the full extent allowable under the law. Unique identifiers (i.e., study id numbers) will be used to link questionnaires, consent forms, and laboratory data. We will generate this unique code number on the forms before they are given out - the same id number will be on the consent form, mailed and interview questionnaires, the biological specimen containers, and the environmental samples from their current home. The participant's study id number will also be linked to, but not posted on, environmental samples from historic residences. An additional code will also be assigned to environmental samples from homes not owned by the participant or his/her parent.

The consent form and the first page of the mailed and interview questionnaire will have the participant's name, other personal identifiers, and the participant's unique study id number. These forms and pages will be stored in locked files at CDC, separate from the completed data collection forms. Participant addresses will be collected in the recruitment process to allow for environmental sampling of current residence and reporting of results. Residential information will be included in the research database, identified using a unique code number when entering the questionnaire data. CDC, as the principal investigator, will maintain the master list that matches the code number to the participant. CDC and NSHD will protect the confidentiality of the participants to the full extent allowable by law. Study databases will not include personal identifiers; data will be entered under study id number only. CDC will also keep a master file of the global positioning system (GPS) reading for each water sample. The GPS reading will be used to construct geographical maps of any contaminants identified. CDC will share the

research database containing the environmental and biological laboratory results and the GPS readings with ATSDR for spatial analysis. Once the final maps are constructed, the GPS reading will be stripped from the database. Specific procedures will be taken to protect the confidentiality of the study data including password protection of electronic files at CDC and unique identifiers that will not include any information that could potentially be used to identify study participants. We are asking participants to donate their DNA to CDC for leukemia research. The DNA specimen will be linked to pertinent questionnaire data and the findings from the exposure assessment. The genetic studies would not be useful medically and will only be reported back to the study donor if individually relevant (see "Risks", above; see Appendix A for informed consent documents – 'What will happen' and 'Confidentiality' sections).
USGS will have a database of water testing results for Churchill County that includes the GPS readings for homes participating in this study. Even though USGS will be kept blind as to which homes housed cases or controls, USGS will prevent external release of the GPS codes that could identify homes participating in this study.

Compensation/incentives:
No one will be paid to be in this study (see "Anticipated benefits", above).

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Table 1. Year of Birth and Sex Categories

Year of birth Category and Sex	Cases	Controls
2000-2001 Girls	0	0
2000-2001 Boys	0	0
1998-1999 Girls	2	8
1998-1999 Boys (as of Dec 2001)	1	4
1996-1997 Girls	2	8
1996-1997 Boys	0	0
1994-1995 Girls	1	4
1994-1995 Boys	3	12
1992-1993 Girls	0	0
1992-1993 Boys	0	0
1990-1991 Girls	0	0
1990-1991 Boys	1	4
1988-1989 Girls	0	0
1988-1989 Boys	1	4
1986-1987 Girls	0	0
1986-1987 Boys	0	0
1984-1985 Girls	0	0
1984-1985 Boys	0	0
1982-1983 Girls	2	8
1982-1983 Boys	0	0
1980-1981 Girls	1	4
1980-1981 Boys	1	4
Total	**14**	**56**
Modified Total Dec, 2001	**15**	**60**

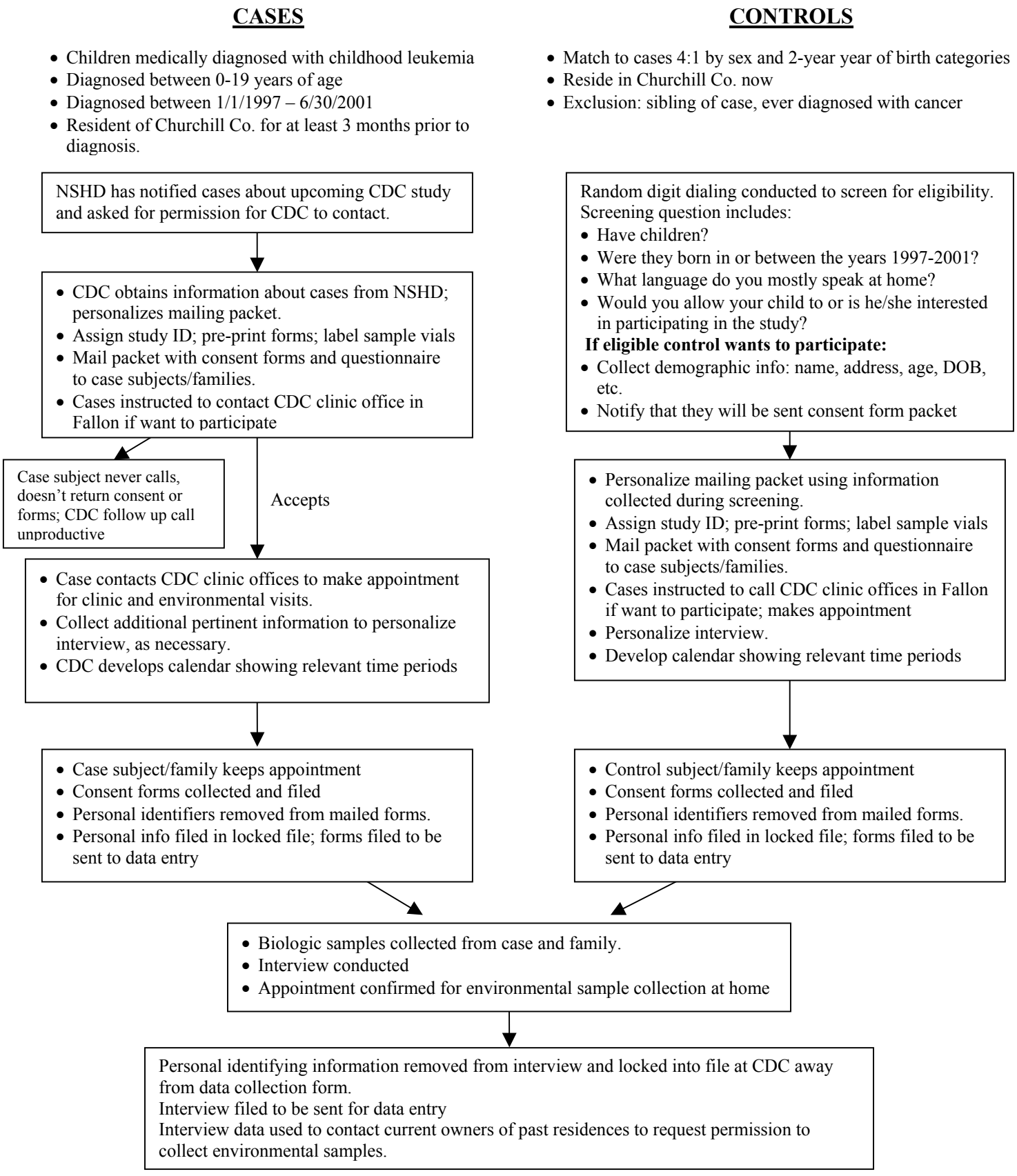
Table 2: Candidate list of substances to be analyzed for in blood and urine samples from study participants. Additional substances to be measured will depend upon the agents ATSDR identifies in their exposure pathway assessment.

Tube	Analyte(s)	Matrix	Required Volume	Storage Temp	Comments	Contact
7mL EDTA	Pb / Cd	Whole Blood	250 uL	≤ -70°C	***This tube MUST be collected FIRST***	Robert Jones
This blood fraction must be aliquoted before spinning down.	Mercury (Total and Inorganic)	Whole Blood	650 uL	≤ -70°C	**Whole blood will be aliquoted into a 2 mL cryovial before processing to obtain the plasma and the Buffy coat components**	Robert Jones
	Selenium	Plasma	250 uL	≤ -70°C		Robert Jones
This blood must be spun down and aliquoted in the field	Organochlorine Pesticides	Plasma	1.0 mL	≤ -70°C	*PCBs could also be analyzed from this aliquot*	Wayman Turner 770-488-7974 Wturner@cdc.gov
	Lipids	Plasma	0.5 mL	≤ -70°C		Wayman Turner
	DNA	***Buffy coat***		≤ -70°C	MUST be frozen –70 C or colder. Buffy coat will be separated from plasma and stored frozen for future genetic studies	Peg Gallagher 770-488-3612 mgallaher1@cdc.gov
	Amp RT DNA – PCR on oncoviruses Serology – Leukemia viruses MOP (primers on cellular RNA) HTLV serology – Bharat FeLV serology	Plasma		≤ -70°C		NCID
	Long Term Storage	Plasma		≤ -70°C		NCEH

Tube	Analyte(s)	Matrix	Required Volume	Storage Temp	Comments	Contact
7mL Gray Top	Blood VOC: 1,1,1-trichloroethane 1,4-dichlorobenzene benzene carbon tetrachloride chloroform dimethylfuran ethylbenzene m-/p-xylene methylene chloride tert-butylmethylether o-xylene styrene tetrachloroethylene toluene trichloroethylene	Whole Blood	7 mL	4°C Do NOT Freeze	***Blood must be collected into a specially treated and screened gray-top vacutainer. Blood sample collection must closely follow the VOC blood collection protocol. Sample can not be opened prior to VOC analysis.***	Ben Blount 770-488-7894 Bblount@cdc.gov
7 mL EDTA	Long Term storage	Plasma		≤ -70°C	MUST be frozen -70°C or colder.	NCEH
This blood must be spun down and aliquoted in the field	DNA	Buffy coat	***Sample aliquoted to 3 separate vials in the field***	≤ -70°C	MUST be frozen -70°C or colder.	NCID
Full Void Urine	Mercury	Urine	1.25 mL	≤ -70°C	***Must be preserved separately in the field***	Robert Jones
	Creatinine	***Urine***	0.25 mL	≤ -70°C		Robert Jones
	Pesticides: Organophosphates Pyrethroids Chlorphenoxy herbicides Carbamates Atrazine	***Urine***	25 mL minimum for 5 tests	≤ -70°C	Amount will vary depending upon pesticides requested. More volume is needed to allow for reanalysis.	Dana Barr 770-488-7886 dbarr@cdc.gov

Tube	Analyte(s)	Matrix	Required Volume	Storage Temp	Comments	Contact
	As	***Urine***	0.5 mL	≤ -70°C		Robert Jones
	Uranium^{235}	Urine	0.5 mL	≤ -70°C		Dan Paschal 770-488-7985 DPaschal@cdc.gov
The urine will be a full void that is collected in a pre-screened collection cup. A 1.2 mL sample will then be aliquoted into the Hg tube.	Antimony Barium Beryllium Cadmium Cesium Cobalt Lead Molybdenum Platinum Thallium Tungsten Uranium^{238}	Urine	2 mL	≤ -70°C		Robert Jones 770-488-7991 770-488-4097(FAX) rljones@cdc.gov
	Chromium (Total)	Urine	0.5 mL	≤ -70°C		Robert Jones
	Nickel	Urine	0.5 mL	≤ -70°C		Robert Jones
	Manganese	Urine	0.5 mL	≤ -70°C	***Requires method development***	Robert Jones
	As (Speciated)	***Urine***	0.5 mL	≤ -70°C	***Requires method development***	Robert Jones
Buccal smear	DNA	***Buccal smear***	2 cytobrushes	Room Temp	Can be shipped on Dry Ice	Peg Gallagher

Figure 1. Study Flow



Appendix A: Consent and Assent Forms

Appendix A1: Adult Case Consent

Do not write in this space

(Adult Case)

CONSENT TO PARTICIPATE

Exposure Assessment of Case-Children with Acute Lymphocytic or Myelocytic Leukemia and a Reference Population in Churchill County, Nevada

Thank you for agreeing to receive this packet of information about the study of childhood leukemia in Churchill County being conducted by the Centers for Disease Control and Prevention (CDC). You have been sent this consent form because we would like to invite you to join our study of leukemia. We are working with the Nevada State Health Division to further understand this illness. We hope you will take the time to review this form and consent to be a part of this study. If you have any questions about this form at any time while filling it out, please call 775/423-0617 and we will be happy to help you in any way we can.

Instructions

You have received this packet because you indicated on a recent phone call that you were willing to receive information about a study about childhood leukemia in Churchill County, Nevada. Please read this consent form. If you decide that you would like to be a part of the study, please sign the consent form where indicated at the end of this form. It is important that you and your immediate family members also take part in this study. Immediate family members include your mother, father, and any full, half, or step-siblings who live with you. A separate consent form for them to review and sign is included with this packet. An appointment will be scheduled for you and your family to visit the CDC offices in Fallon, Nevada.

Please bring the signed consent form and the completed questionnaire with you to your appointment at the CDC clinic offices in Fallon, Nevada. When you come to the CDC clinic offices for your visit, we will collect samples of blood, urine and cheek cells from you, and will interview your parent(s)/guardian(s) about your mother's pregnancy with you, your family's medical history, and your current and past residences in Churchill County. During your visit, we will schedule a time for the members of our environmental team to collect environmental samples from your current home. These samples may include drinking water, household dust, play yard soil, and indoor air.

Your visit to the CDC clinic offices may last as long as two hours.

Purpose

Recently, the Nevada State Health Division (NSHD) identified a greater number of cases of Acute Lymphocytic Leukemia (ALL) and Acute Myelocytic Leukemia (AML) in Churchill County than would be expected by chance alone. The NSHD has asked the CDC to conduct a research study to look into the increase of this illness.

According to the Nevada State Health Division, you were diagnosed with ALL/AML between 1997 and 2001. We want to see if contact with certain chemicals, radioactive elements, or infectious agents are related to your illness.

This study has two main components, a biological assessment and an environmental assessment. During the biological assessment, we will to take samples of your blood, urine, and cells from inside your cheeks. We may also do genetic studies for leukemia research using DNA collected from you. The DNA samples

will only be used for research about leukemia and for no other purpose. Two questionnaires are also included in the biological assessment, one in this mailing packet, and an interview questionnaire that will be administered to your parent(s)/guardian(s) in person during your clinic visit.

During the environmental assessment component, we will take samples from your current home and from past homes you have lived in within Churchill County.

We are asking you to volunteer to be in this study. You have the right to refuse. There is no penalty for doing so. Before you decide, you should know what is involved and have all your questions answered. If you have any questions about the study or about these consent forms, please call us at 775/423-0617 or toll-free at 888/608-4623. We'll be happy to answer any questions you may have.

Cost/Compensation
There is no cost for you to be in this study. You will receive no payment for being in this study.

What will happen?
If you choose to be in this study, we will draw about 21 ml (about 1 to 1 1/2 tablespoons) of blood from a vein in your arm. First we will clean the skin by gently rubbing it with alcohol. The needle stick may hurt a little for a few seconds. The person taking the blood will be very careful. It will not hurt to give a sample of cheek cells. We will collect cheek cells by brushing the inside of each cheek with a soft brush for 30 seconds. You will provide 32.5ml (approximately 1 ounce) of urine. It will not hurt to give a urine sample.

DNA will come from a portion of your blood sample and from your cheek cell sample. These specimens will be stored at CDC using a research code number. Any genetic studies performed with your DNA are for leukemia research only. Experts will advise CDC about which genetic research studies to perform. Genetic research may include identifying variations in genes that direct how the body handles toxic substances or fixes damaged DNA. Genetic research may also include testing for certain viruses thought to be associated with cancer, such as Epstein-Barr virus. The genetic research will not provide information specifically useful for your medical treatment. However, this genetic research may advance our understanding of leukemia.

CDC will also store some of the blood and urine collected in this study by a code number, in case we need to do more tests in the future. Your blood and urine will not be tested for HIV, or the presence of alcohol or drugs.

During the study, we will interview your parent(s)/guardian(s) about your medical and pre-natal history to build upon the recent survey conducted by NSHD. We will ask about your daily activities and water use. The interview will be assigned a research code number; all personal identification information will be removed. Answers to the interview questions will be kept confidential.

We will attempt to collect environmental samples (soil, dust, water, and air) from all of the homes you lived in within Churchill County, Nevada, between 1 year prior to your birth until present. This includes any home within Churchill County that your mother lived in while she was pregnant with you. This will not include any home outside of Churchill County, Nevada. Sample collection at your home may take more than 1 hour. The current owner/occupant of homes you have lived in must give us permission to collect environmental samples from their homes.

Benefits
You will be notified of the results of the tests done on your blood and urine to see if you had contact with certain chemicals, radioactive elements, or infectious agents. You will be given the test results for samples taken from the home(s) you currently own. Results from other homes will be given to the current property owner/occupant. A report summarizing our findings will be given to all participants of

this study. This report will not have any information that would identify you.
By providing DNA for genetic testing, you will be helping us and other medical professionals to understand why some people get ALL/AML and others do not. You will receive a general report of the research findings that will not include any personal identifying information. However, should the genetic research done on your DNA identify something that could significantly affect your health or reproductive choices, we will notify you personally. If this were to happen, we would advise you to share this information with your healthcare provider, using your own resources.

Confidentiality
We will protect your privacy to the extent allowable by law. We will not put your name on the blood, urine, or cheek cell samples. Instead, these samples will be identified using a research code number. We will keep all the research records and test results in locked files and only research staff will be allowed to look at them.

CDC will store a part of your blood and urine samples in the event that further laboratory tests are needed. CDC will give the laboratory test results to the NSHD only by code number.

Questionnaires and consent forms that contain personal identification information will be stored in a locked file, separate from the questionnaire data. Data entry personnel will not be given nor have access to your personal identification information.

CDC will store your DNA for future genetic research using only a research code number. The code number will allow CDC to link the laboratory tests and questionnaire data to the genetic studies. CDC will report the findings of genetic research as a summary of the results all DNA studies. Despite all these safeguards, it may be possible to determine your identity due to the small number of children developing leukemia in Churchill County, Nevada.

The U.S. Geological Survey (USGS) will collect drinking water from each home and attach a research code number to the sample. USGS will locate each home they test by using satellites, known as a global positioning system (GPS) reading. The GPS readings will be used to map the study findings and will not be available as public information. USGS will not keep your name, phone number, or street address. USGS will provide the water testing results to NSHD and CDC by code number.

The environmental team, which may be made up of representatives from state, local, and federal agencies collaborating on the study, will take the indoor air, household dust, and play yard soil samples from your home(s). Each home setting will be labeled with a research code number. A contracted laboratory will test these samples and provide the results to CDC and NSHD by code number.

You will be provided with the results of the tests done on your blood, urine, and the results of the tests of your current home. In order to tell you these results, NSHD and CDC will keep a master list that matches your research code numbers with you. This master list will be kept in a locked file separate from the collected samples and completed questionnaire. NSHD will protect your confidentiality to the extent allowable by law. When we talk or write about this study, we will not include your name or any facts that might identify you.

Your name, telephone number, and address are on this consent form to allow us to contact you while we are conducting this research study. We will keep this consent form in a locked file separate from the rest of the study data.

Right to Refuse/Withdraw
It is your choice whether to be in this study. You may skip any question you don't want to answer. You may stop answering questions any time you want. You can expect the same medical care from your doctor whether you are in the study or not in the study. There is no penalty or loss of entitled benefits if you choose not to be in this study. You may stop being in this study at any time without losing any entitled benefits. If at any time in the future, you would like to have your interview information, or the samples from your home, or your blood, urine, or cheek cell samples destroyed or removed from the study, please call Dr. Carol Rubin (phone number below).

For more information
We will give you a copy of this form to keep. If you have any questions, concerns, or complaints about this study, please contact:

For questions related to this research study or questions related to injury from the study
Dr. Randall Todd, Nevada State Health Division (775-684-5946)
Dr. Carol Rubin, Centers for Disease Control and Prevention, (1-404-498-1340 and leave a message).

For questions related to your research rights
Dr. John Livengood, Centers for Disease Control and Prevention, Deputy Associate Director for Science (1-404-639-7260)

Thank you for considering being in this study.

Carol Rubin, D.V.M., M.P.H.
Centers for Disease Control and Prevention

Randall Todd, Dr.P.H.
Nevada State Health Division

Case Adult:
As described above, we are inviting you to be part of this research study. You may be in the study by indicating your consent to the items below. You may consent to all, some, or none of the items.

To be in this study, please sign your initials in the box next to each item you agree to.

	The removal from you of up to 21 ml (1 to 1 ½ tablespoons) of blood by vein puncture.
	The collection from you of 32.5ml (approximately 1 ounce) of urine in a cup.
	The removal of cells from the inside of your mouth with a cheek brush (soft bristle swab) to provide DNA to study genes that may play a role in ALL/AML.
	The storage of a portion of your blood, urine, and cheek cell samples at CDC to be used for future studies about the causes of ALL/AML.

