

Sierra Vista Child Leukemia Assessment: 2006 Update

-- Leukemia Rate --

-- Environmental Information --



**Bureau of Public Health
Statistics**

Arizona Cancer Registry

**Bureau of Epidemiology and
Disease Control**

Office of Environmental Health

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Tim Flood, MD

Bureau Medical Director

Sierra Vista Child Leukemia Assessment

-- 2006 Update of Leukemia Rate --

Background

In 2001 parents in Sierra Vista and university faculty noticed and reported an apparent elevated number of child leukemia cases. In response the Arizona Cancer Registry of the Arizona Department of Health Services (ADHS) accelerated the reporting of child leukemia cases from the Sierra Vista area. The registry is authorized by state law to analyze rates of cancer.

In 2002 the ADHS published an environmental evaluation of the area. (http://www.azdhs.gov/phs/oe/pdfs/sierra_vista_sept12.pdf) That evaluation documented the counts and rate of child leukemia to date, and reviewed the status of selected environmental factors.

In visits and conversations with many of the families, the parents expressed their concerns about the situation. Some of these concerns are addressable through a statistical assessment of the leukemia data. The following report updates the information in the previous report by recalculating the leukemia rate, further characterizing the cases, and reviewing the status of air, water, and soil of Sierra Vista.

Leukemia rate

Case Ascertainment

Since receiving notice of a suspected elevation of child leukemia cases, the ADHS has derived information about leukemia cases from a variety of sources: direct reports from pediatric hematologists and local doctors, the Arizona Cancer Registry (ACR), local healthcare facilities, parents, local residents, and even former residents. In addition to counting cases that meet the standard case definition for a resident case, there was interest in recording other cases that also had an association with the Sierra Vista area. The counting of resident cases allows for calculation of a local incidence rate and comparison to the rates in Arizona and the US. The counting of the associated cases adds an important and complementary perspective.

The cases from the Sierra Vista area were reported to the ACR in an accelerated manner by the patients' healthcare providers. While this intensive, special, "rapid-reporting" of cases allows an up-to-date counting of local cases, it occurs about two years *earlier* than the usual reporting system through hospitals. So, we have a much more current count from Sierra Vista than we do for the state as a whole. We recognize the importance of presenting the most current local information, but this lag in statewide data does not allow us to compare contemporary time frames.

Case Definitions

The case definition remains the same as in the previous report. We are careful in distinguishing resident cases (used in calculating incident rates) from other cases with a link to the area; these linked, but non-resident cases are used to consider the scope and geographic factors when all cases are combined. National standards for coding the residence at the date of initial diagnosis¹ were strictly followed.

Redefinition of the Sierra Vista area

In producing counts and rates for the previous (2002) report we used zip code of the child's residence at diagnosis to define a SV area case. In the 2002 report we defined the area to include the following 6 zip codes: 85613, 85635, 85636, 85650, 85670, and 85671. However, zip codes are not created for health purposes; rather, they are a convenient tool for moving mail.

Use of CHAAs

By the end of 2003 we had determined that zip codes were not a satisfactory method for assigning residence. Instead, the state cancer registry program is moving to a geography-based assignment of residence. We realized that many communities, large and small, urban and rural, Indian reservations, etc., are interested in their cancer counts and rates. These interests are based on many different aspects of cancer, including perceived clusters, and especially their efforts for cancer control. In response, the ADHS Bureau of Public Health Statistics created Community Health Analysis Areas ("CHAAs") that are geography-based. These areas are almost identical to the ADHS Primary Care Areas, which the agency has used for many years in determining the needs for healthcare services and providers around the state.

(<http://www.azdhs.gov/hsd/profiles/index.htm>) The release of the U.S. Census 2000 required that we modify the PCAs to better reflect some areas that were rapidly growing.