I have read the consent form (or someone has read it to me). I agree to be in this study, with my initials above indicating which parts of the study I agree to participate in.

Signature of Case Adult: _____ Today's Date:___/___/___

Name of Case Adult (print): _____

Street Address: _____

_____

City: _____

State: ____ Zip: _____

Phone number: _____

Appendix A1 (cont'd): Adolescent (age 12-17) Case Assent

Do not write in this space

(Adolescent Case Assent:
12-17 years old)

CONSENT TO PARTICIPATE

Exposure Assessment for Case-Children with Acute Lymphocytic or Myelocytic Leukemia and a Reference Population in Churchill County, Nevada

Your parents have said that you could take part in a study of childhood leukemia in Churchill County. We would like to invite you to join our study. We hope you will agree to be a part of this study. If you have any questions about this form at any time while filling it out, please don't hesitate to ask.

Instructions
Please read this assent form. It contains information about the study and what will happen if you decide to participate. If you agree to take part in this study, please sign at the end of the form.

If you decide to take part in this study, we will collect samples of your blood, urine and cells from the inside of your cheek.

Purpose
Recently, the Nevada State Health Division (NSHD) identified a greater number of cases of childhood leukemia (ALL/AML) in Churchill County than expected by chance alone. NSHD has asked the Centers for Disease Control and Prevention (CDC) to conduct a research study. We want to see if contact with certain chemicals, radioactive elements, or infectious agents are related to you getting sick with leukemia.

To do this, we will take samples of your blood and urine and will take samples from the homes where you are currently living and where you have lived in the past within Churchill County. In the future, we may also do genetic studies with your DNA for leukemia research. Your DNA will be used only to help us understand genetic factors related to ALL/AML and for no other purpose.

We would like to include you in this research study. We are asking for you to volunteer to be in this study. You have the right to refuse and there is no penalty for doing so. Before you decide, you should know what is involved and have all your questions answered. If you have any questions as you read through this form, please ask.

What will happen?
If you choose to be in this study, we will draw about 21 ml (about 1 to 1 1/2 tablespoons) of blood from a vein in your arm. First we will clean the skin by gently rubbing it with alcohol. The needle stick may hurt a little for a few seconds. The person taking the blood will be very careful. It will not hurt to give a sample of cheek cells. We will collect cheek cells by brushing the inside of each cheek with a soft brush for 30 seconds. You will provide 32.5ml (approximately 1 ounce) of urine. It will not hurt to give a urine sample.

Your specimens will not have your name or other personal identifying information on them. Your blood and urine will not be tested for HIV, or the presence of alcohol or drugs.

Right to Refuse/Withdraw
It is your choice whether to be in this study. You can expect the same medical care from your doctor whether you are in the study or not in the study. There is no penalty or loss of entitled benefits if you choose not to be in this study. You may stop being in this study at any time without losing any entitled benefits. If at any time in the future, you would like to have your blood, urine, or cheek cell samples destroyed or removed from the study, please call Dr. Carol Rubin (phone number below).

For more information
We will give you a copy of this form to keep. If you have any questions, concerns, or complaints about this study, please contact:

For questions related to this research study or questions related to injury from the study
Dr. Randall Todd, Nevada State Health Division (775-684-5946)
Dr. Carol Rubin, Centers for Disease Control and Prevention, (1-404-498-1340 and leave a message).

For questions related to your research rights
Dr. John Livengood, Centers for Disease Control and Prevention, Deputy Associate Director for Science (1-404-639-7260)

Thank you for considering being in this study.

Carol Rubin, D.V.M., M.P.H.
Centers for Disease Control and Prevention

Randall Todd, Dr.P.H.
Nevada State Health Division

As described above, you are being asked to participate in a research study. You may participate by indicating your consent to the items below. You may consent to all, some, or none of the items.

To be in this study, please sign your initials in the box next to each item you agree to.

	The removal of up to 21 ml (1 to 1 ½ tablespoons) of blood by vein puncture.
	The collection of 32.5ml (approximately 1 ounce) of urine in a cup.
	The removal of cells from the inside of your mouth with a cheek brush (soft bristle swab) to provide DNA to study genes that may play a role in ALL/AML.
	The storage of a portion of your blood, urine, and cheek cell samples at CDC to be used for future studies about the causes of ALL/AML.

I have read the consent form (or someone has read it to me) and I agree to be in this study, with my initials above indicating which parts of the study I agree to participate in.

_____ _____

(Signature) (Date)

_____

(Printed name)

Street Address: _____

City: _____ State: ____ Zip: _____

Phone number (area code): _____

Appendix A2: Adult Reference Consent

(Adult Control)

Do not write in this space

CONSENT TO PARTICIPATE

Exposure Assessment of Case-Children with Acute Lymphocytic or Myelocytic Leukemia and a Reference Population in Churchill County, Nevada

Thank you for agreeing to receive this packet of information about the Centers for Disease Control and Prevention (CDC) study of childhood leukemia in Churchill County. You have been sent this consent form because we would like to invite your family to join our study of leukemia. We are working with the Nevada State Health Division to further understand this illness. We hope you will take the time to review this form and consent to be a part of this study. If you have any questions about this form at any time while filling it out, please call 775/423-0617 or toll-free at 888/608-4623 and we will be happy to help you in any way we can.

Instructions

You have received this packet because you indicated on a recent phone call that you were willing to receive information about a study about childhood leukemia in Churchill County, Nevada. Please read this consent form. If you decide that you would like to be a part of the study, please sign the consent form where indicated at the end of this form. It is important that both you and your parent(s)/guardian(s) participate. A separate consent form for them to review and sign is included with this packet. An appointment will be scheduled for you and your parent(s)/guardian(s) at the CDC offices in Fallon, Nevada.

Please bring the signed consent form and the completed questionnaire with you to your appointment at the CDC clinic offices in Fallon, Nevada. When you come to the CDC clinic offices for your visit, we will collect samples of blood, urine and cheek cells from you, and will interview your parent(s)/guardian(s) about your mother's pregnancy with you, your family's medical history, and your current and past residences in Churchill County. During your visit, we will schedule a time for the members of our environmental team to collect environmental samples from your current home. These samples may include drinking water, household dust, play yard soil, and indoor air.

Your visit to the CDC clinic offices may last as long as two hours.

Purpose

Recently, the Nevada State Health Division (NSHD) identified a greater number of cases of Acute Lymphocytic Leukemia (ALL) and Acute Myelocytic Leukemia (AML) in Churchill County than would be expected by chance alone. The NSHD has asked the CDC to conduct a research study to look into the increase of this illness.

We want to see if contact with certain chemicals, radioactive elements, or infectious agents are related to getting sick with ALL/AML. We are looking for healthy young people to serve as a comparison group for those who got sick with ALL/AML. We would like to include you in this research study. We selected you by chance to match the age and sex of one of the people who got sick with ALL/AML.

As part of this study, we want to take samples from you (blood, urine, and cells from the inside of your cheek), and your home (soil, dust, water, and air). We will

test your blood and urine for contact with certain chemicals, radioactive elements, and infectious agents. We may also want to do genetic studies with your DNA for leukemia research. Your DNA will be used only to help us understand genetic factors related to ALL/AML and for no other purpose. You will only be informed of the results of your genetic tests if they are relevant to you as an individual.

We would like to include you in this research study. We are asking for you to volunteer to be in this study. You have the right to refuse and there is no penalty for doing so. Before you decide, you should know what is involved and have all your questions answered. Please call us at 775/423-0617 or toll-free at 888/608-4623. We'll be happy to answer any questions you may have.

What will happen?

If you choose to be in this study, we will draw about 21 ml (about 1 to 1 1/2 tablespoons) of blood from a vein in your arm. First we will gently rub your skin with alcohol to clean it. The needle stick in your skin may hurt a little for a few seconds. The person taking the blood will be very careful. You will provide 32.5ml (approximately 1 ounce) of urine. It will not hurt to give a sample of urine. In addition, we will collect a sample of the cells from the inside of your mouth (cheek cells). We will collect cheek cells by brushing the inside of each cheek with a soft brush for 30 seconds.

We will obtain your DNA from a portion of your blood sample and from your cheek cell samples. These specimens will be stored at CDC using a research code number. CDC will keep your personal identification information in a locked file separate from the samples. The genetic studies performed on your DNA are for leukemia research purposes only. Experts will advise CDC about which genetic research studies to perform. Genetic research may include identifying variations in genes that direct how the body handles toxic substances or fixes damaged DNA. Genetic research may also include testing for certain viruses thought to be associated with cancer, such as Epstein-Barr virus. This research will not provide information useful for your medical treatment, though you will be informed of your results if they are relevant to you as an individual. However, the genetic research may yield important findings for larger groups.

CDC will also store some of the blood and urine collected in this study by a code number, in case we need to do more tests. We would only do further testing if we identified a specific environmental contaminant in this study. Your blood and urine will not be tested for HIV, or the presence of alcohol or drugs.

We will also ask your parent(s)/guardian(s) some questions during an interview. Their answers will be kept private. Your visit to the CDC's clinic offices in Fallon, Nevada may take as long as two hours.

We will attempt to collect environmental samples (soil, dust, water, and air) from the home(s) where you and/or your parent(s)/ guardian(s) have lived in Churchill County. Sample collection at your home may take more than 1 hour. To collect environmental samples from your previous home(s), we will need permission from the current owner(s)/occupant(s).

Benefits

You will be notified of the results of the blood and urine tests that were done to see if you had contact with certain chemicals, radioactive elements, or infectious agents. You will also be given the test results for samples taken from your current home. A report summarizing our findings will be given to the participants of this study. This report will not have any information that would identify you, your family, or your home.

By providing DNA for genetic testing, you will be helping us and other medical professionals to understand why some people get ALL/AML and others do not. We will notify you if our genetic studies identify something that could significantly affect your

health or reproductive choices. If this were to happen, we would advise you to share this information with your healthcare provider.

Confidentiality

We will protect your privacy to the extent allowable by law. We will not put your name on the survey or on the blood, urine, or cheek cell samples. Instead, we will use a code number. We will keep all the research records and test results in locked files and only research staff will be allowed to look at them. CDC will store a part of your blood and urine samples in the event that further laboratory tests are needed. CDC will give the laboratory test results to the NSHD only by code number.

CDC will store your DNA for future genetic research using only a research code number. The code number will allow CDC to link the laboratory tests and questionnaire data to the genetic studies. CDC will only release genetic research results if they are individually relevant. CDC will report the findings of any genetic research as a summary of all DNA included in those studies.

The U.S. Geological Survey (USGS) will collect drinking water from each home and attach a research code number to the sample. USGS will locate each home they test by using satellites, known as a global positioning system (GPS) reading. The GPS readings will be used to map the study findings and will not be available as public information. USGS will not keep your name, phone number, or street address. USGS will provide the water testing results to NSHD and CDC by code number.

The environmental team, which may be made up of representatives from state, local, and federal agencies collaborating on the study, will take the indoor air, household dust, and play yard soil samples from your home(s). Each home setting will be labeled with a research code number. A contracted laboratory will test these samples and provide the results to CDC and NSHD by code number.

You will be provided with the results of the tests done on your blood, urine, and the results of the tests of your current home. In order to tell you these results, NSHD and CDC will keep a master list that matches your research code numbers with you. NSHD will then notify you of these results. Because the genetic studies are for research purposes only, you will only receive results from the genetic studies if they are individually relevant. CDC and NSHD will protect your confidentiality to the extent allowable by law. When we talk or write about this study, we will not include your name or any facts that might identify anyone in your family.

Your name, telephone number, and address are on this consent form to allow us to contact you while we are conducting this research study. We will keep this consent form in a locked file separate from the rest of the study data.

Right to Refuse/Withdraw

It is your choice whether to be in this study. You may skip any question you don't want to answer. You may stop answering questions any time you want. You can expect the same medical care from your doctor whether you are in the study or not in the study. There is no penalty or loss of entitled benefits if you choose not to be in this study. You may stop being in this study at any time without losing any entitled benefits. If at any time in the future, you would like to have your interview information, or the samples from your home, or your blood, urine, or cheek cell samples destroyed or removed from the study, please call Dr. Carol Rubin (phone number below).

For more information

We will give you a copy of this form to keep. If you have any questions, concerns, or complaints about this study, please contact:

For questions related to this research study or questions related to injury from the study

Dr. Randall Todd, Nevada State Health Division (775-684-5946)
Dr. Carol Rubin, Centers for Disease Control and Prevention, (1-404-498-1340 and leave a message).

For questions related to your research rights

Dr. John Livengood, Centers for Disease Control and Prevention, Deputy Associate Director for Science (1-404-639-7260)

Thank you for considering being in this study.

Carol Rubin, D.V.M., M.P.H.
Centers for Disease Control and Prevention

Randall Todd, Dr.P.H.
Nevada State Health Division

As described above, you are being asked to participate in a research study. You may participate by indicating your consent to the items below. You may consent to all, some, or none of the items.

To be in this study, please sign your initials in the box next to each item you agree to.

	The removal of up to 21 ml (1 to 1 ½ tablespoons) of blood by vein puncture.
	The collection of 32.5ml (approximately 1 ounce) of urine in a cup.
	The removal of cells from the inside of your mouth with a cheek brush (soft bristle swab) to provide DNA to study genes that may play a role in ALL/AML.
	The storage of a portion of your blood, urine, and cheek cell samples at CDC to be used for future studies about the causes of ALL/AML.
	The collection of samples of drinking water, household dust, play yard soil, and indoor air from the home(s) you and/or your parent(s)/guardian(s) currently live in within Churchill County.

I have read the consent form (or someone has read it to me) and I agree to be in this study, with my initials above indicating which parts of the study I agree to participate in.

_____ _____

(Signature) (Date)

_____

(Printed name)

Street Address: _____

City: _____ State: ____ Zip: _____

Phone number (area code): _____

Appendix A2 (cont'd): Adolescent (age 12-17) Reference Assent

Do not write in this space

(Adolescent Control Assent: Age12-17 years)

CONSENT TO PARTICIPATE

Exposure Assessment for Case-Children with Acute Lymphocytic or Myelocytic Leukemia and a Reference Population in Churchill County, Nevada

Your parents have said that you could take part in a study of childhood leukemia in Churchill County. We would like to invite you to join our study. We hope you will agree to be a part of this study. If you have any questions about this form at any time while filling it out, please don't hesitate to ask.

Instructions
Please read this assent form. It contains information about the study and what will happen if you decide to participate. If you agree to take part in this study, please sign at the end of the form.

If you decide to take part in this study, we will collect samples of your blood, urine and cells from the inside of your cheek.

Purpose
Recently, the Nevada State Health Division (NSHD) identified a greater number of cases of childhood leukemia (ALL/AML) in Churchill County than would be expected by chance alone. NSHD has asked the Centers for Disease Control and Prevention (CDC) to conduct a research study. We want to see if contact with certain chemicals, radioactive elements, or infectious agents are related to people getting sick with leukemia.

To do this, we will take samples of your blood and urine and samples from the home where you currently live and where you have lived in the past within Churchill County. In the future, we may also do genetic studies with your DNA for leukemia research. Your DNA will be used only to help us understand genetic factors related to ALL/AML and for no other purpose.

We would like to include you in this research study. We are asking for you to volunteer to be in this study. You have the right to refuse and there is no penalty for doing so. Before you decide, you should know what is involved and have all your questions answered. If you have any questions as you read through this form, please ask.

What will happen?
If you choose to be in this study, we will draw about 21 ml (about 1 to 1 1/2 tablespoons) of blood from a vein in your arm. First we will gently rub your skin with alcohol to clean it. The needle stick in your skin may hurt a little for a few seconds. The person taking the blood will be very careful. It will not hurt to give a sample of your cheek cells. We will collect cheek cells by brushing the inside of each cheek with a soft brush for 30 seconds. You will provide 32.5ml (approximately 1 ounce) of urine. It will not hurt to give a urine sample.

Your specimens will not have your name or other personal identifying information on them. Your blood and urine will not be tested for HIV, or the presence of alcohol or drugs.

Right to Refuse/Withdraw
It is your choice whether to be in this study. You can expect the same medical care from your doctor whether you are in the study or not in the study. There is no penalty or loss of entitled benefits if you choose not to be in this study. You may stop being in this study at any time without losing any entitled benefits. If at any time in the future, you would like to have your blood, urine, or cheek cell samples destroyed or removed from the study, please call Dr. Carol Rubin (phone number below).

For more information

We will give you a copy of this form to keep. If you have any questions, concerns, or complaints about this study, please contact:

For questions related to this research study or questions related to injury from the study

Dr. Randall Todd, Nevada State Health Division (775-684-5946)

Dr. Carol Rubin, Centers for Disease Control and Prevention, (1-404-498-1340 and leave a message).

For questions related to your research rights

Dr. John Livengood, Centers for Disease Control and Prevention, Deputy Associate Director for Science (1-404-639-7260)

Thank you for considering being in this study.

Carol Rubin, D.V.M., M.P.H.
Centers for Disease Control and Prevention

Randall Todd, Dr.P.H.
Nevada State Health Division

As described above, you are being asked to participate in a research study. You may participate by indicating your consent to the items below. You may consent to all, some, or none of the items.

To be in this study, please sign your initials in the box next to each item you agree to.

	The removal of up to 21 ml (1 to 1 ½ tablespoons) of blood by vein puncture.
	The collection of 32.5ml (approximately 1 ounce) of urine in a cup.
	The removal of cells from the inside of your mouth with a cheek brush (soft bristle swab) to provide DNA to study genes that may play a role in ALL/AML.
	The storage of a portion of your blood, urine, and cheek cell samples at CDC to be used for future studies about the causes of ALL/AML.

I have read the consent form (or someone has read it to me) and I agree to be in this study, with my initials above indicating which parts of the study I agree to participate in.

_____ _____

(Signature) (Date)

_____

(Printed name)

Street Address: _____

City: _____ State: ____ Zip: _____

Phone number (area code): _____

Appendix A3: Child Assent (age 7 to less than 12)

Please do not write in this space

(Child Assent: Age 7-11)

ASSENT TO PARTICIPATE

Exposure Assessment of Case-Children with Acute Lymphocytic or Myelocytic Leukemia and a Reference Population in Churchill County, Nevada

I am talking to you today because I want to invite you to join a study about leukemia, which is a type of cancer. This study is going to see if something that children eat, drink, breathe, or touch might make them very sick. It will only take a few minutes of your time and might help children who are sick. There is little risk to being in this study, which means that nothing bad is likely to happen to you for being in this study. We would like to get a sample of your blood and your urine and the cells inside your cheek. It may hurt a little bit to give the blood sample, but it won't hurt at all to give the urine or your cheek cells. Your cheek cells will be collected by brushing the inside of your cheek with a soft brush.

You should ask us any questions you have about being in this study and you can refuse to be in this study for any reason. If you agree to be in this study, you can stop being in this study at any time, if you wish. Your parents have said it is all right for you to be in the study.

What will happen?

If you let us, we will take a small amount of blood from a vein in your arm by putting a small needle in the vein for a few seconds. First we will gently rub your skin with alcohol to clean it.

We will also ask your parents some questions about your health and some things about them. All the answers they give us are private. We will not tell anyone who is not working on this study what they said.

Will it hurt?

The needle stick in your skin may hurt a little for a few seconds. The person taking the blood will be very careful. It will not hurt to give a sample of urine or cheek cells.

Benefits

We are doing this study to help answer questions about why some children get very sick.

Please check the items you agree to:

[ ] You agree to give a sample of your cheek cells, blood and urine for this study.

[ ] You agree to let CDC store some of your blood, urine, and cheek cells for future use for research.

_____ _____

(Child's signature) (Date)

_____

(Child's printed name)

Street Address: _____

City: _____ State: ____ Zip: _____

Phone number: _____

Appendix A4: Case Families Consent

Do not write in this space

(Case Family)

CONSENT TO PARTICIPATE

Exposure Assessment of Case-Children with Acute Lymphocytic or Myelocytic Leukemia and a Reference Population in Churchill County, Nevada

Thank you for agreeing to receive this packet of information about the Centers for Disease Control and Prevention (CDC) study of childhood leukemia in Churchill County. You have been sent this consent form because we would like to invite your family to join our study of leukemia. We are working with the Nevada State Health Division to further understand this illness. We hope you will take the time to review this form and consent to be a part of this study. If you have any questions about this form at any time while filling it out, please call 775/423-0617 or toll-free at 888/608-4623 and we will be happy to help you in any way we can.