It was a challenge to designate as many CHAAs as possible to give local residents specific information about their local communities, but at the same time make them large enough to have enough population upon which stable disease rates could be calculated. These interests compete with each other. A compromise resulted in the designations of 126 CHAAs.

(<http://www.azdhs.gov/phs/azchaa/>). It is important to note that there is no completely satisfactory way to combine or split these areas, and that any delineation is somewhat artificial. The biggest difficulties occur at the urban/rural interface and in rapidly growing communities.

The website about the CHAAs provides much information about the counts and rates of selected cancers of public health interest, including those for which preventive measures are possible (eg, lung cancer, breast cancer, colorectal cancer). The Q&A webpage

(http://www.azdhs.gov/phs/azchaa/cha_a.pdf) provides additional information about the use of CHAAs in Arizona. We believe the use of these areas will reduce the problem of deciding what to define as the area of analysis when residents ask questions about cancer in "their area." For all intents and purposes, the CHAAs are the smallest geographic units that are practical for producing cancer rates. Even so, in many CHAAs the counts of rare cancers are too small for

¹ See National Program for Cancer Registration and North American Association of Central Cancer Registries.

yearly analysis and some aggregation is required to stabilize the rate. We recognize that the CHAAs will be useful for a while; but, as the state continues to grow, rural areas will become urbanized and the CHAAs will need to be updated or replaced.

In the case of Cochise county, we consulted with the Cochise County Health Department and they agreed with designations that resulted in six CHAAs for the county, including the CHAA for Sierra Vista.

Definition of Leukemia

The defining document is the International Classification of Disease for Oncology (ICD-O). While the specific morphology definitions changed in the middle of our study period, these changes do not affect the calculation of total leukemia cases. Our definition is compatible with the one used and published by the National Program for Cancer Registration (NPCR). (<http://www.cdc.gov/cancer/npcr/uscs/2002/pdf/appendixJ.pdf>)

Denominator for Arizona

We used the population figures available from Claritas, a commercial company that uses US Census data to derive intercensal population figures (see Table 1). The Claritas figures compare reasonably well with other figures we obtained from the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute. Cancer registries across the United States commonly use these figures when calculating state-specific rates. But, note the yearly variation of up to 3.6% in the population estimates from these two supposedly authoritative sources.

Table 1. Population figures for children age 0-14 years of age.

	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006
Sierra Vista CHAA	11646	11733	11849	11962	12078	12190	12370	12502	12486	13221	13285	13221
Arizona (Claritas)	994317	1023523	1055729	1086968	1119199	1150466	1181068	1206736	1230609	1278013	1321551	1348765
Arizona (SEER)	N/A	N/A	1036893	1078652	1120576	1159574	1211507	1247004	1274805	N/A	N/A	N/A
Difference			18836	8316	-1377	-9108	-30439	-40268	-44196			
% difference			1.8%	0.8%	-0.1%	-0.8%	-2.6%	-3.3%	-3.6%			

Denominators for SV CHAA

We built the CHAA denominators from the Claritas disks which provide yearly estimates of population, by age group, by gender, by race, at the block group level. For the year 2001, we interpolated the value by using the census data for 2000 and the Claritas estimate for 2002. ARC-GIS software was used for this geographic and demographic work.