Instructions

You have received this packet because you indicated on a recent phone call that you were willing to receive information about a study on childhood leukemia in Churchill County, Nevada. Please read this consent form. If you decide that you would like you and your family to be a part of the study, please sign the consent form where indicated at the end of this form. You will be consenting for yourself, the case child if he/she is under 18 years old, and the case child's siblings who are under 18 years old. If the case child has adult siblings 18 years old or over, that sibling should sign for him/herself where appropriate at the end of this form. If the case child is over 18 years old, a separate consent form for him/her is included in this packet. Please then complete the enclosed questionnaire and call the CDC clinic offices in Fallon at 775/423-0617 to make an appointment for you and your family to visit the CDC clinic offices.

Please bring the signed consent form and the completed questionnaire forms with you to your appointment at the CDC clinic offices in Fallon, Nevada. When you come to the CDC clinic offices for your visit, we will collect samples of blood, urine and cheek cells from you and your family, and will interview you about medical histories (including pregnancy with the case child), and current and past residences in Churchill County. During your visit, we will schedule a time for the members of our environmental team to collect environmental samples from your current home. These samples may include drinking water, household dust, play yard soil, and indoor air.

Your visit to the CDC clinic offices may last as long as two hours.

Purpose

Recently, the Nevada State Health Division (NSHD) identified a greater number of cases of Acute Lymphocytic Leukemia (ALL) and Acute Myelocytic Leukemia (AML) in Churchill County than would be expected by chance alone. The NSHD has asked the Centers for Disease Control and Prevention (CDC) to conduct a research study to look into the increase.

According to the Nevada State Health Division, your child was diagnosed with ALL/AML between 1997 and 2001. For clarification purposes and to avoid confusion among this child and his/her

siblings, we will refer to your child with leukemia as the "case child." We want to see if contact with certain chemicals, radioactive elements, or infectious agents were related to this illness. It is important that your child with leukemia and his or her immediate family members take part in this study. Immediate family members include the child's mother, father, and any full, half, or step-siblings who live with your child.

This study has two main components, a biological assessment and an environmental assessment. During the biological assessment, we would like to take samples of your family's blood, urine, and cells from inside their cheeks. We may also want to do genetic studies for leukemia research using DNA collected from each family member. The DNA samples will only be used for research about leukemia and for no other purpose. During the environmental assessment component, we would like to take samples from your family's current home and from past homes your family has lived in within Churchill County.

We are asking you and each member of your family to volunteer to be in this study. Each person has the right to refuse. There is no penalty for doing so. Before you decide, you should know what is involved and have all your questions answered. If you have any questions about the study or about these consent forms, please call us at 775/423-0617 or toll-free at 888/608-4623. We'll be happy to answer any questions you may have.

Cost/Compensation

There is no cost for the family to be in this study. Your family will receive no payment for being in this study.

What will happen?

From each family member choosing to be in this study, we will draw about 21 ml (about 1 to 1 1/2 tablespoons) of blood from a vein in his or her arm. First we will clean the skin by gently rubbing it with alcohol. The needle stick may hurt a little for a few seconds. The person taking the blood will be very careful. It will not hurt to give a sample of cheek cells. We will collect cheek cells by brushing the inside of each cheek with a soft brush for 30 seconds. Each family member will provide 32.5ml (approximately 1 ounce) of urine. It will not hurt to give a urine sample.

DNA will come from a portion of each person's blood sample and from his or her cheek cell samples. These specimens will be stored at CDC using a research code number. Any genetic studies performed with your family's DNA are for leukemia research only. Experts will advise CDC about which genetic research studies to perform. Genetic research may include identifying variations in genes that direct how the body handles toxic substances or fixes damaged DNA. Genetic research may also include testing for certain viruses thought to be associated with cancer, such as Epstein-Barr virus. The genetic research will not provide information useful for your family's medical treatment, specifically. However, this genetic research may advance our understanding of leukemia.

CDC will also store some of the blood and urine collected in this study by a code number, in case we need to do more tests in the future. Your family's blood and urine will not be tested for HIV, or the presence of alcohol or drugs.

During the study, we will interview you about the case child's medical and pre-natal history to build upon the recent survey conducted by NSHD. We will ask about your and the case child's daily activities and water use. The interview will be assigned a research code number; all personal identification information will be removed. Answers to the interview questions will be kept confidential.

We will attempt to collect environmental samples (soil, dust, water, and air) from all of the homes you lived in within Churchill County, Nevada, between 1 year prior to the case child's date of birth until present. This includes any home within Churchill County that the case child's mother lived in while she was pregnant with him/her. This will not include any home outside of Churchill County, Nevada. The current owner(s)/occupant(s) of homes where you

have lived in the past must give us permission to collect environmental samples from their homes. Sample collection at your home may take more than 1 hour.

Benefits

You will be notified of the results of the tests done on your family's blood and urine to see if your family had contact with certain chemicals, radioactive elements, or infectious agents. You will be given the test results for samples taken from your current home. Results from other homes will be given to the current property owner/occupant. A report summarizing our findings will be given to all participants of this study. This report will not have any information that would identify you, your family, or your home.

By providing DNA for genetic testing, you will be helping us and other medical professionals to understand why some people get ALL/AML and others do not. You will receive a general report of the research findings that does not include any personal identifying information. However, should the genetic research done on your DNA identify something that could significantly affect your health or reproductive choices, we will notify you personally. If this were to happen, we would advise you to share this information with your healthcare provider, using your own resources.

Confidentiality

We will protect your family's privacy to the extent allowable by law. We will not put your names on the blood, urine, or cheek cell samples. Instead, these samples will be identified using a research code number. We will keep all the research records and test results in locked files and only research staff will be allowed to look at them.

CDC will store a part of your and your family's blood and urine samples in the event that further laboratory tests are needed. CDC will give the laboratory test results to the NSHD only by code number.

CDC will store your family's DNA for future genetic research using only a research code number. The code number will allow CDC to link the laboratory tests and questionnaire data to the genetic studies. CDC will report the findings of genetic research as a summary of all DNA included in those studies. Despite all these safeguards, it may be possible to determine your family's identity due to the small number of children developing leukemia in Churchill County, Nevada.

Questionnaires and consent forms that contain personal identification information will be stored in a locked file, separate from the questionnaire data. Data entry personnel will not be given nor have access to your personal identification information.

The U.S. Geological Survey (USGS) will collect drinking water from each home and attach a research code number to the sample. USGS will locate each home they test by using satellites, known as a global positioning system (GPS) reading.

The GPS readings will be used to map the study findings and will not be available as public information. USGS will not keep your (or any family member's) name, phone number, or street address. USGS will provide the water testing results to NSHD and CDC by code number.

The environmental team, which may be made up of representatives from state, local, and federal agencies collaborating on the study, will take the indoor air, household dust, and play yard soil samples from your home(s). Each home setting will be labeled with a research code number. A contracted laboratory will test these samples and provide the results to CDC and NSHD by code number.

You will be provided with the results of the tests done on your blood, urine, and the results of the tests of your current home. In order to tell you these results, NSHD and CDC will keep a master list that matches your research code numbers with you. This master list will be kept in a locked file separate from the collected samples and completed questionnaire. NSHD will protect your confidentiality to the extent allowable by law. When we talk or write about this study, we will not include your name or any

facts that might identify anyone in your family.

Your names, telephone number, and address are on this consent form to allow us to contact you while we are conducting this research study. We will keep this consent form in a locked file separate from the rest of the study data.

Right to Refuse/Withdraw
It is your choice whether to be in this study. You may skip any question you don't want to answer. You may stop answering questions any time you want. You can expect the same medical care from your doctor whether you are in the study or not in the study. There is no penalty or loss of entitled benefits if you choose not to be in this study. You may stop being in this study at any time without losing any entitled benefits. If at any time in the future, you would like to have your interview information, or the samples from your home, or your blood, urine, or cheek cell samples destroyed or removed from the study, please call Dr. Carol Rubin (phone number below).

For more information
We will give you a copy of this form to keep. If you have any questions, concerns, or complaints about this study, please contact:

For questions related to this research study or questions related to injury from the study
Dr. Randall Todd, Nevada State Health Division (775-684-5946)
Dr. Carol Rubin, Centers for Disease Control and Prevention, (1-404-498-1340 and leave a message).

For questions related to your research rights
Dr. John Livengood, Centers for Disease Control and Prevention, Deputy Associate Director for Science (1-404-639-7260)

Thank you for considering being in this study.

Carol Rubin, D.V.M., M.P.H.
Centers for Disease Control and Prevention

Randall Todd, Dr.P.H.
Nevada State Health Division

Case Child's Parent/Guardian 1:
As described above, we are inviting you to be part of this research study. You may be in the study by indicating your consent to the items below. You may consent to all, some, or none of the items.

To be in this study, please sign your initials in the box next to each item you agree to.

	A direct (in-person) interview that includes questions about you and your family's health, usual activities, and history of cancer.
	The removal from you of up to 21 ml (1 to 1 ½ tablespoons) of blood by vein puncture.
	The collection from you of 32.5ml (approximately 1 ounce) of urine in a cup.
	The removal of cells from the inside of your mouth with a cheek brush (soft bristle swab) to provide DNA to study genes that may play a role in ALL/AML.
	The storage of a portion of your blood, urine, and cheek cell samples at CDC to be used for future studies about the causes of ALL/AML.
	The collection of samples of drinking water, household dust, play yard soil, and indoor air from your current home in Churchill County.

I have read the consent form (or someone has read it to me). I agree to be in this study, with my initials above indicating which parts of the study I agree to participate in.

Signature of Parent/Guardian 1: _____ Date:___/___/___

Name of Parent/Guardian 1 (print): _____

Street Address: _____

_____

City: _____

State: ____ Zip: _____

Phone number: _____

Case Child's Parent/Guardian 2:
As described above, we are inviting you to be part of this research study. You may be in the study by indicating your consent to the items below. You may consent to all, some, or none of the items.

To be in this study, please sign your initials in the box next to each item you agree to.

	A direct (in-person) interview that includes questions about you and your family's health, usual activities, and history of cancer.
	The removal from you of up to 21 ml (1 to 1 ½ tablespoons) of blood by vein puncture.
	The collection from you of 32.5ml (approximately 1 ounce) of urine in a cup.
	The removal of cells from the inside of your mouth with a cheek brush (soft bristle swab) to provide DNA to study genes that may play a role in ALL/AML.
	The storage of a portion of your blood, urine, and cheek cell samples at CDC to be used for future studies about the causes of ALL/AML.
	The collection of samples of drinking water, household dust, play yard soil, and indoor air from your current home in Churchill County.

I have read the consent form (or someone has read it to me). I agree to be in this study, with my initials above indicating which parts of the study I agree to participate in.

Signature of Parent/Guardian 2: _____ Date:___/___/___

Name of Parent/Guardian 2 (print): _____

Other Related Adult Living with Case Child
As described above, we are inviting you to be part of this research study. You may be in the study by indicating your consent to the items below. You may consent to all, some, or none of the items.

To be in this study, please sign your initials in the box next to each item you agree to.

	The removal from you of up to 21 ml (1 to 1 ½ tablespoons) of blood by vein puncture.
	The collection from you of 32.5ml (approximately 1 ounce) of urine in a cup.
	The removal of cells from the inside of your mouth with a cheek brush (soft bristle swab) to provide DNA to study genes that may play a role in ALL/AML.
	The storage of a portion of your blood, urine, and cheek cell samples at CDC to be used for future studies about the causes of ALL/AML.

I have read the consent form (or someone has read it to me). I agree to be in this study, with my initials above indicating which parts of the study I agree to participate in.

Signature of Other Related Adult living with Case Child: _____
Date:___/___/___

Name of Other Related Adult living with Case Child (print): _____

As described above, we are inviting your children to be part of this research study. You may allow your children to be in the study by indicating your consent to the items below. You may consent to all, some, or none of the items.

I (Parent or Legal Guardian) have read the consent form and agree that my children listed below may be in this study. In addition, I indicate with my initials which parts of the study that each child can participate in.

Child 1: Case Child

Child's Name:

_____

first middle father's surname mother's surname

Signature of Parent/ Guardian: _____ Date:___/___/___

Name of Parent/Guardian (print): _____

By my initials, I consent for this child to participate in the following parts of this research study.

	The removal from him/her of up to 21 ml (1 to 1 ½ tablespoons) of blood by vein puncture.
	The collection from him/her of 32.5ml (approximately 1 ounce) of urine in a cup.
	The removal of cells from the inside of his/her mouth with a cheek brush (soft bristle swab) to provide DNA to study genes that may play a role in ALL/AML.
	The storage of a portion of his/her blood, urine, and cheek cell samples at CDC to be used for future studies about the causes of ALL/AML.

Child 2
Child's Name:

_____
first middle father's surname mother's surname

By my initials, I consent for this child to participate in the following parts of this research study

	The removal from him/her of up to 21 ml (1 to 1 ½ tablespoons) of blood by vein puncture.
	The collection from him/her of 32.5ml (approximately 1 ounce) of urine in a cup.
	The removal of cells from the inside of his/her mouth with a cheek brush (soft bristle swab) to provide DNA to study genes that may play a role in ALL/AML.
	The storage of a portion of his/her blood, urine, and cheek cell samples at CDC to be used for future studies about the causes of ALL/AML.

Child 3
Child's Name:

_____
first middle father's surname mother's surname

By my initials, I consent for this child to participate in the following parts of this research study

	The removal from him/her of up to 21 ml (1 to 1 ½ tablespoons) of blood by vein puncture.
	The collection from him/her of 32.5ml (approximately 1 ounce) of urine in a cup.
	The removal of cells from the inside of his/her mouth with a cheek brush (soft bristle swab) to provide DNA to study genes that may play a role in ALL/AML.
	The storage of a portion of his/her blood, urine, and cheek cell samples at CDC to be used for future studies about the causes of ALL/AML.

Child 4
Child's Name:

_____
first middle father's surname mother's surname

By my initials, I consent for this child to participate in the following parts of this research study

	The removal from him/her of up to 21 ml (1 to 1 ½ tablespoons) of blood by vein puncture.
	The collection from him/her of 32.5ml (approximately 1 ounce) of urine in a cup.
	The removal of cells from the inside of his/her mouth with a cheek brush (soft bristle swab) to provide DNA to study genes that may play a role in ALL/AML.
	The storage of a portion of his/her blood, urine, and cheek cell samples at CDC to be used for future studies about the causes of ALL/AML.

Child 5
Child's Name:

_____
first middle father's surname mother's surname

By my initials, I consent for this child to participate in the following parts of this research study

	The removal from him/her of up to 21 ml (1 to 1 ½ tablespoons) of blood by vein puncture.
	The collection from him/her of 32.5ml (approximately 1 ounce) of urine in a cup.
	The removal of cells from the inside of his/her mouth with a cheek brush (soft bristle swab) to provide DNA to study genes that may play a role in ALL/AML.
	The storage of a portion of his/her blood, urine, and cheek cell samples at CDC to be used for future studies about the causes of ALL/AML.

Appendix A5: Reference Families Consent

Do not write in this space

(Control Family)

CONSENT TO PARTICIPATE

Exposure Assessment of Case-Children with Acute Lymphocytic or Myelocytic Leukemia and a Reference Population in Churchill County, Nevada

Thank you for agreeing to receive this packet of information about the (Centers for Disease Control and Prevention) CDC study of childhood leukemia in Churchill County. You have been sent this consent form because we would like to invite your family to join our study of leukemia. We are working with the Nevada State Health Division to further understand this illness. We hope you will take the time to review this form and consent to be a part of this study. If you have any questions about this form at any time while filling it out, please call 775/423-0617 or toll-free at 888/608-4623 and we will be happy to help you in any way we can.

Instructions

You have received this packet because you indicated on a recent phone call that you were willing to receive information about a study on childhood leukemia in Churchill County, Nevada. Please read this consent form. If you decide that you would like you and your family to be a part of the study, please sign the consent form where indicated at the end of this form. You will be consenting for yourself and the child selected to be a control subject for this study (the "control child"). If the control child is over 18 years old, a separate consent form for him/her is included in this packet. Please then complete the enclosed questionnaire and call the CDC clinic offices in Fallon at 775/423-0617 to make an appointment for you and your family to visit the CDC clinic offices.

Please bring the signed consent form and the completed questionnaire forms with you to your appointment at the CDC clinic offices in Fallon, Nevada. When you come to the CDC clinic offices for your visit, we will collect samples of blood, urine and cheek cells from you and the control child, and will interview you about medical histories, pregnancy with the control child, and current and past residences in Churchill County. During your visit, we will schedule a time for the members of our environmental team to collect environmental samples from your current home. These samples may include drinking water, household dust, play yard soil, and indoor air. We may also collect these environmental samples from other homes you have lived in within Churchill County, Nevada.

Your visit to the CDC clinic offices may last as long as two hours.

Purpose

Recently, the Nevada State Health Division (NSHD) identified a greater number of cases of Acute Lymphocytic Leukemia (ALL) and Acute Myelocytic Leukemia (AML) in Churchill County than would be expected by chance alone. The NSHD has asked the Centers for Disease Control and Prevention (CDC) to conduct a research study to look into the increase.

We want to see if contact with certain chemicals, radioactive elements, or infectious agents were related to this illness. It is important that the control child and his or her parent(s)/guardian(s) take part in this study.

This study has two main components, a biological assessment and an environmental assessment. During the biological assessment, we would like to take samples of your and the control child's blood, urine, and cells from inside the cheek. We may also want to do genetic studies for leukemia research using DNA collected from you and the control child. The DNA samples will only be used for research about leukemia and for no other purpose. During the environmental assessment component, we would like to take samples from your family's current home and from past homes your family has lived in within Churchill County.

We are asking you and your child selected to be a control to volunteer to be in this study. Each person has the right to refuse. There is no penalty for doing so. Before you decide, you should know what is involved and have all your questions answered. If you have any questions about the study or about these consent forms, please call us at 775/423-0617 or toll-free at 888/608-4623. We'll be happy to answer any questions you may have.

Cost/Compensation
There is no cost to be in this study. Your family will receive no payment for being in this study.

What will happen?
From each study participant, we will draw about 21 ml (about 1 to 1 1/2 tablespoons) of blood from a vein in the arm. First we will clean the skin by gently rubbing it with alcohol. The needle stick may hurt a little for a few seconds. The person taking the blood will be very careful. It will not hurt to give a sample of cheek cells. We will collect cheek cells by brushing the inside of each cheek with a soft brush for 30 seconds. Study participants will provide 32.5ml (approximately 1 ounce) of urine. It will not hurt to give a urine sample.

DNA will come from a portion of each person's blood sample and from his or her cheek cell samples. These specimens will be stored at CDC using a research code number. Any genetic studies performed with your family's DNA are for leukemia research only. Experts will advise CDC about which genetic research studies to perform. Genetic research may include identifying variations in genes that direct how the body handles toxic substances or fixes damaged DNA. Genetic research may also include testing for certain viruses thought to be associated with cancer, such as Epstein-Barr virus. This research may advance our understanding of leukemia.

CDC will also store some of the blood and urine collected in this study by a code number, in case we need to do more tests in the future. Blood and urine samples will not be tested for HIV, or the presence of alcohol or drugs.

During the study, we will interview you about the control child's medical and pre-natal history to build upon the recent survey conducted by NSHD. We will ask about your and the control child's activities and water use. The interview will be assigned a research code number; all personal identification information will be removed. Answers to the interview questions will be kept confidential.

We will attempt to collect environmental samples (soil, dust, water, and air) from your current home in Churchill County, Nevada. Sample collection at your home may take more than 1 hour. To collect environmental samples from previous homes you have lived in, we will need permission from the current owner/occupant.

Benefits

You will be notified of the results of the tests done on your and your child's blood and urine to see if your family had contact with certain chemicals, radioactive elements, or infectious agents. You will be given the test results for samples taken from your current home. A report summarizing our findings will be given to all participants of this study. This report will not have any information that would identify you, your family, or your home.

By providing DNA for genetic testing, you will be helping us and other medical professionals to understand why some people get ALL/AML and others do not. You will receive a general report of the

research findings that will not include any personal identifying information. However, should the genetic research done on your DNA identify something that could significantly affect your health or reproductive choices, we will notify you personally. If this were to happen, we would advise you to share this information with your healthcare provider, using your own resources.

Confidentiality

We will protect your family's privacy to the extent allowable by law. We will not put your names on the blood, urine, or cheek cell samples. Instead, these samples will be identified using a research code number. We will keep all the research records and test results in locked files and only research staff will be allowed to look at them.

CDC will store a part of your and your child's blood and urine samples in the event that further laboratory tests are needed. CDC will give the laboratory test results to the NSHD only by code number.

CDC will store DNA for future genetic research using only a research code number. The code number will allow CDC to link the laboratory tests and questionnaire data to the genetic studies. CDC will report the findings of genetic research as a summary of all DNA included in those studies.

Questionnaires and consent forms that contain personal identification information will be stored in a locked file, separate from the questionnaire data. Data entry personnel will not be given nor have access to your personal identification information.

The U.S. Geological Survey (USGS) will collect drinking water from each home and attach a research code number to the sample. USGS will locate each home they test by using satellites, known as a global positioning system (GPS) reading.

The GPS readings will be used to map the study findings and will not be available as public information. USGS will not keep your (or any family member's) name, phone number, or street address. USGS will provide the water testing results to NSHD and CDC by code number.

The environmental team, which may be made up of representatives from state, local, and federal agencies collaborating on the study, will take the indoor air, household dust, and play yard soil samples from your home(s). Each home setting will be labeled with a research code number. A contracted laboratory will test these samples and provide the results to CDC and NSHD by code number.

You will be provided with the results of the tests done on your blood, urine, and the results of the tests of your current home. In order to tell you these results, NSHD and CDC will keep a master list that matches your research code numbers with you. This master list will be kept in a locked file separate from the collected samples and completed questionnaire. NSHD will protect your confidentiality to the extent allowable by law. When we talk or write about this study, we will not include your name or any facts that might identify anyone in your family.

Your names, telephone number, and address are on this consent form to allow us to contact you while we are conducting this research study. We will keep this consent form in a locked file separate from the rest of the study data.

Right to Refuse/Withdraw
It is your choice whether to be in this study. You may skip any question you don't want to answer. You may stop answering questions any time you want. You can expect the same medical care from your doctor whether you are in the study or not in the study. There is no penalty or loss of entitled benefits if you choose not to be in this study. You may stop being in this study at any time without losing any entitled benefits. If at any time in the future, you would like to have your interview information, or the samples from your home, or your blood, urine, or cheek cell samples destroyed or removed from the study, please call Dr. Carol Rubin (phone number below).

For more information
We will give you a copy of this form to keep. If you have any questions, concerns, or complaints about this study, please contact:

For questions related to this research study or questions related to injury from the study
Dr. Randall Todd, Nevada State Health Division (775-684-5946)
Dr. Carol Rubin, Centers for Disease Control and Prevention, (1-404-498-1340 and leave a message).

For questions related to your research rights
Dr. John Livengood, Centers for Disease Control and Prevention, Deputy Associate Director for Science (1-404-639-7260)

Thank you for considering being in this study.

Carol Rubin, D.V.M., M.P.H.
Centers for Disease Control and Prevention

Randall Todd, Dr.P.H.
Nevada State Health Division

Control Child's Parent/Guardian 1:
As described above, we are inviting you to be part of this research study. You may be in the study by indicating your consent to the items below. You may consent to all, some, or none of the items.

To be in this study, please sign your initials in the box next to each item you agree to.

	A direct (in-person) interview that includes questions about you and your family's health, usual activities, and history of cancer.
	The removal from you of up to 21 ml (1 to 1 ½ tablespoons) of blood by vein puncture.
	The collection from you of 32.5ml (approximately 1 ounce) of urine in a cup.
	The removal of cells from the inside of your mouth with a cheek brush (soft bristle swab) to provide DNA to study genes that may play a role in ALL/AML.
	The storage of a portion of your blood, urine, and cheek cell samples at CDC to be used for future studies about the causes of ALL/AML.
	The collection of samples of drinking water, household dust, play yard soil, and indoor air from your current home in Churchill County.

I have read the consent form (or someone has read it to me). I agree to be in this study, with my initials above indicating which parts of the study I agree to participate in.

Signature of Parent/Guardian 1: _____ Date:___/___/___

Name of Parent/Guardian 1 (print): _____

Street Address: _____

_____

City: _____

State: ____ Zip: _____

Phone number: _____

Control Child's Parent/Guardian 2:
As described above, we are inviting you to be part of this research study. You may be in the study by indicating your consent to the items below. You may consent to all, some, or none of the items.

To be in this study, please sign your initials in the box next to each item you agree to.

	A direct (in-person) interview that includes questions about you and your family's health, usual activities, and history of cancer.
	The removal from you of up to 21 ml (1 to 1 ½ tablespoons) of blood by vein puncture.
	The collection from you of 32.5ml (approximately 1 ounce) of urine in a cup.
	The removal of cells from the inside of your mouth with a cheek brush (soft bristle swab) to provide DNA to study genes that may play a role in ALL/AML.
	The storage of a portion of your blood, urine, and cheek cell samples at CDC to be used for future studies about the causes of ALL/AML.
	The collection of samples of drinking water, household dust, play yard soil, and indoor air from your current home in Churchill County.

I have read the consent form (or someone has read it to me). I agree to be in this study, with my initials above indicating which parts of the study I agree to participate in.

Signature of Parent/Guardian 2: _____ Date:___/___/___

Name of Parent/Guardian 2 (print): _____

As described above, we are inviting your child to be part of this research study. You may allow your child to be in the study by indicating your consent to the items below. You may consent to all, some, or none of the items.

I (Parent or Legal Guardian) have read the consent form and agree that my child listed below may be in this study. In addition, I indicate with my initials which parts of the study that my child can participate in.

Control Child

Child's Name:

_____

first middle father's surname mother's surname

Signature of Parent/ Guardian: _____ Date:___/___/___

Name of Parent/Guardian (print): _____

By my initials, I consent for this child to participate in the following parts of this research study.

	The removal from him/her of up to 21 ml (1 to 1 ½ tablespoons) of blood by vein puncture.
	The collection from him/her of 32.5ml (approximately 1 ounce) of urine in a cup.
	The removal of cells from the inside of his/her mouth with a cheek brush (soft bristle swab) to provide DNA to study genes that may play a role in ALL/AML.
	The storage of a portion of his/her blood, urine, and cheek cell samples at CDC to be used for future studies about the causes of ALL/AML.

Appendix B: Questionnaire

B1: Mail Packet

B2: Interview

Appendix B1: Mail Packet

Name
Address
City, State, Zip

Dear _____,

Thank you for agreeing to review the enclosed materials related to the study of leukemia and environmental exposures in Churchill County. This study is being conducted by the Nevada State Health Division and the Centers for Disease Control and Prevention, along with the cooperation of state and federal environmental agencies. The study has many parts, including this mail-out packet, the collection of biological samples (that is, blood, urine, and cheek cells) from you and members of your family, the collection of environmental samples (for example, soil and dust) from your home, and a personal interview. As we discussed on the telephone, the first step is this mailing packet; please review the materials in this packet carefully.

This packet includes the study consent form(s) and an 8-part questionnaire. The consent form(s) are several pages long. It is very important that you read through it carefully so that you understand the purpose of the study and your role in it. Your signature on these form(s) tells us that you want to participate in this study. If you have any questions about completing the consent form(s), please call us at **775/423-0617 or toll-free at 888/608-4623.** We are happy to assist you.

The other forms in this packet ask for general information about your family members, the homes that you have lived in, the jobs, military history, hobbies, and recreational activities of you and other adults living in your household, and your child's school attendance and travel history.

If you decide to participate in this study, please contact the CDC clinic offices in Fallon, Nevada, to make an appointment. During this appointment, we will collect samples of blood, urine, and cheek cells and will conduct the personal interview. The number to call to make the appointment is **775/423-0617.**

Please bring your signed consent and completed questionnaire form with you to your appointment. Unfortunately, if you do not have them with you, it will be necessary to re-schedule your appointment.

The success of this study depends on you! We appreciate you taking the time to complete the forms. Thank you very much for your help.

Sincerely yours,

Carol Rubin, DVM, MPH
Centers for Disease Control and Prevention

Randall Todd, DrPH
Nevada State Health Division

Do not write in this space

Exposure Assessment of Children with Acute Lymphocytic or Myelocytic Leukemia and a Reference Population in Churchill County, Nevada

Child's Name:
Child's Address:

Please complete this form only after you have signed the consent form.

Thank you for taking the time to complete this form. It asks for general information about (Child's Name) and his/her family, and for specific information about where he/she and his/her family have lived, current occupations, hobbies and recreational activities, school attendance, and immunization and travel histories.

If you have any questions about the form or don't understand what is being asked, **please call 775/423-0617 or 888/608-4623**; we'll be happy to help you any way we can.

Please mark boxes with an X.

To protect your child's identity, we have not included his/her name on the following pages. Rather, we refer to him/her as the "study child". This page, which includes his/her personal information, will be separated from the rest of the questionnaire and stored in a separate locked filing cabinet.

Once again, thank you for agreeing to participate in this important study.

Do not write in this space

Part I. Demographic Information

1. When was the study child born? _____/_____/_____
(mm) (dd) (yyyy)

2. Where was the study child born?

_____ _____ _____
(City) (State) (Country)

3. What was the duration of the study child's pregnancy in weeks? _____
❑ Don't know

4. What is the study child's sex?
❑ Male
❑ Female

5. Is the study child Spanish/Hispanic/Latino? **Please mark one**
❑ No, not Spanish /Hispanic/Latino
❑ Yes, Mexican, Mexican Am., Chicano
❑ Yes, Puerto Rican
❑ Yes, Cuban
❑ Yes, other Spanish/Hispanic/Latino _____ (please specify)

6. What is the study child's race? **Please mark all that apply**
❑ White
❑ Black, African American, or Negro
❑ American Indian or Alaska Native
❑ Asian Indian
❑ Chinese
❑ Filipino
❑ Other Asian
❑ Japanese
❑ Korean
❑ Vietnamese
❑ Native Hawaiian
❑ Guamanian or Chamorro
❑ Samoan
❑ Other Pacific Islander

7. Was the study child adopted?
❑ Yes
❑ No
❑ Refuse to answer

8. How old was the study child's biological father at the time the study child was born?
_____ years

9. Where was the study child's biological father born?

_____ _____ _____
(City) (State) (Country)
❑ Don't Know
❑ Refuse to answer

10. How old was the study child's biological mother at the time the study child was born?
____ years

11. Where was the study child's biological mother born?

_____ _____ _____
(City) (State) (Country)
❑ Don't Know
❑ Refuse to answer

12. How many households does the study child currently live in? By this we mean households where the child routinely spends large amounts of time. For example, a child who spends one week living in a maternal household and one week living in a paternal household would be considered to live in two households. ____

13. How many adults currently live in the study child's household(s)? _____

14. What language is usually spoken at the study child's home?
Please mark only one; please specify language if you mark "other"
❑ English ❑ Spanish ❑ Other (please specify) _____

15. How many full siblings does the study child have? Full siblings are brothers and/or sisters who have the same biological mother **and** biological father as the study child. _____

- ❑ Don't Know
- ❑ Refuse to answer

16. Please provide the following information about the study child full siblings.

First name	**Date of birth**	**Sex** (please mark one)
_____	_____/_____/_____ (mm) (dd) (yyyy)	❑ Male ❑ Female
_____	_____/_____/_____ (mm) (dd) (yyyy)	❑ Male ❑ Female
_____	_____/_____/_____ (mm) (dd) (yyyy)	❑ Male ❑ Female
_____	_____/_____/_____ (mm) (dd) (yyyy)	❑ Male ❑ Female
_____	_____/_____/_____ (mm) (dd) (yyyy)	❑ Male ❑ Female
_____	_____/_____/_____ (mm) (dd) (yyyy)	❑ Male ❑ Female

17. How many half siblings does the study child have? Half siblings are brothers and/or sisters who have the same mother but different father as the study child, **or** have the same father but different mother as the study child. (**please write number here)** _____
    - ❑ Don't Know
    - ❑ Refuse to answer

18. Please provide the following information about the study child half siblings.

First name	**Date of birth**	**Sex** (please mark one)
_____	_____/_____/_____ (mm) (dd) (yyyy)	❑ Male ❑ Female
_____	_____/_____/_____ (mm) (dd) (yyyy)	❑ Male ❑ Female
_____	_____/_____/_____ (mm) (dd) (yyyy)	❑ Male ❑ Female

19. Please provide the following information about other children who have lived with the study child for 6 months or more:

First name	**Date of birth**	**Sex** (please mark one)
_____	_____/_____/_____ (mm) (dd) (yyyy)	❑ Male ❑ Female
_____	_____/_____/_____ (mm) (dd) (yyyy)	❑ Male ❑ Female

20. How many children (full or half siblings or unrelated children) currently live in the same household as the study child? ___
    - ❑ Don't Know
    - ❑ Refuse to answer

Part II. List of Residences

A. Residences of the study child's mother during her pregnancy with the study child

1. This section should be filled out by the adult who can provide the most complete information about where the study child's mother lived while she was pregnant with him/her.

What was the street address of the residence(s) the study child's mother lived in while she was pregnant with him/her?	**When did the study child's mother <u>start</u> living here?** (mm/yyyy)	**When did the study child's mother <u>stop</u> living here?** (mm/yyyy)	**Did the parents/guardians of the study child own or rent this residence?**	**How many other adults and children also lived at this residence at this time?** Adults (18 yrs or over) Children (less than 18 yrs)
Street: City: State: Zip: Country: *Residence 1* (during pregnancy)			❑ Own ❑ Rent Landlord's name: _____	Adults: _____ Children: _____
Street: City: State: Zip: Country: *Residence 2* (during pregnancy)			❑ Own ❑ Rent Landlord's name: _____	Adults: _____ Children: _____
Street: City: State: Zip: Country: *Residence 3* (during pregnancy)			❑ Own ❑ Rent Landlord's name: _____	Adults: _____ Children: _____

B. Residences of the study child

Please list the address of the homes the study child lived in, for at least 6 months in a row, and the dates he/she lived at these addresses during the time period between (DOB) and his/her date of diagnosis/June 30, 2001.

What was the street address of the residence(s) the study child lived in between (DOB) and his/her date of diagnosis/June 30, 2001?	**When did the study child start living here?** (mm/yyyy)	**When did the study child stop living here?** (mm/yyyy)	**Did the parents/guardians of the study child own or rent this residence?**	**How many adults and children also lived at this residence at this time?** Adults (18 yrs or over) Children (less than ≤18 yrs)
Street: City: State: Zip: Country: *Residence 1*			❑ Own ❑ Rent Landlord's name: _____	Adults: _____ Children: _____
Street: City: State: Zip: Country: *Residence 2*			❑ Own ❑ Rent Landlord's name: _____	Adults: _____ Children: _____
Street: City: State: Zip: Country: *Residence 3*			❑ Own ❑ Rent Landlord's name: _____	Adults: _____ Children: _____
Street: City: State: Zip: Country: *Residence 4*			❑ Own ❑ Rent Landlord's name: _____	Adults: _____ Children: _____

If you need additional space to list your past homes, please use the back of this sheet.

Part III. List of Jobs and Military Service

In this section, we would like to get information about the current occupation of each adult who currently lives with the study child. We are interested in paid and volunteer work as well as part-time and full-time jobs, jobs at home and/or jobs on a farm.

Please complete questions 1 through 4 below for each adult, including yourself, who lives in the same household with the study child. Begin by identifying the relationship of each adult to the study child.

==========

Adult 1

What is the relationship of Adult 1 to the study child: _____
(for example, mother, father, stepmother/father, mother's boyfriend/father's girlfriend, family friend, etc.)

1. Does Adult 1 have an occupation at present? (This includes paid and volunteer work as well as part-time and full-time jobs, jobs at home and/or jobs on a farm) **Please mark one box**

❑ Yes ❑ No ❑ Don't know/Not sure ❑ Refuse to answer

2. If you answered "yes" to question 1, please fill in the table below concerning Adult 1's present job. If you answered "no" or "don't know" or refused to answer question 1, please **skip to question 3**.

What is Adult 1's present job(s) title (please list all current occupations)	**What is the name of the company or employer?**	**Where is this job located?** City, state. Give country if not in the U.S.	**How long has Adult 1 worked/volunteered here?**

Please continue this table on the back of this page if you need more space.

3. Did Adult 1 serve in the U.S. Armed Forces between (date) and the study child's date of diagnosis/June 30, 2001? **Please mark one box.**

❑ Yes ❑ No ❑ Don't know/Not sure ❑ Refuse to answer

4. If you answered "yes" to question 3, please fill in the table on the next page for each country that you served in. If you answered "no" or "don't know" to question 3, **please skip to next adult**.
If there are no other adults living with the study child, please **skip to Part IV**.

Country of service	**Date service began** (mm/yyyy)	**Date service ended** (mm/yyyy) (if current, enter "present")	**Branch of the Armed Forces**	**Type of job**	**Please indicate if Adult 1 worked with or had contact with chemical or biological agents**
					❑ None ❑ Don't know If yes, specify: _____ _____
					❑ None ❑ Don't know If yes, specify: _____ _____
					❑ None ❑ Don't know If yes, specify: _____ _____
					❑ None ❑ Don't know If yes, specify: _____ _____

Please continue this table on the back of this page if you need more space.

End of Adult 1

Adult 2

What is the relationship of Adult 2 to the study child: _____ (for example, mother, father, stepmother, stepfather, uncle, grandmother, family friend, etc)

1. Does Adult 2 have an occupation at present?
   (This includes paid and volunteer work as well as part-time and full-time jobs, jobs at home and/or jobs on a farm) **Please mark one box**
   ❑ Yes ❑ No ❑ Don't know/Not sure ❑ Refuse to answer

2. If you answered "yes" to question 1, please fill in the table below concerning Adult 2's present job. If you answered "no" or "don't know" or refused to answer question 1, please **skip to question 3**.

What is Adult 2's present job(s) title	**What is the name of the company or employer?**	**Where is this job located?** City, state. Give country if not in the U.S.	**How long has Adult 2 worked/volunteered here?**

Please continue this table on the back of this page if you need more space.

3. Did Adult 2 serve in the U.S. Armed Forces between (date) and the study child's date of diagnosis/June 30, 2001? **Please mark one box**
❑ Yes ❑ No ❑ Don't know/Not sure ❑ Refuse to answer

4. If you answered "yes" to question 3, please fill in the table below for each country that Adult 2 served in. If you answered "no" or "don't know" or refused to answer question 3, **please skip to next adult**.

If there are no other adults living with the study child please **skip to Part IV**.

Country of service	**Date service began** (mm/yyyy)	**Date service ended** (mm/yyyy)	**Branch of the Armed Forces**	**Type of job**	**Please indicate if Adult 2 worked with or had contact with chemical or biological agents**
					❑ None ❑ Don't know If yes, specify: _____ _____

Country of service	**Date service began** (mm/yyyy)	**Date service ended** (mm/yyyy)	**Branch of the Armed Forces**	**Type of job**	**Please indicate if Adult 2 worked with or had contact with chemical or biological agents**
					❑ None ❑ Don't know If yes, specify: _____ _____
					❑ None ❑ Don't know If yes, specify: _____ _____
					❑ None ❑ Don't know If yes, specify: _____ _____

Please continue this table on the back of this page if you need more space.

End of Adult 2

Adult 3

What is the relationship of Adult 3 to the study child: _____ (for example, mother, father, stepmother, stepfather, uncle, grandmother, family friend, etc)

1. Does Adult 3 have an occupation at present?
   (This includes paid and volunteer work as well as part-time and full-time jobs, jobs at home and/or jobs on a farm) **Please mark one box**
   ❑ Yes ❑ No ❑ Don't know/Not sure ❑ Refuse to answer

2. If you answered "yes" to question 1, please fill in the table below concerning Adult 3's present job. If you answered "no" or "don't know" or refused to answer question 1, please **skip to question 3**.

What is Adult 3's present job(s) title	**What is the name of the company or employer?**	**Where is this job located?** City, state. Give country if not in the U.S.	**How long has Adult 3 worked/volunteered here?**

Please continue this table on the back of this page if you need more space.

3. Did Adult 3 serve in the U.S. Armed Forces between (date) and the study child's date of diagnosis/June 30, 2001? **Please mark one box**
   ❑ Yes ❑ No ❑ Don't know/Not sure ❑ Refuse to answer

4. If you answered "yes" to question 3, please fill in the table below for each country that Adult 3 served in. If you answered "no" or "don't know" or refused to answer question 3, **please skip to next adult**.

   If there are no other adults living with the study child please **skip to Part IV**.

Country of service	**Date service began** (mm/yyyy)	**Date service ended** (mm/yyyy)	**Branch of the Armed Forces**	**Type of job**	**Please indicate if Adult 3 worked with or had contact with chemical or biological agents**
					❑ None ❑ Don't know If yes, specify: _____ _____

Country of service	**Date service began** (mm/yyyy)	**Date service ended** (mm/yyyy)	**Branch of the Armed Forces**	**Type of job**	**Please indicate if Adult 3 worked with or had contact with chemical or biological agents**
					❑ None ❑ Don't know If yes, specify: _____ _____
					❑ None ❑ Don't know If yes, specify: _____ _____
					❑ None ❑ Don't know If yes, specify: _____ _____

Please continue this table on the back of this page if you need more space.