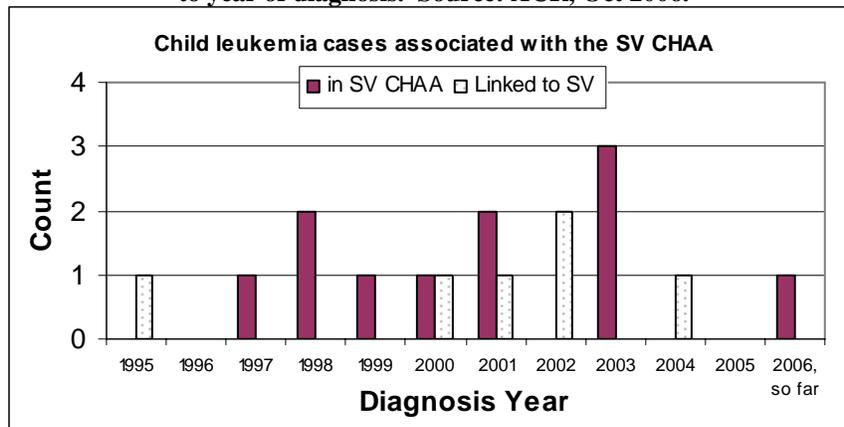
Results

Count

In the period from 1995 to October 2006 the ACR received reports of eleven child cases diagnosed while they resided in the Sierra Vista CHAA. These are defined as the “In SV

CHAA” cases. An additional six cases have been reported (usually by parents who have moved away) with some link to the Sierra Vista area. This link might be strong, for example if the case were diagnosed while living in an adjoining CHAA, or weak if the case lived at some time in Sierra Vista but moved away prior to diagnosis or occasionally visited the area prior to the child’s diagnosis. We refer to these six cases as “linked to Sierra Vista.” Figure 1 shows the distribution of the 17 cases according to year of diagnosis.

Figure 1. Count of child leukemia cases associated with Sierra Vista according to year of diagnosis. Source: ACR, Oct 2006.



Rate and Comparison to Arizona Data

In the previous ADHS report we confirmed a statistically significantly elevated rate in Sierra Vista, 1995-2001, using zip codes as the defining criteria. Now, with several more years of observation the important question we ask is whether the count and incidence rate of cases remains elevated.

Ideally, any comparison of Sierra Vista to Arizona would use identical time frames (the years of diagnosis). Using identical time frames tends to reduce the distorting effect that may be present in case ascertainment year-to-year. The counts and rates of cases reported to the ACR from across the state are shown in Table 2 and Figure 2.

The age-adjusted rate for the Sierra Vista CHAA in the period 1995-2006 was 7.29 cases per 100,000 resident children age 0-14.² The 95% confidence interval of this rate is 3.00-11.59. For comparison, Arizona’s annualized age-adjusted rate in the period 1995-2003 was 4.72 per 100,000 children, and the U.S. annual rate from 1992-2003 varied between 4.2 and 5.2 (See appendix). So, in this analysis with additional years of observation, the Sierra Vista rate remains elevated, but this rate now appears statistically similar to the state and U.S. rate.

² Age-adjusted to the year 2000 standard US population using 3 age strata: 0-4, 5-9, 10-14.

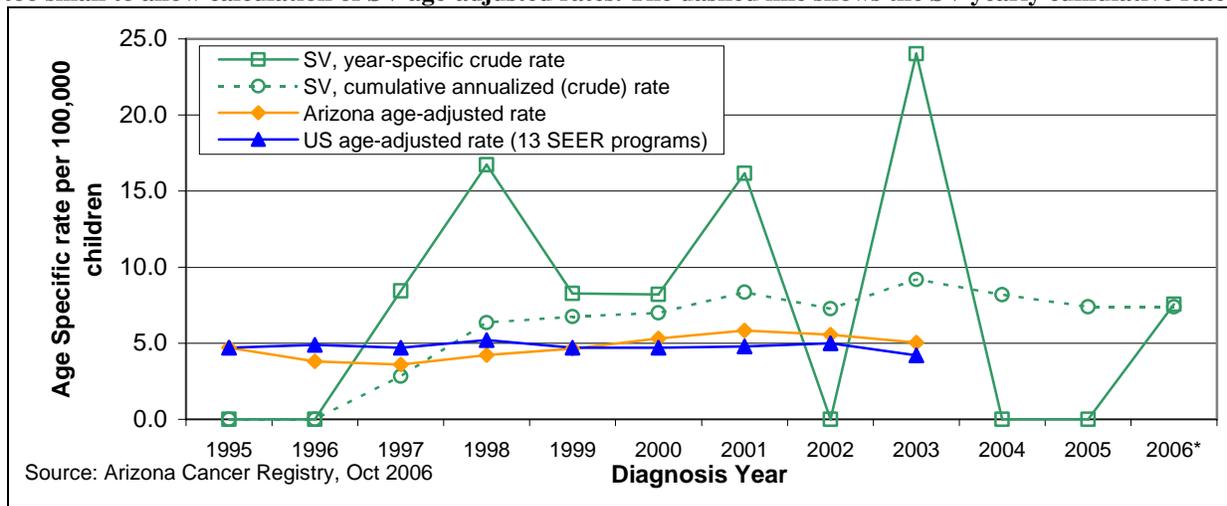
Table 2. Arizona, age-specific incidence rate per 100,000 children age 0-14, leukemia (all types). * indicates years for which data are incomplete. [n.a.: not available; -: not calculated].