End of Adult 3

If you need additional space for other Adults in the study child's household, please call 775/423-0617 and we will send you more tables.

Part IV. Hobbies and Recreational Activities

This section of the questionnaire is about any hobbies and recreational activities that adults in the study child's household may have done during the past 6 months. There are separate tables for the hobbies/activities of each adult who has lived in the study child's household for at least the past 6 months.

Part a. Adult 1: (please specify relationship with the study child): _____
The next few pages ask about Adult 1's hobbies and recreational activities during the past 6 months.

Hobbies and Recreational Activities

1. Below is a table listing several hobbies and activities. For each hobby and activity listed, please indicate if Adult 1 did the hobby/activity and how often <u>on average</u> that hobby/activity was done.

Hobby/Recreational Activity	**Did Adult 1 do this hobby or activity?**	**On average, how frequently during the past 6 months did Adult 1 do this hobby or activity?** (please mark only one)		
		Daily	Weekly	Monthly
Model building	❑ Yes ❑ No ❑ Don't know or Not sure If yes, what type of model? _____			
Artwork (for example: ceramics, painting)	❑ Yes ❑ No ❑ Don't know or Not sure If yes, what type of art? _____			
Furniture stripping	❑ Yes ❑ No ❑ Don't know or Not sure			
Auto/Truck maintenance	❑ Yes ❑ No ❑ Don't know or Not sure			
Electronic repair	❑ Yes ❑ No ❑ Don't know or Not sure			
Leather work	❑ Yes ❑ No ❑ Don't know or Not sure			
Metal work	❑ Yes ❑ No ❑ Don't know or Not sure			
Hiking/Camping	❑ Yes ❑ No ❑ Don't know or Not sure			
Gardening	❑ Yes ❑ No ❑ Don't know or Not sure			
Animal related For example: horseback riding	❑ Yes ❑ No ❑ Don't know or Not sure If yes, specify _____			

Adult 1: Hobbies/Activities Exposure History

Please think about any chemicals or substances that Adult 1 may have used during the past 6 months for hobbies or recreational activities.

1. Below is a table that lists some commonly used chemicals and substances. For each chemical/substance listed, please indicate if Adult 1 used that chemical/substance for hobbies or activities. For each chemical/substance that was used, please indicate how often on average it was used.

Chemicals/Substances used for hobbies or recreational activities	**Did Adult 1 use this chemical for hobbies or recreational activities?** If yes, go to the next column	**On average, how frequently during the past 6 months did Adult 1 use this chemical for hobbies/activities?** (please mark only one)		
		Daily	Weekly	Monthly
Solvents/degreasers used to clean mechanical parts	❑ Yes ❑ No ❑ Don't know or Not sure			
Glues/adhesives	❑ Yes ❑ No ❑ Don't know or Not sure			
Varnishes/lacquers	❑ Yes ❑ No ❑ Don't know or Not sure			
Pesticides (for example, insect repellant, lawn treatment)	❑ Yes ❑ No ❑ Don't know or Not sure			
Plastics	❑ Yes ❑ No ❑ Don't know or Not sure			
Rust preventatives (for example, Rustoleum)	❑ Yes ❑ No ❑ Don't know or Not sure			
Rubber cement	❑ Yes ❑ No ❑ Don't know or Not sure			
Dyes and pigments	❑ Yes ❑ No ❑ Don't know or Not sure			
Petroleum products (for example, hydraulic fluid, motor oil)	❑ Yes ❑ No ❑ Don't know or Not sure			

(Continued)

Chemicals/Substances used for hobbies or recreational activities	**Did Adult 1 use this chemical for hobbies or recreational activities?** If yes, go to the next column	**On average, how frequently during the past 6 months did Adult 1 use this chemical for hobbies/activities?** (please mark only one)		
		Daily	Weekly	Monthly
Metals	❑ Yes ❑ No ❑ Don't know or Not sure			
Paints, paint thinners or paint strippers	❑ Yes ❑ No ❑ Don't know or Not sure			
Other chemicals or substances used for hobbies or recreational activities not listed above. If yes, specify _____ _____	❑ Yes ❑ No ❑ Don't know or Not sure			

End of Adult 1
If no other Adults in household, please go to Part V.

Part b. Adult 2
Hobbies and Recreational activities

The next few pages ask about hobbies and activities Adult 2 has done during the past 6 months.

1. Below is a table listing several hobbies and activities. For each hobby and activity listed, please indicate if Adult 2 did the hobby/activity and how often on average that hobby/activity was done.

Hobby/Recreational Activity	**Did Adult 2 do this hobby or activity?**	**On average, how frequently during the past 6 months did Adult 2 do this hobby or activity? (please mark only one)**		
		Daily	Weekly	Monthly
Model building	❑ Yes ❑ No ❑ Don't know or Not sure If yes, what type of model? _____			
Artwork (example: ceramics, painting)	❑ Yes ❑ No ❑ Don't know or Not sure If yes, what type of art? _____			
Furniture stripping	❑ Yes ❑ No ❑ Don't know or Not sure			
Auto/Truck maintenance	❑ Yes ❑ No ❑ Don't know or Not sure			
Electronic repair	❑ Yes ❑ No ❑ Don't know or Not sure			
Leather work	❑ Yes ❑ No ❑ Don't know or Not sure			
Metal work	❑ Yes ❑ No ❑ Don't know or Not sure			
Hiking/Camping	❑ Yes ❑ No ❑ Don't know or Not sure			
Gardening	❑ Yes ❑ No ❑ Don't know or Not sure			
Animal related For example, horseback riding	❑ Yes ❑ No ❑ Don't know or Not sure If yes, specify _____			

Adult 2: Hobby/Activity Exposure History

Please think about chemicals or substances that Adult 2 may have used for hobbies or recreational activities during the past 6 months.

1. Below is a table that lists some of the commonly used chemicals and substances. For each chemical/substance listed, please indicate if Adult 2 used that chemical/substance for hobbies or activities. For each chemical/substance that was used, please indicate how often on average it was used.

Chemicals/substances used for hobbies or recreational activities	**Did Adult 2 use this chemical for hobbies or recreational activities?** If yes, go to the next column	**On average, how frequently during the past 6 months did Adult 2 use this chemical for hobbies/activities?** (please mark only one)		
		Daily	Weekly	Monthly
Solvents/degreasers used to clean mechanical parts	❑ Yes ❑ No ❑ Don't know or Not sure			
Glues/adhesives	❑ Yes ❑ No ❑ Don't know or Not sure			
Varnishes/lacquers	❑ Yes ❑ No ❑ Don't know or Not sure			
Pesticides (for example, insect repellant, lawn treatment)	❑ Yes ❑ No ❑ Don't know or Not sure			
Plastics	❑ Yes ❑ No ❑ Don't know or Not sure			
Rust preventatives (for example, Rustoleum)	❑ Yes ❑ No ❑ Don't know or Not sure			
Rubber cement	❑ Yes ❑ No ❑ Don't know or Not sure			
Dyes and pigments	❑ Yes ❑ No ❑ Don't know or Not sure			
Petroleum products (for example, hydraulic fluid, motor oil)	❑ Yes ❑ No ❑ Don't know or Not sure			

(continued)

Chemicals/Substances used for hobbies or recreational activities	**Did Adult 2 use this chemical for hobbies or recreational activities?** If yes, go to the next column	**On average, how frequently during the past 6 months did Adult 2 use this chemical for hobbies/activities?** (please mark only one)		
		Daily	Weekly	Monthly
Metals	❑ Yes ❑ No ❑ Don't know or Not sure			
Paints, paint thinners or paint strippers	❑ Yes ❑ No ❑ Don't know or Not sure			
Other chemicals or substances used for hobbies or recreational activities If yes, specify _____ _____	❑ Yes ❑ No ❑ Don't know or Not sure			

End of Adult 2
If no other Adults in household, please go to Part V.

Part c. Adult 3
Hobbies and Recreational activities

The next few pages ask about hobbies and activities Adult 3 has done during the past 6 months.

1. Below is a table listing several hobbies and activities. For each hobby and activity listed, please indicate if Adult 3 did the hobby/activity and how often on average that hobby/activity was done.

Hobby/Recreational Activity	**Did Adult 3 do this hobby or activity?**	**On average, how frequently during the past 6 months did Adult 3 do this hobby or activity? (please mark only one)**		
		Daily	Weekly	Monthly
Model building	❑ Yes ❑ No ❑ Don't know or Not sure If yes, what type of model? _____			
Artwork (example: ceramics, painting)	❑ Yes ❑ No ❑ Don't know or Not sure If yes, what type of art? _____			
Furniture stripping	❑ Yes ❑ No ❑ Don't know or Not sure			
Auto/Truck maintenance	❑ Yes ❑ No ❑ Don't know or Not sure			
Electronic repair	❑ Yes ❑ No ❑ Don't know or Not sure			
Leather work	❑ Yes ❑ No ❑ Don't know or Not sure			
Metal work	❑ Yes ❑ No ❑ Don't know or Not sure			
Hiking/Camping	❑ Yes ❑ No ❑ Don't know or Not sure			
Gardening	❑ Yes ❑ No ❑ Don't know or Not sure			
Animal related For example, horseback riding	❑ Yes ❑ No ❑ Don't know or Not sure If yes, specify _____			

Adult 3: Hobby/Activity Exposure History

Please think about chemicals or substances that Adult 3 may have used for hobbies or recreational activities during the past 6 months.

1. Below is a table that lists some of the commonly used chemicals and substances. For each chemical/substance listed, please indicate if Adult 3 used that chemical/substance for hobbies or activities. For each chemical/substance that was used, please indicate how often on average it was used.

Chemicals/substances used for hobbies or recreational activities	**Did Adult 3 use this chemical for hobbies or recreational activities?** If yes, go to the next column	**On average, how frequently during the past 6 months did Adult 3 use this chemical for hobbies/activities?** (please mark only one)		
		Daily	Weekly	Monthly
Solvents/degreasers used to clean mechanical parts	❑ Yes ❑ No ❑ Don't know or Not sure			
Glues/adhesives	❑ Yes ❑ No ❑ Don't know or Not sure			
Varnishes/lacquers	❑ Yes ❑ No ❑ Don't know or Not sure			
Pesticides (for example, insect repellant, lawn treatment)	❑ Yes ❑ No ❑ Don't know or Not sure			
Plastics	❑ Yes ❑ No ❑ Don't know or Not sure			
Rust preventatives (for example, Rustoleum)	❑ Yes ❑ No ❑ Don't know or Not sure			
Rubber cement	❑ Yes ❑ No ❑ Don't know or Not sure			
Dyes and pigments	❑ Yes ❑ No ❑ Don't know or Not sure			
Petroleum products (for example, hydraulic fluid, motor oil)	❑ Yes ❑ No ❑ Don't know or Not sure			

(continued)

Chemicals/Substances used for hobbies or recreational activities	**Did Adult 3 use this chemical for hobbies or recreational activities?** If yes, go to the next column	**On average, how frequently during the past 6 months did Adult 3 use this chemical for hobbies/activities?** (please mark only one)		
		Daily	Weekly	Monthly
Metals	❑ Yes ❑ No ❑ Don't know or Not sure			
Paints, paint thinners or paint strippers	❑ Yes ❑ No ❑ Don't know or Not sure			
Other chemicals or substances used for hobbies or recreational activities If yes, specify _____ _____	❑ Yes ❑ No ❑ Don't know or Not sure			

End of Adult 3
If you need additional space to report hobbies and activities for other Adults, please call 775/423-0617 and we will send you more tables.

Part V. Other Possible Exposures

1. Has anyone else, other than the adults listed on the previous pages, who has lived with the study child during the last 6 months, had a hobby or activity that routinely involved the use of chemicals/substances?

- ❑ Yes
- ❑ No
- ❑ Don't know/Not sure
- ❑ Refuse to answer

If you answered "yes", please go to **question 2**.
If you answered "no", please go to **question 3**.

2. Which chemicals/substances were used and how often?

a. Name of chemical/substance	b. How often was this used?
1. _____	1. ❑ Daily ❑ Weekly ❑ Monthly
2. _____	2. ❑ Daily ❑ Weekly ❑ Monthly
3. _____	3. ❑ Daily ❑ Weekly ❑ Monthly

3. During the year before the study child was diagnosed with leukemia/June 30, 2001, did any of his/her household members have an illness with fever and/or a rash over a large part of the body that lasted longer than 4 days?

- ❑ Yes
- ❑ No
- ❑ Don't know/Not sure
- ❑ Refuse to answer

If you answered "yes", please go to **question 4**.
If you answered "no", "don't know", or refused to answer the question, please go to **question 6**.

4. Relationship to study child?

Person A _____
Person B _____
Person C _____

5. What was their diagnosis if known?

Person A _____
Person B _____
Person C _____

6. During the year before the study child was diagnosed with leukemia/June 30, 2001, did any playmates of the study child have an illness with fever and/or a rash over a large part of their body that lasted longer than 4 days?

- ❑ Yes
- ❑ No
- ❑ Don't know/Not sure
- ❑ Refuse to answer

If you answered "yes", please go to **question 7**.
If you answered "no", "don't know", or refused to answer the question, please go to **question 8**.

7. What was their diagnosis if known?

Person A _____
Person B _____
Person C _____

8. During the year before the study child was diagnosed with leukemia/June 30, 2001, did the study child routinely play in areas other than in his/her own yard or at school (for example, public playground, agricultural field, dumpsite or landfill)?

- ❑ Yes
- ❑ No
- ❑ Don't know/Not sure
- ❑ Refuse to answer

If you answered "yes", please go to **question 9**.
If you answered "no", "don't know", or refused to answer the question, please go to **question 10**.

9. Please specify where the study child played other than his/her own yard or at school.

_____

10. During the year before the study child was diagnosed with leukemia/June 30, 2001 did the study child ever swim in a natural body of water such as streams, ponds or lakes near Fallon, not including swimming pools?

- ❑ Yes
- ❑ No
- ❑ Don't know/Not sure
- ❑ Refuse to answer

If you answered "yes", please go to **question 11**.
If you answered "no", "don't know", or refused to answer the question, please go to **question 12**.

11. If yes, please describe the body(s) of water that the study child swam in.

_____
_____
_____

12. During the last 6 months, has the study child had any household or outdoor pets?

- ❑ Yes
- ❑ No
- ❑ Don't know/Not sure
- ❑ Refuse to answer

If you answered "yes", please go to **question 13**.
If you answered "no", "don't know", or refused to answer the question, please go to **the next section**.

13. If yes, what type of pet(s)?

_____
_____
_____

Part VI. School Attendance

The adult who can provide the most complete information about the study child's schooling history should complete this section. This includes all public or private day care, pre-school, nursery school, grade or elementary school, and junior high and high school.

1. Please complete the table below, starting with the school or day care center that the study child attended first.

What was the name of the school or daycare the study child attended?	**What city and state was the school/day care located?** If not U.S., please give country	**What dates did the study child attend this school/day care?**		**Approximately how many children were in the study child's class at this school/daycare center?**
		From (mm/yyyy)	**To** (mm/yyyy)	
Name of 1st school/day care				
Name of 2nd school/day care				
Name of 3rd school/day care				
Name of 4th school/day care				
Name of 5th school/day care				
Name of 6th school/day care				
Name of 7th school/day care				
Name of 8th school/day care				
Name of 9th school/day care				
Name of 10th school/day care				

If you need more space to write information about past schooling, please use the back of this sheet.

Part VII: Immunizations

This section asks for information about all the vaccinations or immunizations the study child has ever received. Please complete this form as accurately as possible – it is important that we have a complete record. This information can be obtained from many sources. The study child's current or previous doctor may complete this form, or a parent or guardian may copy the information from the study child's immunization record.

If you are sure that the study child received a particular vaccination/immunization, but you cannot find the record of it, please mark yes and estimate the month and year when he/she received that vaccination/immunization.

If the study child never received a particular vaccination/immunization, mark the "no" box.

If the study child received a vaccination/immunization that is not listed, please write this in one of the rows labeled "Other" and complete the row. Use the back of the page if you need more space.

Vaccinations/Immunizations	**Has the study child ever received this vaccination/ immunization?** Please mark one box	**Month(s) and year(s) when the study child received this vaccination/immunization** (mm/yyyy)	**Where did you obtain the information about this vaccination/ immunization?**
DPT or DTaP (Diphtheria, pertussis, tetanus)	❑ Yes ❑ No ❑ Don't know or Not sure		❑ Doctor's office ❑ Immunization record ❑ Memory/Estimate
DT or dT (Diphtheria, tetanus) vaccine	❑ Yes ❑ No ❑ Don't know or Not sure		❑ Doctor's office ❑ Immunization record ❑ Memory/Estimate
MMR (Combination of measles, mumps, and rubella) vaccine	❑ Yes ❑ No ❑ Don't know or Not sure		❑ Doctor's office ❑ Immunization record ❑ Memory/Estimate
Mumps vaccine	❑ Yes ❑ No ❑ Don't know or Not sure		❑ Doctor's office ❑ Immunization record ❑ Memory/Estimate
Measles (Rubeola) vaccine	❑ Yes ❑ No ❑ Don't know or Not sure		❑ Doctor's office ❑ Immunization record ❑ Memory/Estimate
Rubella (German measles) vaccine	❑ Yes ❑ No ❑ Don't know or Not sure		❑ Doctor's office ❑ Immunization record ❑ Memory/Estimate

Vaccinations/Immunizations	**Has the study child ever received this vaccination/ immunization?** Please mark one box	**Month(s) and year(s) when the study child received this vaccination/immunization** (mm/yyyy)	**Where did you obtain the information about this vaccination/ immunization?**
Chicken pox (Varicella) vaccine	❑ Yes ❑ No ❑ Don't know or Not sure		❑ Doctor's office ❑ Immunization record ❑ Memory/Estimate
Polio vaccine (Sabin) (Oral/Drops)	❑ Yes ❑ No ❑ Don't know or Not sure		❑ Doctor's office ❑ Immunization record ❑ Memory/Estimate
Polio vaccine (Salk) (IPV/Shot)	❑ Yes ❑ No ❑ Don't know or Not sure		❑ Doctor's office ❑ Immunization record ❑ Memory/Estimate
Hib (*Hemophilus influenzae* type b) vaccine	❑ Yes ❑ No ❑ Don't know or Not sure		❑ Doctor's office ❑ Immunization record ❑ Memory/Estimate
Hepatitis A vaccine	❑ Yes ❑ No ❑ Don't know or Not sure		❑ Doctor's office ❑ Immunization record ❑ Memory/Estimate
Hepatitis B vaccine	❑ Yes ❑ No ❑ Don't know or Not sure		❑ Doctor's office ❑ Immunization record ❑ Memory/Estimate
Yellow fever vaccine	❑ Yes ❑ No ❑ Don't know or Not sure		❑ Doctor's office ❑ Immunization record ❑ Memory/Estimate
Other vaccination/immunization not listed	❑ Yes ❑ No ❑ Don't know or Not sure		❑ Doctor's office ❑ Immunization record ❑ Memory/Estimate
Other vaccination/immunization not listed	❑ Yes ❑ No ❑ Don't know or Not sure		❑ Doctor's office ❑ Immunization record ❑ Memory/Estimate

2. Has anyone in the study child's household, other than the study child, received an oral polio vaccine in the last 2 months?

❑ Yes ❑ No ❑ Don't know or Not sure

3. If yes, what is the relationship of this person to the study child?

Person A: _____
Person B: _____
Person C: _____

4. Has anyone in the study child's household, other than the study child, received any vaccination in the last 30 days?

❑ Yes ❑ No ❑ Don't know or Not sure

5. If yes …

a. Who? _____ What immunization(s)? _____ ❑ Don't know

_____

_____

b. Who? _____ What immunization(s)? _____ ❑ Don't know

_____

_____

c. Who? _____ What immunization(s)? _____ ❑ Don't know

_____

_____

Part VIII: Travel History

In this section, we would like information about any travel, including trips within the United States and to other countries, that the study child may have taken between (date) and the study child's date of diagnosis/June 30, 2001. Please also include any trip the study child's mother took while she was pregnant with him/her.

A. Domestic Trips.

1. During the time period between (date) and the study child's date of diagnosis/June 30, 2001, has the study child (or the study child's mother during her pregnancy with the study child) taken a trip to another state within the United States that lasted *7 days or longer*? Think about trips that the study child may have taken over the holidays or during vacations. Please consider **only trips that lasted for 7 days or longer**.

- ❑ Yes
- ❑ No
- ❑ Don't know/Not sure
- ❑ Refuse to answer

If you answered "yes" to question 1, please go to **question 2.**
If you did answered "no", "don't know" or refused to answer the question, please **skip to the next section,** "**International Trips"**.

2. For each of these trips, please complete the following table to provide information about each trip the study child (or the study child's mother during her pregnancy with the study child) took between (date) and the study child's date of diagnosis/June 30, 2001.

Date of Trip (mm/yyyy)	**Destination** (city, state) If more than one state, please list all	**Total Duration of Trip** (number of days)

If you need additional space, please use the back of this page

B. International Trips.

1. During the time period between (date) and the study child's date of diagnosis/June 30, 2001, has the study child (or the study child's mother during her pregnancy with the study child) taken any trips to another country, for any length of time?
   - ❑ Yes
   - ❑ No
   - ❑ Don't know/Not sure
   - ❑ Refuse to answer

If you answered "yes" to the previous question, please go to **question 2.**
If you answered "no", "don't know", or refused to answer the question, then you are finished with this questionnaire. ***Thank you so much for your time!***

2. For each of these trips, please complete the following table to provide information about each trip the study child (or the study child's mother during her pregnancy with the study child) took between (date) and the study child's date of diagnosis/June 30, 2001.

Date of Trip (mm/yyyy)	**Destination** (city, country) If more than one country, please list all	**Total Duration of Trip** (number of days)

If you need additional space, please use the back of this page

You have reached the end of the mailing packet!

Thank you for taking the time to complete this mailing packet. We greatly appreciate your participation in this study!

If you have not already done so, please contact the CDC clinic offices in Fallon, Nevada, at 775/423-0617 to make an appointment for your family's visit. During that visit, we will collect biological samples (blood, urine, cheek cells) and conduct a personal interview. **Please remember to bring your consent form and completed question-naire with you to your clinic visit.**

If you need clarification of any item on any of the forms or have any questions about completing the forms, please do not hesitate to call us at 775/423-0617 or 888/608-4623. We will be happy to assist you.

Again, we thank you for your help with this important study.

Confidential Interview

Place ID label here

Part I. Confidential study subject and interviewee information

1. Date of Interview: _____ (mm/dd/yyyy)

2. Start time: ____ ____: ____ ____ a.m./p.m.

3. End time: ____ ____: ____ ____ a.m./p.m.

Interviewer: The first two pages contain personal information about the study subject. Once the interview is complete and the questionnaire has been filled out, please return to the project manager for filing. This page should not be copied or faxed.

- **Interviewer name** _____
- **Representing CDC and working with the Nevada State Health Division**
- **Confidential to the extent allowed by law**
- **Take your time**
- **Don't know is OK**

Interviewer: Verify study participant's information with interviewee.

4. **Study Child's Name and Address:**
5. **Study Child's Age in Years:**
6. **a) Study Child's Date of Birth:**
   b) Diagnosis Date (if a case):
7. **Study Child's Sex:**

8. Is this information correct? ❑ Yes ❑ No ❑ Don't know/Not sure ❑ Refused to answer

9. **Interviewer:** List any changes/corrections below:

_____
_____
_____
_____

Now I would like to ask you for some more information about you.

9. What is your full name? _____

10. What is your relationship to (child's name)? **Please mark one box.**

❑ Mother/ Stepmother	❑ Maternal grandmother	❑ Maternal grandfather	❑ Maternal aunt	❑ Maternal uncle	❑ Other _____
❑ Father/ Stepfather	❑ Paternal grandmother	❑ Paternal grandfather	❑ Paternal aunt	❑ Paternal uncle	

11. What is your address? _____
_____

12. What is your telephone number, with area code please? _____

Interviewer: If only **one person** participating in the study, **skip to question 17**.
If **two people** are participating in the study, please direct **question 13** to the other adult present for the interview.

13. What is your full name? _____

14. What is your relationship to (child's name)? **Please mark one box.**

❑ Mother/ Stepmother	❑ Maternal grandmother	❑ Maternal grandfather	❑ Maternal aunt	❑ Maternal uncle	❑ Other _____
❑ Father/ Stepfather	❑ Paternal grandmother	❑ Paternal grandfather	❑ Paternal aunt	❑ Paternal uncle	

15. If different from above address, what is your address?
_____
_____

16. If different from above number, what is your telephone number, with area code please?
_____

17. Are you the biological parent(s) of (child's name) ❑Yes ❑No ❑Refused to answer

Interviewer: If information on both biological parents is not captured above, please go to **question 18.**
If information for both biological parents captured above, please **go to next section.**

18. If no, what is/are the name(s) and phone numbers of the biological mother/father?
Mother _____Phone_____
Father _____Phone_____

Place ID label here

Interviewer: Please note that the child's name **should not** be written anywhere on the questionnaire from this point forward. The prompt ("child's name") is for interviewing purposes only. As you read the interview, insert the name of the child you are interviewing at this prompt.

Parts of the interview:

- **Residential history**
- **Medical history of Case/Control child**
- **Pregnancy history**
- **Family Medical history**
- **Nutrition**
- **Other Current Information**

Part II. Residential History

- **Thank you**
- **Different homes where you have lived**
- **Study Child's mother's homes(s) during pregnancy**
- **Study Child's home(s) between birth and June 30, 2001 for 6 months or longer**

Residence of (Child's Name)'s mother IF SHE LIVED HERE WHILE PREGNANT BUT BEFORE BIRTH. ***YELLOW***

Interviewer: Please refer to residence sheet provided. * fill-in & confirm

A. **__ of __**	A1. Date of residence * From: _____ (mm/yy) To: _____ (mm/yy)	**A2. Street ***	**A3. Town or City** *

A4. State/Country/Zip code*

A5. Number of people living in this residence * _____

The following questions refer to the source and use of water in this residence.

B. What was the main source of your drinking water while there? ☐ City or County ☐ Private Well ☐ Other specify _____ ☐ Community Well ☐ Spring ☐ Bottled ☐ Don't know	B1. Name the water company that provided this water (the place where you sent in your water bill) _____ ❑ Don't know/Not sure	**B2. If private well, tested?** ❑ Yes ❑ No If no, go to C	B3. If tested, indicate the following on the back of this page: **Date** ❑ **DK** **Who did testing** ❑ **DK** **Results** ❑ **DK**
C. What was the main source of water used for cooking? ☐ City or County ☐ Private Well ☐ Other specify _____ ☐ Community Well ☐ Spring ☐ Bottled ☐ Don't know	C1. Name the water company that provided this water (the place where you sent in your water bill) ❑ Same as above ❑ Don't know/Not sure	**C2. If private well, tested?** ❑ Yes ❑ No If no, go to D	C3. If tested, indicate the following on the back of this page: **Date** ❑ **DK** **Who did testing** ❑ **DK** **Results** ❑ **DK**
D. What was the main source of the water for bathing? ☐ City or County ☐ Private Well ☐ Other specify _____ ☐ Community Well ☐ Spring ☐ Don't know	D1. Name the water company that provided this water (the place where you sent in your water bill) ❑ Same as above ❑ Don't know/Not sure	**D2. If private well, tested?** ❑ Yes ❑ No If no, go to E	D3. If tested, indicate the following on the back of this page: **Date** ❑ **DK** **Who did testing** ❑ **DK** **Results** ❑ **DK**

E. Did you bathe or shower at this residence? ❑ Yes ❑ No

Now, I am going to ask you about substances that you used in and around this residence. Have you ever used any of the following….

H. Insecticides (e.g., spray to kill bugs) **(not a commercial service)** **H1. Indoor** ❑ Yes ❑ No ❑ DK **H2. Outdoor** ❑ Yes ❑ No ❑ DK	Indoor **H1.1** How often did you use these products? **(answer one only)** ❑ Daily ❑ Weekly ❑ Monthly ❑ Yearly ❑ DK	Outdoor **H2.1** How often did you use these products? **(answer one only)** ❑ Daily ❑ Weekly ❑ Monthly ❑ Yearly ❑ DK
I. Commercial pesticides **I1. Indoor** ❑ Yes ❑ No ❑ DK **I2. Outdoor** ❑ Yes ❑ No ❑ DK	Indoor **I1.1** How often did you use these products? **(answer one only)** ❑ Daily ❑ Weekly ❑ Monthly ❑ Yearly ❑ DK I1.2 Name of commercial pesticide company:	Outdoor **I2.1** How often did you use these products? **(answer one only)** ❑ Daily ❑ Weekly ❑ Monthly ❑ Yearly ❑ DK I2.2 Name of commercial pesticide company:
J. Weed Killer (herbicides) **J2. Outdoor** ❑ Yes ❑ No ❑ DK	**Intentionally Blank**	Outdoor **J2.1** How often did you use these products? **(answer one only)** ❑ Daily ❑ Weekly ❑ Monthly ❑ Yearly ❑ DK
K. Poison to kill rodents (e.g., rats mice, etc) **K1. Indoor** ❑ Yes ❑ No ❑ DK **K2. Outdoor** ❑ Yes ❑ No ❑ DK	Indoor **K1.1** How often did you use these products? **(answer one only)** ❑ Daily ❑ Weekly ❑ Monthly ❑ Yearly ❑ DK	Outdoor **K2.1** How often did you use these products? **(answer one only)** ❑ Daily ❑ Weekly ❑ Monthly ❑ Yearly ❑ DK

Residence of (Child's Name)'s mother THAT SHE LIVED IN DURING PREGNANCY AND AFTER BIRTH. ***BLUE***

Interviewer: Please refer to residence sheet provided. * fill-in & confirm

A. **__ of __**	A1. Date of residence * From: _____ To: _____ (mm/yy) (mm/yy)	**A2. Street ***	**A3. Town or City** *
A4 State/Country * Zip code*	A5. Number of people living in this residence * _____	A6. Did (Child's Name) share his/her bedroom at this residence * ❑ Yes ❑ No	

The following questions refer to the source and use of water in this residence.

B. What was the main source of your drinking water while there? ☐ City or County ☐ Private Well ☐ Other specify _____ ☐ Community Well ☐ Spring ☐ Bottled ☐ Don't know	B1. Name the water company that provided this water (the place where you sent in your water bill) _____ ❑ Don't know/Not sure	**B2. If private well, tested?** ❑ Yes ❑ No If no, go to C	B3. If tested, indicate the following on the back of this page: **Date** ❑ **DK** **Who did testing** ❑ **DK** **Results** ❑ **DK**
C. What was the main source of water used for cooking? ☐ City or County ☐ Private Well ☐ Other specify _____ ☐ Community Well ☐ Spring ☐ Bottled ☐ Don't know	C1. Name the water company that provided this water (the place where you sent in your water bill) ❑ Same as above ❑ Don't know/Not sure	**C2. If private well, tested?** ❑ Yes ❑ No If no, go to D	C3. If tested, indicate the following on the back of this page: **Date** ❑ **DK** **Who did testing** ❑ **DK** **Results** ❑ **DK**
D. What was the main source of the water for bathing? ☐ City or County ☐ Private Well ☐ Other specify _____ ☐ Community Well ☐ Spring ☐ Don't know	D1. Name the water company that provided this water (the place where you sent in your water bill) ❑ Same as above ❑ Don't know/Not sure	**D2. If private well, tested?** ❑ Yes ❑ No If no, go to E	D3. If tested, indicate the following on the back of this page: **Date** ❑ **DK** **Who did testing** ❑ **DK** **Results** ❑ **DK**
E. Did you bathe or shower at this residence? ❑ Yes ❑ No	F. Did (Child's Name) bathe or shower at this residence? ❑ Yes ❑ No		

G. Did (Child's Name) drink formula at this residence? ❑ Yes ❑ No (if no, go to H) ❑ DK/NA	G1. How often did you make the formula with water? ❑ Always ❑ Occasionally ❑ Never	G2. What was the main source of the water used for the formula? ☐ City or County ☐ Private Well ☐ Other specify _____ ☐ Community Well ☐ Spring ☐ Bottled ☐ Don't know	G3. If you made the formula with water, did you boil it before you used it? ❑ Yes ❑ No

Now, I am going to ask you about substances that you used in and around this residence. Have you ever used any of the following….

H. Insecticides (e.g., spray to kill bugs) **(not a commercial service)** **H1. Indoor** ❑ Yes ❑ No ❑ DK **H2. Outdoor** ❑ Yes ❑ No ❑ DK	Indoor **H1.1** How often did you use these products? **(answer one only)** ❑ Daily ❑ Weekly ❑ Monthly ❑ Yearly ❑ DK	Outdoor **H2.1** how often did you use these products? **(answer one only)** ❑ Daily ❑ Weekly ❑ Monthly ❑ Yearly ❑ DK
I. Commercial pesticides **I1. Indoor** ❑ Yes ❑ No ❑ DK **I2. Outdoor** ❑ Yes ❑ No ❑ DK	Indoor **I1.1** How often did you use these products? **(answer one only)** ❑ Daily ❑ Weekly ❑ Monthly ❑ Yearly ❑ DK **I1.2 Name of commercial pesticide company:**	Outdoor **I2.1** How often did you use these products? **(answer one only)** ❑ Daily ❑ Weekly ❑ Monthly ❑ Yearly ❑ DK **I2.2 Name of commercial pesticide company:**
J. Weed Killer (herbicides) **J2. Outdoor** ❑ Yes ❑ No ❑ DK	**Intentionally Blank**	Outdoor **J2.1** How often did you use these products? **(answer one only)** ❑ Daily ❑ Weekly ❑ Monthly ❑ Yearly ❑ DK
K. Poison to kill rodents (e.g., rats mice, etc) **K1. Indoor** ❑ Yes ❑ No ❑ DK **K2. Outdoor** ❑ Yes ❑ No ❑ DK	Indoor **K1.1** How often did you use these products? **(answer one only)** ❑ Daily ❑ Weekly ❑ Monthly ❑ Yearly ❑ DK	Outdoor **K2.1** How often did you use these products? **(answer one only)** ❑ Daily ❑ Weekly ❑ Monthly ❑ Yearly ❑ DK

Places where (Child's Name) lived for <u>at least 6 months</u> in a row AFTER HE/SHE WAS BORN. ***ORANGE***

Interviewer: Please refer to residence sheet provided. * fill-in & confirm

A. **__ to __**	A1. Dates of residence * From: _____ (mm/yy) To: _____ (mm/yy)	**A2. Street ***	**A3. Town or City** *
A4 State/Country * Zip code*	A5. Number of people living in this residence * _____	A6. Did (Child's Name) share his/her bedroom at this residence * ❑ Yes ❑ No	

The following questions refer to the source and use of water in this residence.

B. What was the <u>main</u> source of your drinking water while there? ☐ City or County ☐ Private Well ☐ Other specify _____ ☐ Community Well ☐ Spring ☐ Bottled ☐ Don't know	B1. Name the water company that provided this water (the place where you sent in your water bill) _____ ❑ Don't know/Not sure	**B2. If private well, tested?** ❑ Yes ❑ No If no, go to C	B3. If tested, indicate the following on the back of this page: **Date** ❑ **DK** **Who did testing** ❑ **DK** **Results** ❑ **DK**
C. What was the <u>main</u> source of water used for cooking? ☐ City or County ☐ Private Well ☐ Other specify _____ ☐ Community Well ☐ Spring ☐ Bottled ☐ Don't know	C1. Name the water company that provided this water (the place where you sent in your water bill) ❑ Same as above ❑ Don't know/Not sure	**C2. If private well, tested?** ❑ Yes ❑ No If no, go to D	C3. If tested, indicate the following on the back of this page: **Date** ❑ **DK** **Who did testing** ❑ **DK** **Results** ❑ **DK**
D. What was the <u>main</u> source of the water for bathing? ☐ City or County ☐ Private Well ☐ Other specify _____ ☐ Community Well ☐ Spring ☐ Don't know	D1. Name the water company that provided this water (the place where you sent in your water bill) ❑ Same as above ❑ Don't know/Not sure	**D2. If private well, tested?** ❑ Yes ❑ No If no, go to E	D3. If tested, indicate the following on the back of this page: **Date** ❑ **DK** **Who did testing** ❑ **DK** **Results** ❑ **DK**
E. Did you bathe or shower at this residence? ❑ Yes ❑ No	F. Did (Child's Name) bathe or shower at this residence? ❑ Yes ❑ No		

G. Did (Child's Name) drink formula at this residence? ❑ Yes ❑ No (if no, go to H) ❑ DK/NA	G1. How often did you make the formula with water? ❑ Always ❑ Occasionally ❑ Never	G2. What was the main source of the water used for the formula? ☐ City or County ☐ Private Well ☐ Other specify _____ ☐ Community Well ☐ Spring ☐ Bottled ☐ Don't know	G3. If you made the formula with water, did you boil it before you used it? ❑ Yes ❑ No

Now, I am going to ask you about substances that you used in and around this residence. Have you ever used any of the following….

H. Insecticides (e.g., spray to kill bugs) **(not a commercial service)** **H1. <u>Indoor</u>** ❑ Yes ❑ No ❑ DK **H2. <u>Outdoor</u>** ❑ Yes ❑ No ❑ DK	<u>Indoor</u> **H1.1** How often did you use these products? **(answer one only)** ❑ Daily ❑ Weekly ❑ Monthly ❑ Yearly ❑ DK	<u>Outdoor</u> **H2.1** how often did you use these products? **(answer one only)** ❑ Daily ❑ Weekly ❑ Monthly ❑ Yearly ❑ DK
I. Commercial pesticides **I1. <u>Indoor</u>** ❑ Yes ❑ No ❑ DK **I2. <u>Outdoor</u>** ❑ Yes ❑ No ❑ DK	<u>Indoor</u> **I1.1** How often did you use these products? **(answer one only)** ❑ Daily ❑ Weekly ❑ Monthly ❑ Yearly ❑ DK **I1.2 Name of commercial pesticide company:**	<u>Outdoor</u> **I2.1** How often did you use these products? **(answer one only)** ❑ Daily ❑ Weekly ❑ Monthly ❑ Yearly ❑ DK **I2.2 Name of commercial pesticide company:**
J. Weed Killer (herbicides) **J2. <u>Outdoor</u>** ❑ Yes ❑ No ❑ DK	**Intentionally Blank**	<u>Outdoor</u> **J2.1** How often did you use these products? **(answer one only)** ❑ Daily ❑ Weekly ❑ Monthly ❑ Yearly ❑ DK
K. Poison to kill rodents (e.g., rats mice, etc) **K1. <u>Indoor</u>** ❑ Yes ❑ No ❑ DK **K2. <u>Outdoor</u>** ❑ Yes ❑ No ❑ DK	<u>Indoor</u> **K1.1** How often did you use these products? **(answer one only)** ❑ Daily ❑ Weekly ❑ Monthly ❑ Yearly ❑ DK	<u>Outdoor</u> **K2.1** How often did you use these products? **(answer one only)** ❑ Daily ❑ Weekly ❑ Monthly ❑ Yearly ❑ DK

Part III. Medical History

- **Three parts: Child, Mother's pregnancy, Family**

A. Child's Medical History

a. Illnesses

Interviewer: Explanations/descriptions of illnesses will follow the illness name. Read the prompt only upon request for explanation.

Before June 30, 2001, was (Child's Name) diagnosed by a physician with …	**YES**	**NO**	**DK**	**Did illnesses occur more than once?**		**At what age was (Child's Name) first diagnosed with this illness?**
				YES	**NO**	
Arthritis (joint pain with heat/swelling/ inflammation of the joint for 3 days or longer, or refusal to bear weight/move an arm or leg for 3 days or longer, or limping for 3 days or more. **Interviewer: Record only symptoms NOT due to injury (for example, no broken bone, sprain, fall, etc.)**						
Fever of 101 degrees F or higher lasting for 5 days or more.						
Rash over large areas of the body that stayed for 3 days or greater and **does not** include measles, chicken pox, poison ivy/oak, bites, or allergic reaction.						
Autoimmune disorder for example, Lupus, thyroid disease						
Anemia (low red blood count or hemoglobin)						
Aplastic anemia (very low red blood count)						
Neutropenia or low white blood count						
Thrombocytopenia or low platelets (example: ITP or idiopathic thrombocytopenia purpura)						
Infectious mononucleosis (EBV) (viral illness)						
Diarrhea (3 or more loose stools/day) without blood lasting 5 days or >, or treated with antibiotics by a doctor						
Bloody diarrhea of any duration						
Hepatitis (inflammation of the liver from infection/medications)						
Allergic skin rash (example is eczema)						
Hay fever						
Asthma						
Chicken pox (Varicella)						
German measles (Rubella)						
Measles (Rubeola)						
Mumps						
Fifth's disease (infection that gives a "slapped cheek" appearance						
Fever blisters ("cold sores", herpes simplex)						

Before June 30, 2001, was (Child's Name) <u>diagnosed by a physician</u> with …	**YES**	**NO**	**DK**	**Did illnesses occur more than once?**		**At what age was (Child's Name) first diagnosed with this illness?**
				YES	**NO**	
Urinary tract infection						
Epilepsy, seizures, or convulsions						
Severe injury to the head requiring medical attention						
Immune deficiency or immunosuppression (for example: HIV)						
CMV or Cytomegalovirus (congenital infection or infection in children with an immune deficiency)						
Toxoplasmosis (congenital infection or infection in children with an immune deficiency) ("cat litter disease")						
Organ transplant						

2. Has a physician, nurse practitioner, or other health professional ever told you that (Child's Name) had any other serious disease? **Please mark one**

- ❑ Yes ❑ Don't know/Not sure
- ❑ No ❑ Refused to answer

Interviewer: If subject does answer "yes", go to **question 3**. If subject answers "no", don't know, or refused to answer go to next page.