Diagnosis Year	Sum, all state cases	State population of children	Age-specific (crude) rate	Age-adjusted rate
1995	47	996,962	4.71	4.63
1996	39	1,023,503	3.81	3.73
1997	38	1,056,310	3.60	3.55
1998	46	1,086,928	4.23	4.20
1999	52	1,119,748	4.64	4.60
2000	61	1,150,466	5.30	5.25
2001	69	1,183,307	5.83	5.77
2002	67	1,206,736	5.55	5.51
2003*	62	1,230,609	5.04	4.96
2004*	n.a.	n.a.	--	--
2005*	n.a.	n.a.	--	--
2006*	n.a.	n.a.	--	--
1995-2003*	481	10,054,569	4.78	4.72

Table 3. Sierra Vista, age-specific incidence rate (per 100,000 children) for children age 0-14, leukemia.

Diagnosis Year	Sum, all Sierra Vista CHAA, resident cases	Sierra Vista CHAA, resident population	Annual, Age-specific (crude) rate	Running, Annualized crude rate	Annualized, age-adjusted rate
1995	0	11,646	0.00	0.00	--
1996	0	11,733	0.00	0.00	--
1997	1	11,849	8.44	2.84	--
1998	2	11,962	16.72	6.36	--
1999	1	12,078	8.28	6.75	--
2000	1	12,190	8.20	7.00	--
2001	2	12,370	16.17	8.35	--
2002	0	12,502	0.00	7.27	--
2003	3	12,486	24.03	9.19	--
2004	0	13,221	0.00	8.19	--
2005	0	13,285	0.00	7.39	--
2006*	1	13,221	7.56	7.41	--
1995-2006*	11	148,543	7.41	7.41	7.29

Figure 2. Age-specific leukemia rates, age 0-14. We show the SV crude rates because the annual counts are too small to allow calculation of SV age-adjusted rates. The dashed line shows the SV yearly cumulative rate.



Characteristics of Cases

In characterizing the cases we include cases that are diagnosed in the Sierra Vista CHAA and cases described previously as “Linked” to Sierra Vista. There are eleven cases included under the term “SV,” and six that fit under the term “Linked.” In this section we show all cases known to date.

The following graphs display the information concerning age, birth year, gender, leukemia subtype, and birth place. Complete data were unavailable for some cases.

Figure 3. Age at diagnosis for cases diagnosed 1995-2006. The spike noted at age 2 is seen also in national and state statistics.

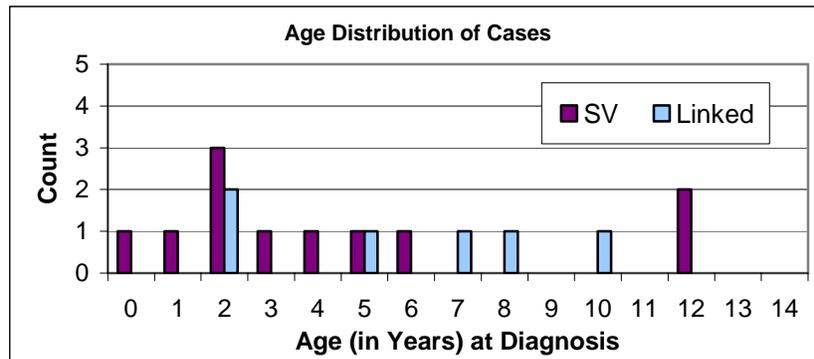


Figure 4. Year of birth of cases diagnosed between 1995 and 2006.

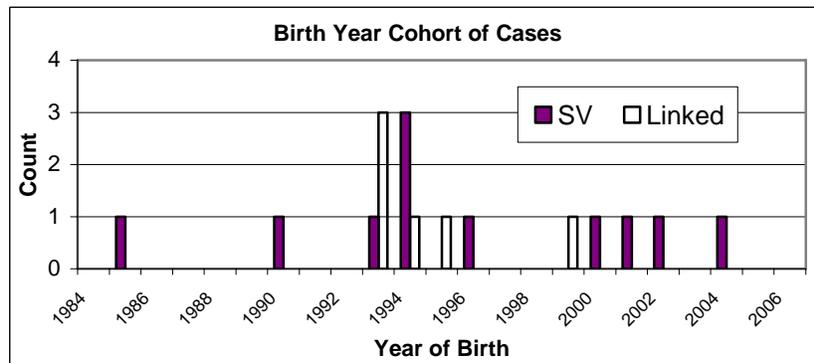


Figure 5. Gender of cases diagnosed between 1995 and 2006.

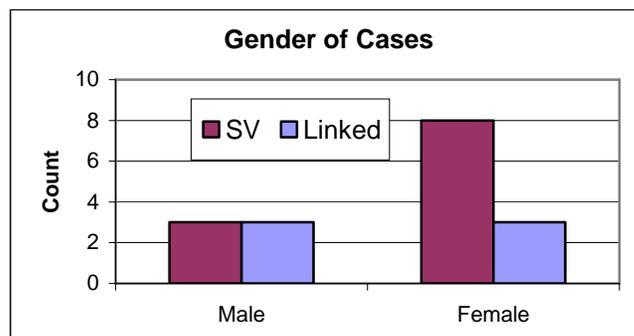
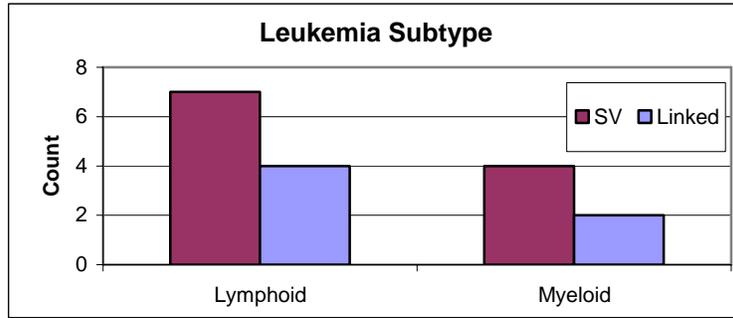


Figure 6. Histologic classification of leukemia for cases diagnosed 1995-2006.



The proportion of female cases exceeds that of male cases. This is an unusual finding in state and national data, where males are at slightly higher risk than females. A small spike in the birth years 1993-1994 also is noted, but unexplainable.