3. If yes, what was the diagnosis(es)?

_____

_____

b. Medical procedures

I am now going to ask you about medical procedures (Child's Name) may have received from (dob) to June 30, 2001.

1. Before June 30, 2001, did (Child's Name) ever have an x-ray or a radiology scan, excluding dental x-rays? …"not related to his/her diagnosis", **if a case.**

❑ Yes ❑ Don't know/Not sure
❑ No ❑ Refused to answer

Interviewer: If subject answer "yes", please go to **question 2** If subject answers "no", don't know, or refused to answer go to **question 3**

2. Can you tell me what type of x-ray or radiology scan (Child's Name) received and when he/she received it? Remember, we are only talking about the time period between (dob) and June 30, 2001.

Type:	**On what part(s) of the body?**	**How long before June 30, 2001 did (Child's Name) have this x-ray/scan done?**
❑Regular (diagnostic) x-ray	_____	____ ❑days ❑months ❑years
	_____	____ ❑days ❑months ❑years
	_____	____ ❑days ❑months ❑years
❑CT or "CAT" scan	_____	____ ❑days ❑months ❑years
	_____	____ ❑days ❑months ❑years
❑MRI	_____	____ ❑days ❑months ❑years
	_____	____ ❑days ❑months ❑years
❑Upper GI		____ ❑days ❑months ❑years
❑Other		____ ❑days ❑months ❑years
❑Don't know or not sure		

_____

3. Has (Child's Name) had his/her tonsils removed?
   - ❑ Yes, At what age did (Child's Name) have his/her tonsils removed? _____
   - ❑ No
   - ❑ Don't know/Not sure
   - ❑ Refused to answer

4. Has (Child's Name) had his/her appendix removed?
   - ❑ Yes, At what age did (Child's Name) have his/her appendix removed? _____
   - ❑ No
   - ❑ Don't know/Not sure
   - ❑ Refused to answer

I am now going to ask you about medications (Child's Name) may have taken prior to June 30, 2001 and then his/her present medications.

c. (Child's Name)'s Medications

Interviewer: **Hand the interviewee the medication list.**
Mark Yes/No/DK one time for each row (medication group), even if (Child's Name) took several medicines listed in that section.

1.

Let's start with medications used to treat asthma, pain or inflammation that (Child's Name) may have taken between (dob) and June 30, 2001….	**YES**	**NO**	**DK**	**Age** Approximate age that (Child's Name) took the medication	**Duration** Approximate length of time (in days) that the child took the medication
Azulfidine or Sulfasalazine (used in inflammatory bowel disease)					
Azolid or Phenylbutazone					
Corticosteroids/Glucocorticoids: Cortisone Hydrocortisone tablets (*not cream)* Methylprednisolone or Prednisone Pediapred oral solution or Prelone syrup Solu-Medrol					
Cuprimine or Depen or Penicillamine					
Enbrel or eternacept (immunosuppressant agent)					
Imuran or azathioprine (immunosuppressant agent)					
Inhaler for asthma: *[List names]*					
Plaquenil or Chloroquine					
Rheumatrex or Methotrexate					
Cyclosporin					
Chloramphenicol or Chloromycetin					

2. Before June 30, 2001, did (Child's Name) ever take any home remedies, folk medicines, or herbal products for at least one week?

- ❑ Yes ❑ Don't know/Not sure
- ❑ No ❑ Refused to answer

Interviewer: If subject answer "yes", please go to **question 3**
If subject answers "no", "don't know" or refuses to answer, please go to **question 4**

3. Can you tell me which home remedies, folk medicines, or herbal products (Child's Name) took for at least one week? _____

_____

4. **At present**, is (Child's Name) taking any over the counter medications, prescription medications, home remedies, folk medicines, vitamins, or herbal products?

- ❑ Yes ❑ Don't know/Not sure
- ❑ No ❑ Refused to answer

Interviewer: If subject answered "yes", please go to **question 5.**
If subject answered "no", **please go to the next section**

5. Can you tell me which over the counter medications, prescription medications, home remedies, folk medicines, or herbal products (Child's Name) is taking at present?

_____

_____

B. Maternal Pregnancy History Source: _____

OK. Now I am going to ask you some questions specifically about your pregnancy with (Child's Name) and some questions about (Child's Name) when he/she was a baby.

a. Pregnancy with Participating Child

1. Did you or (Child's Name)'s father take any medications or have any medical procedures to help you become pregnant with (Child's Name)?

❑ Yes ❑ Don't know/Not sure
❑ No ❑ Refused to answer

Interviewer: If subject answered "yes", please go to **question 2.**
If subject answered "no, or "don't know" or refused to answer, please go to **question 3.**

2. Which medications or procedures were used?

_____
_____
_____

3. At the time you became pregnant with (Child's Name), were you using any method of contraception or birth control?

❑ Yes ❑ Don't know/Not sure
❑ No ❑ Refused to answer

Interviewer: If subject answered "yes", go to **question 4**.
If subject answered "no, or "don't know" or refused to answer, please go to **question 5.**

4. Which method(s) were you using?

_____
_____

5. When you were pregnant with (Child's Name), how far in your pregnancy were you when you had your first prenatal health care visit? _____ (**months**) of pregnancy

6. We are interested in any illnesses or medical conditions you may have had during your pregnancy with (Child's Name). I am going to read you a list of medical conditions. Please tell me if you had that medical condition when you were pregnant with (Child's Name).

During your pregnancy with (Child's Name), did you have…	If **yes**, go to next column If **no,** go to the next row	**During which month(s) of your pregnancy did you have this condition?** (record the range if applicable)	**Did you take medication(s) for [the condition]?** **Interviewer:** If yes, go to next column	**Which medication(s) did you take?**	**During what month(s) of your pregnancy did you take this medication?** (record the range if applicable)	**Medication 1** **How long was this taken during your pregnancy** (mark only one box)	**Medication 2** **How long was this taken during your pregnancy** (mark only one box)
Diabetes (including gestational diabetes; sometimes called sugar diabetes or diabetes mellitus)	❑ Yes ❑ No ❑ Don't know or Not sure	_____ month(s) ❑ Don't know	❑ Yes ❑ No ❑ Don't know or Not sure	1._____ 2._____ ❑ Don't know/Not sure	_____ month(s) _____ month(s)	❑ ___ days ❑ ___ weeks ❑ ___ months ❑ DK	❑ ___ days ❑ ___ weeks ❑ ___ months ❑ DK
High blood pressure	❑ Yes ❑ No ❑ Don't know or Not sure	_____ month(s) ❑ Don't know	❑ Yes ❑ No ❑ Don't know or Not sure	1. _____ 2._____ ❑ Don't know/Not sure	_____ month(s) _____ month(s)	❑ ___ days ❑ ___ weeks ❑ ___ months ❑ DK	❑ ___ days ❑ ___ weeks ❑ ___ months ❑ DK
Epilepsy (seizures)	❑ Yes ❑ No ❑ Don't know or Not sure	_____ month(s) ❑ Don't know	❑ Yes ❑ No ❑ Don't know or Not sure	1. _____ 2._____ ❑ Don't know/Not sure	_____ month(s) _____ month(s)	❑ ___ days ❑ ___ weeks ❑ ___ months ❑ DK	❑ ___ days ❑ ___ weeks ❑ ___ months ❑ DK
Flu	❑ Yes ❑ No ❑ Don't know or Not sure	_____ month(s) ❑ Don't know	❑ Yes ❑ No ❑ Don't know or Not sure	1. _____ 2._____ ❑ Don't know/Not sure	_____ month(s) _____ month(s)	❑ ___ days ❑ ___ weeks ❑ ___ months ❑ DK	❑ ___ days ❑ ___ weeks ❑ ___ months ❑ DK
Kidney, bladder, or urinary tract infection	❑ Yes ❑ No ❑ Don't know or Not sure	_____ month(s) ❑ Don't know	❑ Yes ❑ No ❑ Don't know or Not sure	1. _____ 2._____ ❑ Don't know/Not sure	_____ month(s) _____ month(s)	❑ ___ days ❑ ___ weeks ❑ ___ months ❑ DK	❑ ___ days ❑ ___ weeks ❑ ___ months ❑ DK
Pelvic inflammatory disease (PID, vaginal discharge and lower abdominal pain)	❑ Yes ❑ No ❑ Don't know or Not sure	_____ month(s) ❑ Don't know	❑ Yes ❑ No ❑ Don't know or Not sure	1. _____ 2._____ ❑ Don't know/Not sure	_____ month(s) _____ month(s)	❑ ___ days ❑ ___ weeks ❑ ___ months ❑ DK	❑ ___ days ❑ ___ weeks ❑ ___ months ❑ DK
Fever	❑ Yes ❑ No ❑ Don't know or Not sure	_____ month ❑ Don't know	❑ Yes ❑ No ❑ Don't know or Not sure	1. _____ 2._____ ❑ Don't know/Not sure	_____ month(s) _____ month(s)	❑ ___ days ❑ ___ weeks ❑ ___ months ❑ DK	❑ ___ days ❑ ___ weeks ❑ ___ months ❑ DK

7. When you were pregnant with (Child's Name), did you take any other medications that you haven't already mentioned, including over-the-counter medications, prescription medications, home remedies, folk remedies, vitamins, or herbal remedies?

❑ Yes ❑ Don't know/Not sure
❑ No ❑ Refused to answer

Interviewer: If subject answered "yes", please go to **question 8**.
If subject answered "no" or "don't know" or refused to answer, please go to **question 10**.

8. Which medications or remedies did you take?

a. _____
b. _____
c. _____
d. _____
❑ Unknown

9. During what trimester did you use those medicines or remedies?
Trimester 1, 2, and/or 3

a. _____
b. _____
c. _____
d. _____
❑ Unknown

OK. I'm now going to ask you some questions about certain medical procedures you may have had while you were pregnant with (Child's Name).

10. During your pregnancy, did you have any x-rays or radiology scans, excluding dental x-rays and ultrasounds?

❑ Yes ❑ Don't know/Not sure
❑ No ❑ Refused to answer

Interviewer: If subject answered "yes", go to **question 11**.
If subject answered "no" or "don't know" or refused to answer, please go to **question 15**.

11. How many x-rays or radiology scans did you have? _____(**fill in number**)

12. Please consider the <first> x-ray or scan that you had:
    a. What kind of x-ray or scan did you have?
        ❑Regular (diagnostic) x-ray
        ❑CT or "CAT" scan
        ❑MRI
        ❑Upper GI
        ❑Don't know or not sure
        ❑Other _____

    b. What part of the body was x-rayed or scanned? _____
    c. In which month of pregnancy was this x-ray or scan done? _____

13. Please consider the <second> x-ray or scan that you had:
    a. What kind of x-ray or scan did you have?
        ❑Regular (diagnostic) x-ray
        ❑CT or "CAT" scan
        ❑MRI
        ❑Upper GI
        ❑Don't know or not sure
        ❑Other __

    b. What part of the body was x-rayed or scanned? _____
    c. In which month of pregnancy was this x-ray or scan done? _____

14. Please consider the <third> x-ray or scan that you had:
    a. What kind of x-ray or scan did you have?
        ❑Regular (diagnostic) x-ray
        ❑CT or "CAT" scan
        ❑MRI
        ❑Upper GI
        ❑Don't know or not sure
        ❑Other __

    b. What part of the body was x-rayed or scanned? _____
    c. In which month of pregnancy was it done? _____

(Continue on back of page if more than three x-rays/scans.)

The next set of questions also relate to your activities or behaviors during your pregnancy with (Child's Name).

15. Did you have any pets while you were pregnant with (Child's Name)?
- ❑ Yes ❑ Don't know/Not sure
- ❑ No ❑ Refused to answer

Interviewer: If subject answered "yes", please go to **question 16.**
If subject answered "no" or "don't know" or refused to answer, please go to **question 17**.

16. What type of pet(s) did you have? _____

17. During your pregnancy with (Child's Name), did you live or work on an agricultural or livestock farm, or a ranch?
- ❑ Yes ❑ Don't know/Not sure
- ❑ No ❑ Refused to answer

Interviewer: If subject answered "yes", please go to **question 20.**
If subject answered "no" or "don't know" or refused to answer, please go to **question 18**.

18. Even though you did not live or work on a farm or ranch, did you visit one of these places while you were pregnant with (Child's Name)?
- ❑ Yes ❑ Don't know/Not sure
- ❑ No ❑ Refused to answer

Interviewer: If subject answered "yes", please go to **question 19.**
If subject answered "no" or "don't know" or refused to answer, please go to **question 20**.

19. On average, how many times during your pregnancy did you visit the farm or ranch?
❑ 0-5 ❑ 6-10 ❑ 11-20 ❑ more than 20 days

20. During your pregnancy with (Child's Name), did you ever swim in natural bodies of waters, such as streams, ponds, lakes or oceans? **This does not include swimming pools**.
- ❑ Yes ❑ Don't know/Not sure
- ❑ No ❑ Refused to answer

Interviewer: If subject answered "yes", please go to **question 21.**
If subject answered "no" or "don't know" or refused to answer, please go to **question 22**.

21. Can you please tell me which body of water or type of body of water (e.g. pond) you swam in during your pregnancy with (Child's Name).

Name (Type) of body of water	*County*	*State*

22. Looking at this list, did you use any of these chemicals/substances during your pregnancy?

Interviewer: Please show study participants the list of chemicals. Mark all that apply.

Mother

❑ Solvents (degreasers) used to clean mechanical parts	❑ Don't know
❑ Glues/adhesives	❑ Don't know
❑ Varnishes/lacquers	❑ Don't know
❑ Pesticides (for example, insect repellant, lawn treatment)	❑ Don't know
❑ Rust preventatives (for example, Rustoleum)	❑ Don't know
❑ Rubber cement	❑ Don't know
❑ *Dyes and pigments*	❑ *Don't know*
❑ Petroleum products (for example, motor oil, gasoline)	❑ Don't know
❑ Metals	❑ Don't know
❑ Paint, paint thinners, or paint strippers	❑ Don't know
❑ Other _____	❑ Don't know
❑ None	
❑ Refused to answer	

23. Have you <u>ever</u> smoked cigarettes?

❑ Yes ❑ Don't know/Not sure
❑ No ❑ Refused to answer

Interviewer: If subject answered "yes", please go to **question 24.**
If subject answered "no" or "don't know" or refused to answer, please go to **question 29.**

24. Were you smoking cigarettes during the three months before you were pregnant with (Child's Name)?

❑ Yes ❑ Don't know/Not sure
❑ No ❑ Refused to answer

Interviewer: If subject answered "yes", please go to **question 25**.
If subject answered "no" or "don't know" or refused to answer, please go to **question 26.**

25. During the three months prior to your pregnancy with (Child's Name), on average, about how many cigarettes did you smoke per week?

_____**(fill in number) [1 pack = 20 cigarettes]**

26. Did you smoke cigarettes at any time during your pregnancy with (Child's Name)?

❑ Yes ❑ Don't know/Not sure
❑ No ❑ Refused to answer

Interviewer: If subject answered "yes", please go to **question 27**.
If subject answered "no" or "don't know" or refused to answer, please go to **question 29.**

27. How many months in total during your pregnancy did you smoke cigarettes? ___

28. During the time you smoked during your pregnancy, on average, about how many cigarettes did you smoke per week? _____(**fill in number**) **[1 pack = 20 cigarettes]**

29. While you were pregnant with (Child's Name), did anyone else regularly smoke cigarettes around you in the house, at your workplace or at your school, if you attended school?
- ❑ Yes ❑ Don't know/Not sure
- ❑ No ❑ Refused to answer

Interviewer: If subject answered "yes", go to **question 30**.
If subject answered "no", "don't know" or refused to answer, please go to **question 33**.

30. During which trimester(s) of your pregnancy, did this person(s) smoke cigarettes around you in the house, at your workplace or at your school?

Trimester 1, 2, and/or 3

Person A _____
Person B _____
Person C _____

31. On average, how many days per month did this person(s) smoke cigarettes around you?

Person A	❑ 0-5	❑ 6-10	❑ 11-20	❑ more than 20 days
Person B	❑ 0-5	❑ 6-10	❑ 11-20	❑ more than 20 days
Person C	❑ 0-5	❑ 6-10	❑ 11-20	❑ more than 20 days

32. How many cigarettes per day did (s)he regularly smoke around you? **[1 pack=20 cigarettes]**

Person A ____ per day
Person B ____ per day
Person C ____ per day

33. Did you drink alcohol during your pregnancy with (Child's Name)?
- ❑ Yes ❑ Don't know/Not sure
- ❑ No ❑ Refused to answer

Interviewer: If subject answered "yes", please go to **question 34**.
If subject answered "no", "don't know" or refused to answer, please go to **Section b.** below.

34. During which months of your pregnancy did you drink alcohol and how much did you drink during these months? One drink is equivalent to one can of beer, one 8oz glass of wine, or one shot of liquor such as whiskey or vodka. **Write number of drinks consumed in the space provided below the months the mother drank.**

Months	1	2	3	4	5	6	7	8	9	10
Number of drinks per month?										

b. Delivery and Feeding of the Participating Child

Thank you for answering my questions about your pregnancy with (Child's Name). Now I am going to ask you some questions about (Child's Name)'s birth and how he/she was fed as an infant.

35. How much did (Child's Name) weigh at birth? _____ pounds ____ ounces

36. What was (Child's Name) length at birth? _____ inches ❑ Don't know/Not sure

37. Did you ever breastfeed (Child's Name)?
❑ Yes ❑ Don't know/Not sure
❑ No ❑ Refused to answer

Interviewer: If subject answered "yes", please go to **question 38**.
If subject answered "no", "don't know", or refused to answer, please go to **question 44**.

38. How long did you breastfeed him/her? _____ weeks _____ months

39. Did you ever have a fever of 101 degrees F or higher lasting 5 days or longer while breastfeeding (Child's Name)?
❑ Yes ❑ Don't know/Not sure
❑ No ❑ Refused to answer

40. We're interested in learning about any medicines or preparations that you may have taken during the time you breastfed (Child's Name); these include injections, and drugs you took by mouth. For each medicine or preparation, please tell me if you took it when you were breastfeeding (Child's Name).

While you were breastfeeding (Child's Name), did you take…	**Interviewer:** If yes, go to next column	**How frequently during this time did you use the medications?**
Multi-vitamin supplements	❑ Yes ❑ No ❑ Don't know or Not sure	❑ Daily ❑ Weekly ❑ Monthly ❑ Yearly ❑ Don't know
Antibiotics	❑ Yes ❑ No ❑ Don't know or Not sure	❑ Daily Total # days ____ ❑ Weekly ❑ Monthly ❑ Yearly ❑ Don't know

While you were breastfeeding (Child's Name), did you take…	**Interviewer:** If yes, go to next column	**How frequently during this time did you use the medications?**
Steroids (for example, Prednisone, Prelone, Pediapred, Cortisone, Cortef, Hydrocortone, or Medrol) **[Interviewer:** please note Clinical names: prednisolone, methylprednisolone, or hydrocortisone**]** (NOT CREAM)	❑ Yes ❑ No ❑ Don't know or Not sure	❑ Daily Total # days ____ ❑ Weekly ❑ Monthly ❑ Yearly ❑ Don't know
Were there any other medications/herbal products you took while you were breastfeeding? _____ _____ _____	❑ Yes ❑ No ❑ Don't know or Not sure	❑ Daily Total # days ____ ❑ Weekly ❑ Monthly ❑ Yearly ❑ Don't know

41. Did you receive vaccines for polio, hepatitis B, flu or any other disease while breastfeeding (Child's Name)?
    - ❑ Yes ❑ Don't know/Not sure
    - ❑ No ❑ Refused to answer

Interviewer: If subject answered "yes", please go to **question 42**.
If subject answered "no", "don't know", or refused to answer, please go to **question 43**.