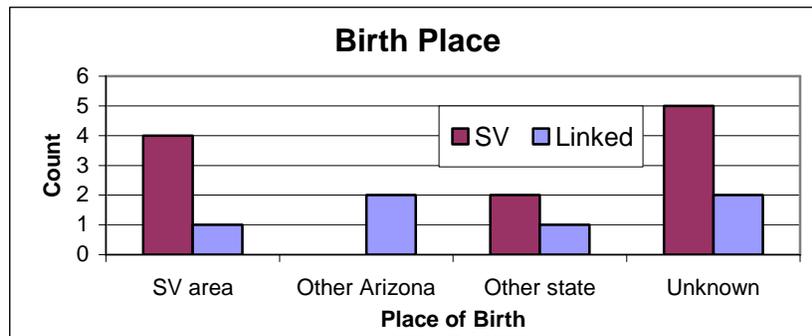
Residence Mapping

Some parents asked whether particular neighborhoods were at risk. In response, we requested that parents provide us with a detailed list of their residences for use in mapping to see if there was a common pattern. We expended considerable effort in seeking complete residential information about all cases and their parents.

The dataset contained valid street addresses at diagnosis for all resident cases. In addition, many parents were able to provide other addresses in the Sierra Vista area where they had lived prior to the child’s diagnosis date. However, some parents were not available for this exercise or chose not to participate.

Information about the place of birth is presented in Figure 7.

Figure 7. Location of birth of cases diagnosed 1995-2006 while residing in Sierra Vista or with a link to Sierra Vista.



Ten cases spent a range of 0-71 months in Sierra Vista prior to diagnosis; data on length of residence for seven cases could not be obtained. For the addresses received, no families had lived in one location the entire time, and four families had lived in five or six locations prior to diagnosis. The mapping of addresses did not reveal any clear pattern, and there was no

clustering of the addresses in any particular neighborhood. As expected, there were some cases who had lived at Ft. Huachuca, but these locations did not predominate.

Discussion

While many scientific articles have been published since 2001 concerning child leukemia, there still is little known about the factors that cause childhood leukemia. Nevertheless, considerable progress has been made in identifying genetic alterations that are present in the leukemic cells and the genome of cases. These alterations are important for identifying effective, and less harmful, chemotherapy. The alterations of underlying genetic structure or of the intracellular proteins also may lead to identification of the external factors that cause the alterations in the first place. But, so far, not enough cases have been studied with the new instruments and technology to allow scientists to pinpoint these elusive underlying or external factors.

Lacking an understanding of the cause of child leukemia makes it impossible for our public health response to make preventive recommendations. We have reached the limit of a public health response to the identified cluster. Further understanding about the causes of child leukemia will require advances in genetically categorizing large numbers leukemia cases and comparing their various exposure factors including infections and exposure to environmental factors in a broad sense. The NCI website <http://cancergenome.nih.gov/index.asp> describes the kinds of activities that are needed.³

At least two of the six “remote” cases experienced undiagnosable illness while living in the Sierra Vista area prior to definitive diagnosis when they lived elsewhere. Presumably, some of the cases diagnosed in Sierra Vista also became ill elsewhere before moving to Sierra Vista where they lived when diagnosed. A lengthy prodromal period is not uncommon with some cases of leukemia. The epidemiologic term for the interval between the action that causes a disease and the disease onset is the *induction* period.⁴ Hematologists and cancer specialists at the National Cancer Institute continue to search for the causes and factors that underlie child leukemia. Much more research is needed to discover the precise underlying mechanism of leukemia’s etiology.

Limitations

We relied on one source for the estimate of the Sierra Vista population of children. Because the US census is conducted only every ten years, our estimate of the area’s intercensal population may be in error. This is likely to be true in any of Arizona’s growing areas, including Sierra Vista.

Cases that resided at the margin of areas that border Sierra Vista likely had significant interaction with the services available in this regionally attractive town. This interaction is not well captured

³ http://cancergenome.nih.gov/media/Sep_13_2006_press_release.pdf

⁴ Ashengrau A and Seage GR III. *Essential of Epidemiology in Public Health*. Page 214; Jones and Bartlett Publ; 2003.

in the calculation of incidence rate. But we believe their inclusion in the graphs that characterize all cases improves their consideration in the big picture.