42. Which vaccines did you receive while breastfeeding (Child's Name)?

_____
_____

43. How old was (Child's Name) when you started to supplement breastfeeding with formula or food? _____ months ❑ Don't know/Not sure

44. Did (Child's Name) drink soy-based infant formula?
    - ❑ Yes ❑ Don't know/Not sure
    - ❑ No ❑ Refused to answer

Interviewer: If subject answered "yes", please go to **question 45**.
If subject answered "no", don't know", or refused to answer, please go to **question 46**.

45. How long did (Child's Name) drink soy-based infant formula? _____ months
❑ Don't know/Not sure

You may consider these next few questions to be sensitive, but I would like to reassure you that

this information will be kept completely confidential to the extent allowed by law. Would you be more comfortable answering these questions to me directly, with no one else in the room?

46. During or just before your pregnancy did you or (Child's Name)'s father use any recreational drugs, such as cocaine, marijuana, LSD, amphetamines or heroin?

Mother
❑ Yes ❑ Don't know/Not sure
❑ No ❑ Refused to answer

Father
❑ Yes ❑ Don't know/Not sure
❑ No ❑ Refused to answer

47. **If yes**, please list the drug(s).

Mother
A. Drug 1: _____
Drug 2:_____

Father
B. Drug 1: _____
Drug 2:_____

48. Do you **presently** use any recreational drugs, such as cocaine, marijuana, LSD, amphetamines or heroin?

Mother/Guardian 1
❑ Yes ❑ Don't know/Not sure
❑ No ❑ Refused to answer

Father/Guardian 2
❑ Yes ❑ Don't know/Not sure
❑ No ❑ Refused to answer

49. **If yes**, please list the drug(s) and when you last used it.

Mother/Guardian 1
A. Drug 1: _____
Drug 2:_____

B. Drug 1: When last used? _____
Drug 2: When last used? _____

Father/Guardian 2
A. Drug 1: _____
Drug 2:_____

B. Drug 1: When last used? _____
Drug 2: When last used? _____

C. Family Medical History

- **Final section of Medical History segment**
- **Questions about family history of cancer and birth defects.**
- **Do you need a bathroom break? Something to drink? (Don't forget Urine Cups)**

Interviewer: Repeat the questions in each column heading for each relative listed in the first column.

Think about (Child's Name)'s (relative from list below)…	**Was (this relative) ever diagnosed with any type of cancer?** if "yes" go to next column	**What type of cancer did (this relative) have? What part of the body was affected by cancer?**	**How old was (this relative) when diagnosed?** (years)	**Was (this relative) born with a birth defect?** if "yes" go to next column	**What type of birth defect was (this relative) born with?**
Mother (Biological)	❑ Yes ❑ No ❑ Don't know/Not sure		❑ DK/Not sure	❑ Yes ❑ No ❑ Don't know/Not sure	
Father (Biological)	❑ Yes ❑ No ❑ Don't know/Not sure		❑ DK/Not sure	❑ Yes ❑ No ❑ Don't know/Not sure	
Full Sister ❑ NA	❑ Yes ❑ No ❑ Don't know/Not sure		❑ DK/Not sure	❑ Yes ❑ No ❑ Don't know/Not sure	
Full Sister ❑ NA	❑ Yes ❑ No ❑ Don't know/Not sure		❑ DK/Not sure	❑ Yes ❑ No ❑ Don't know/Not sure	
Full Sister ❑ NA	❑ Yes ❑ No ❑ Don't know/Not sure		❑ DK/Not sure	❑ Yes ❑ No ❑ Don't know/Not sure	
Full Brother ❑ NA	❑ Yes ❑ No ❑ Don't know/Not sure		❑ DK/Not sure	❑ Yes ❑ No ❑ Don't know/Not sure	
Full Brother ❑ NA	❑ Yes ❑ No ❑ Don't know/Not sure		❑ DK/Not sure	❑ Yes ❑ No ❑ Don't know/Not sure	
Full Brother ❑ NA	❑ Yes ❑ No ❑ Don't know/Not sure		❑ DK/Not sure	❑ Yes ❑ No ❑ Don't know/Not sure	

Think about (Child's Name)'s <u>(relative from list below)</u>.	**Was <u>(this relative)</u> ever diagnosed with any type of cancer?** if "yes" go to next column	**What type of cancer did <u>(this relative)</u> have? What part of the body was affected by cancer?**	**How old was <u>(this relative)</u> when diagnosed?** (years)	**Was <u>(this relative)</u> born with a birth defect?** if "yes" go to next column	**What type of birth defect was <u>(this relative)</u> born with?**
Maternal half-brother ❑ NA [Brother of (Child's Name) who has the **same mother** but **different father**]	❑ Yes ❑ No ❑ Don't know/Not sure		❑ DK/Not sure	❑ Yes ❑ No ❑ Don't know/Not sure	
Maternal half-sister ❑ NA [Sister of (Child's Name) who has the **same mother** but **different father**]	❑ Yes ❑ No ❑ Don't know/Not sure		❑ DK/Not sure	❑ Yes ❑ No ❑ Don't know/Not sure	
Paternal half-brother ❑ NA [Brother of (Child's Name) who has the **same father** but **different mother**]	❑ Yes ❑ No ❑ Don't know/Not sure		❑ DK/Not sure	❑ Yes ❑ No ❑ Don't know/Not sure	
Paternal half-sister ❑ NA [Sister of (Child's Name) who has the **same father** but **different mother**]	❑ Yes ❑ No ❑ Don't know/Not sure		❑ DK/Not sure	❑ Yes ❑ No ❑ Don't know/Not sure	
Maternal Grandmother	❑ Yes ❑ No ❑ Don't know/Not sure		❑ DK/Not sure	❑ Yes ❑ No ❑ Don't know/Not sure	
Maternal Grandfather	❑ Yes ❑ No ❑ Don't know/Not sure		❑ DK/Not sure	❑ Yes ❑ No ❑ Don't know/Not sure	
Paternal Grandmother	❑ Yes ❑ No ❑ Don't know/Not sure		❑ DK/Not sure	❑ Yes ❑ No ❑ Don't know/Not sure	
Paternal Grandfather	❑ Yes ❑ No ❑ Don't know/Not sure		❑ DK/Not sure	❑ Yes ❑ No ❑ Don't know/Not sure	

Other (with cancer or birth defect) _____ ❑ NA	❑ Yes ❑ No ❑ Don't know/Not sure		❑ DK/Not sure	❑ Yes ❑ No ❑ Don't know/Not sure	
Other (with cancer or birth defect) _____ ❑ NA	❑ Yes ❑ No ❑ Don't know/Not sure		❑ DK/Not sure	❑ Yes ❑ No ❑ Don't know/Not sure	
Other (with cancer or birth defect) _____ ❑ NA	❑ Yes ❑ No ❑ Don't know/Not sure		❑ DK/Not sure	❑ Yes ❑ No ❑ Don't know/Not sure	

2. Now I want to ask you questions about infections that anyone in (Child's Name)'s household may have had.

Between (dob) and (Child's Name)'sJune 30, 2001, was anyone who lived in his/her household diagnosed with…	column	**How is this person(s) in your household related to (Child's Name)?**
Hepatitis B	❑ Yes ❑ No ❑ Don't know or Not sure	_____
Hepatitis C	❑ Yes ❑ No ❑ Don't know or Not sure	_____
Epstein Barr Virus (EBV) (mononucleosis)	❑ Yes ❑ No ❑ Don't know or Not sure	_____
Human T-cell lymphotropic virus (HTLV) (Rare non-HIV disease)	❑ Yes ❑ No ❑ Don't know or Not sure	_____

3. Has anyone in (Child's Name) household ever tried to donate blood but was told they could not donate?

❑ Yes ❑ Don't know/Not sure
❑ No ❑ Refused to answer

Interviewer: If subject answered yes, please go to **question 4**.
If subject answers "no", "don't know", or refused to answer, please go to **the next section**.

4. If yes, how are they related to (Child's Name)? **Mark the appropriate boxes**

❑ Mother/Guardian 1
❑ Father/Guardian 2
❑ Sibling 1
❑ Sibling 2
❑ Other _____

5. Why were they not allowed to donate blood?

Mother/Guardian 1 _____
Father/Guardian 2 _____
Sibling 1 _____
Sibling 2 _____
Other _____

Part IV. Nutrition

- **(Child's Name)'s eating habits over the past month**

1. For each food item I name, I would like you to tell me if (Child's Name) ate it during the past month.

Did (Child's Name) eat…	**Interviewer:** If yes, go to next column	**How often during the past month did (Child's Name) eat this food?**
Smoked or cured meats, such as ham, bacon, sausage, hot dogs, and lunch meats	❑ Yes ❑ No ❑ Don't know or Not sure	❑ Daily ❑ Weekly ❑ Monthly
Fresh fish or fresh shellfish	❑ Yes ❑ No ❑ Don't know or Not sure	❑ Daily ❑ Weekly ❑ Monthly
Soy-based foods, such as tofu, soy milk, and soy burgers (not including soy-based formula)	❑ Yes ❑ No ❑ Don't know or Not sure	❑ Daily ❑ Weekly ❑ Monthly
Fresh vegetables	❑ Yes ❑ No ❑ Don't know or Not sure	❑ Daily ❑ Weekly ❑ Monthly
Locally-grown cantaloupe	❑ Yes ❑ No ❑ Don't know or Not sure	❑ Daily ❑ Weekly ❑ Monthly
Other fresh fruit, besides locally-grown cantaloupe	❑ Yes ❑ No ❑ Don't know or Not sure	❑ Daily ❑ Weekly ❑ Monthly

Part V: Other Current Information

I want to ask you a few questions concerning other current information.

1. In the last 24 hours have you used any of the following chemicals/substances?
   Please mark all that apply.

Interviewer: Please give list of chemicals to study participants

Mother

- ❑ Solvents (degreasers) used to clean mechanical parts ❑ Don't know
- ❑ Glues/adhesives ❑ Don't know
- ❑ Varnishes/lacquers ❑ Don't know
- ❑ Pesticides (for example, insect repellant, lawn treatment) ❑ Don't know
- ❑ Rust preventatives (for example, Rustoleum) ❑ Don't know
- ❑ Rubber cement ❑ Don't know
- ❑ Dyes and pigments ❑ Don't know
- ❑ Petroleum products (for example, motor oil, gasoline) ❑ Don't know
- ❑ Metals ❑ Don't know
- ❑ Paint, paint thinners, or paint strippers ❑ Don't know
- ❑ Other _____ ❑ Don't know
- ❑ None
- ❑ Refused to answer

Father

- ❑ Solvents (degreasers) used to clean mechanical parts ❑ Don't know
- ❑ Glues/adhesives ❑ Don't know
- ❑ Varnishes/lacquers ❑ Don't know
- ❑ Pesticides (for example, insect repellant, lawn treatment) ❑ Don't know
- ❑ Rust preventatives (for example, Rustoleum) ❑ Don't know
- ❑ Rubber cement ❑ Don't know
- ❑ Dyes and pigments ❑ Don't know
- ❑ Petroleum products (for example, motor oil, gasoline) ❑ Don't know
- ❑ Metals ❑ Don't know
- ❑ Paint, paint thinners, or paint strippers ❑ Don't know
- ❑ Other _____ ❑ Don't know
- ❑ None
- ❑ Refused to answer

2. Presently, do you have a water treatment system? ❑ Yes ❑ No
   If yes, What kind of system is it?
   - ❑ Filter _____
   - ❑ RO unit (reverse osmosis)
   - ❑ Other _____

3. Do you presently smoke cigarettes?

Mother/Guardian 1		Father/Guardian 2	
❑ Yes	❑ Don't know/Not sure	❑ Yes	❑ Don't know/Not sure
❑ No	❑ Refused to answer	❑ No	❑ Refused to answer

Interviewer: If subject answers "yes", please go to **question 4.**
If subject answered "no", "don't know", or refused to answer, please go to **question 5.**

4. On average, about how many cigarettes do you smoke per day?
Mother/Guardian 1 _____(**fill in number**)
Father/Guardian 2 _____(**fill in number**)

5. Do you presently chew tobacco?

Mother/Guardian 1		Father/Guardian 2	
❑ Yes	❑ Don't know/Not sure	❑ Yes	❑ Don't know/Not sure
❑ No	❑ Refused to answer	❑ No	❑ Refused to answer

6. Do you presently drink alcohol?

Mother/Guardian 1		Father/Guardian 2	
❑ Yes	❑ Don't know/Not sure	❑ Yes	❑ Don't know/Not sure
❑ No	❑ Refused to answer	❑ No	❑ Refused to answer

Interviewer: If subject answers "yes", please go to **question 7.**
If subject answered "no", "don't know", or refused to answer, please go to **question 8.**

7. On average, how many drinks of alcohol do you have per week (one drink is equal to one can of beer, one glass of wine, one cocktail or one shot of liquor, such as whisky or vodka).

Mother/Guardian 1	Father/Guardian 2
❑ 0 drinks	❑ 0 drinks
❑ 1-2 drinks	❑ 1-2 drinks
❑ 3-5 drinks	❑ 3-5 drinks
❑ >5 drinks	❑ >5 drinks
❑ Don't know or not sure	❑ Don't know or not sure

8. Do you presently use any prescription medications?

Mother/Guardian 1		Father/Guardian 2	
❑ Yes	❑ Don't know/Not sure	❑ Yes	❑ Don't know/Not sure
❑ No	❑ Refused to answer	❑ No	❑ Refused to answer

Interviewer: If subject answers "yes", please go to **question 9.**
If subject answered "no", "don't know", or refused to answer, please go to **the next section.**

9. Please list your current medications:
Mother/Guardian 1 _____
Father/Guardian 2 _____

Part VI: Secondary Demographics

We've reached the last segment of the interview. These are the last few questions.

1. What is the highest level of education that you completed?
- ❑ No formal schooling
- ❑ 1-8 years schooling
- ❑ 9-11 years schooling
- ❑ High school graduate or GED (high school equivalent)
- ❑ 1-3 years college
- ❑ Completed technical college
- ❑ 4 years of college or Bachelors degree
- ❑ 1 or more years of graduate or professional school
- ❑ Don't know/Not sure
- ❑ Refused

2. What is the highest level of education that (Child's Name) father or male guardian completed?
- ❑ No formal schooling
- ❑ 1-8 years schooling
- ❑ 9-11 years schooling
- ❑ High school graduate or GED (high school equivalent)
- ❑ 1-3 years college
- ❑ Completed technical college
- ❑ 4 years of college or Bachelors degree
- ❑ 1 or more years of graduate or professional school
- ❑ Don't know/Not sure
- ❑ Refused

3. Which of the following categories best describes your total household income last year before taxes? Include the income of everyone who is part of your household. If farming is your household's main source of income please give an estimate of the <u>previous year's farm income.</u>
- ❑ Under $20,000
- ❑ $21,000 - $40,000
- ❑ $41,000 – $75,000
- ❑ $76,000 – $100,000
- ❑ More than $100,000
- ❑ Don't know/Not sure
- ❑ Refused

Thank you very much for your time!
- **The interview is complete**
- **Instructions for urine samples**
- **Schedule environmental sampling**

Appendix C

Script for telephone recruitment
(Random Digit Dialing)

Nevada Control Identification -- Telephone Screener Script

I. INTRODUCTION:
Hello, my name is _____. I am calling on behalf of the Nevada State Health Division and the Centers for Disease Control and Prevention.

Q1. Is this a residence?

IF YES, CONTINUE

IF NO: I'm sorry. I am looking for a household. Goodbye. **COMPUTER WILL CODE AS *BUSINESS* AND BRING UP NEXT NUMBER TO DIAL**

II. SCREENING:
Recently the Nevada State Health Division identified a greater number of children with leukemia in Churchill County than usually observed in a similar population in the United States. The Nevada State Health Division has asked the Centers for Disease Control and Prevention to conduct a research study.

Your telephone number was selected randomly. We are looking for young people to serve as a comparison group for those who got sick with leukemia. I would like to ask a household member who is 18 years of age or older a few questions to determine if your family might be eligible to participate.

IF SPEAKING TO AN APPROPRIATE RESPONDENT, CONTINUE

IF A NEW RESPONDENT COMES TO THE PHONE, <u>REPEAT PARAGRAPHS I AND II</u> AND CONTINUE

IF ADULT MEMBER OF HOUSEHOLD IS NOT AVAILABLE TO COME TO THE PHONE, ASK: When could I call back to reach an adult member of this household? **GO TO APPOINTMENT TAB AND RECORD DATE AND TIME OF SUGGESTED CALL BACK**

IF SPANISH SPEAKING INTERVIEWER IS NEEDED, RECORD "YES" FOR LANGUAGE ON COMMENTS TAB AND SET SOFT APPOINTMENT

IF HOUSEHOLD ADULT REFUSES PRIOR TO OR DURING SCREENING BEFORE ELIGIBLE CHILD IS IDENTIFIED, SELECT THE REFUSAL TAB

Q2. Do you have children born between 1980 and 1998 who currently live in Churchill County?

IF YES, CONTINUE

IF NO: Thank you, but we are only identifying potential participants with children of those ages. We appreciate your willingness to answer our questions. Good-bye.

Q3. I am going to read a list of birth years and genders. Please stop me if I reach a group that includes one of your children who lives in Churchill County. Do you have:

a. Any girls born in 1998 or 1999? YES or NO
b. Any girls born in 1996 or 1997? YES or NO
c. Any boys born in 1994 or 1995? YES or NO
d. Any boys born in 1990 or 1991? YES or NO
e. Any boys born in 1988 or 1989? YES or NO
f. Any girls born in 1982 or 1983? YES or NO
g. Any girls born in 1980 or 1981? YES or NO
h. Any boys born in 1980 or 1981? YES or NO

(COMPUTER WILL STOP AFTER FIRST YES ANSWER AND CONTINUE WITH Q4)

(COMPUTER WILL TALLY YES ANSWERS AND REMOVE A CATEGORY AS THE QUOTA IS REACHED)

IF ALL (REMAINING) ANSWERS ARE NO: Thank you, but you do not have children at an age eligible for our study. We appreciate your willingness to answer our questions. Good-bye.

Q4. Has this child (GENDER BORN IN 19XX-19YY FROM Q3) ever been diagnosed with leukemia or another type of cancer? **(IF TWO CHILDREN FALL INTO THE SELECTED CATEGORY, ASK RESPONDENT TO CONSIDER THE YOUNGEST CHILD)**

IF YES: We are only identifying potential participants that have not been affected by cancer. I will continue asking about any other of your children who live in Churchill County. **REPEAT Q3 STARTING WITH THE NEXT AGE/GENDER CATEGORY**

IF NO, CONTINUE

Q5. Would you be willing to participate in this study and to have your child (GENDER BORN IN 19XX-19YY FROM Q3) participate? Participation includes answering questions to help us learn more about potential risks for childhood leukemia; collecting urine, blood, and cheek cell samples from your child and the child's parents; and collecting environmental samples from your house including dust, soil, water and indoor air. May I send you some information about the study? There is no obligation, even once you receive the material in the mail. You may choose not to participate at any time.

IF YES, CONTINUE

IF NO: Thank you for your willingness to answer our questions. Good-bye.

Q6. May I have your name, address, and the best telephone number to use to reach you in the future?

Name _____

Street _____

City_____ ZIP _____

Phone number _____

Q7.May I have the name and date of birth of the child eligible for our study? (GENDER BORN IN 19XX-19YY FROM Q3)

Name DOB

_____ _____

Q8.Does this child (GENDER BORN IN 19XX-19YY FROM Q3) currently live in your home?

IF YES, GO TO THANK YOU

IF NO: May I please have the name and relationship of the person whom the child lives with (or the child's name if they live alone), and the address and telephone number at that home in Churchill County so that we can contact them about possible study participation?

Name _____

Relationship _____

Street _____

City _____ ZIP _____

Phone number _____

(PHONE NUMBER WILL BE REMOVED FROM SAMPLE SO THAT SAME CHILD OR SIBLING CANNOT BE SCREENED INTO STUDY AS A CONTROL)

Thank you. A package with full study details, consent materials, and names and phone numbers for study staff will be sent to you within a few weeks. We appreciate your time. Good-bye.