Conclusions

Based on information in this update, we draw these conclusions about Sierra Vista cases:

- The relatively small count of cases weakens our ability to draw definitive conclusions about any patterns. This is true even with the additional years of observation and expanded criteria linking cases to the area.
- Since 2001, when parents noted the elevated rate, the rate appears to have peaked in 2003. The local rate since 2004 is comparable to, though somewhat higher than, the state rate. Several more years of observation may reveal a clearer trend.
- In this small population the addition (or removal) of a case causes a wide swing in the annual rate which is statistically unstable.
- The count of female cases was greater than the count of male cases. This finding is unexplained and is unusual because males have the higher rate in state and national data.
- The patterns appear unremarkable for age at diagnosis, birth cohort year, leukemia subtype, and birth place.
- There is no apparent clustering within Sierra Vista.
- Our public health response is severely limited by the lack of understanding of the underlying cause of leukemia.

Future Actions

On a two-year basis, the Arizona Cancer Registry plans to update the child leukemia rates for the state as a whole, and the CHAAs. This non-confidential information will be posted on the website for viewing by the public and medical community.

Continued rapid-reporting of leukemia cases from Sierra Vista is no longer indicated. Any new cases will be captured and reported through the regular reporting system at hospitals.

Environmental Data Review

-- 2006 Update --

Water Quality

All public drinking water systems in Arizona must comply with the Maximum Contaminant Levels (MCLs) established by the United States Environmental Protection Agency (USEPA) since 1989. In the previous report, twenty public water systems were reviewed. There were no indications that industrial solvent, gasoline, arsenic or radiochemicals were at levels of concern. There were changes in a few companies since the last report, for instance one company merged with two others. Sixteen of the sixteen public water systems that service the Sierra Vista area were reviewed for this report. The available information indicated that none of the sixteen water systems exceeded the MCLs, including but not limited to gross alpha radioactivity, arsenic, and benzene, from 2002 to November 2006 (personal communication, Gehlsen). That indicates that the drinking water in the Sierra Vista area does not represent a health threat.

Groundwater quality at Fort Huachuca has been monitored by the Arizona Department of Environmental Quality (ADEQ). The chemical concentrations in groundwater monitoring wells and leachate wells are updated every six months for the South Range Landfill, and reviewed now at intervals of 5 years for the East Range Mine Shaft. Their report states that concentrations for primary metals and volatile organic compounds (VOCs) are within the Arizona Aquifer Water Quality Standards (personal communication, Stonebrink). In Arizona, all aquifers are considered to be drinking water aquifers unless they are specifically exempt (ARS §49-224).

Ambient Air

Stationary sources of air pollution such as factories are required to meet federal and state air quality standards. Emission inventory can be used to estimate the air quality. Based on the available 2005 emission inventories for Sierra Vista area, the largest stationary source in the area is the Huachuca Concrete Plant. This facility emits 10.36 pounds per day (lbs/day) of particulate matter, 4.15 lbs/day of VOCs, and 0.07 lbs/day of hazardous air pollutants (personal communication, Celaya). The emissions from the facility are typical of many concrete block manufacturers. The facility is classified as a low emitter because of the low level of pollutants emitted by the facility. All other facilities in the area emit very low levels of airborne contaminants.

There are many non-point sources of air pollutions such as automobiles, trucks and aircraft that can affect air quality. Emissions from vehicular traffic in the Sierra Vista area are relatively small since Sierra Vista has a relatively small population (approximately 41,000, according to the US Census Bureau). Fort Huachuca has an active airfield called the Libby Army Airfield. The runway at Libby Army Airfield is shared with the Sierra Vista Municipal Airport. There are 99 aircraft based at the facility. Approximately half of the aircraft are single engine airplanes, nine are multiple engine airplanes, eight are helicopters, and one is an ultralight. Twenty-eight of the 99 airplanes are military aircraft. The average airport operation activity is approximately

318 flights per day. Approximately 78% of the daily flights are conducted by the military, with the remaining flights spread among local, transient, and commercial aviation.

Aviation fuel (Avgas and Jet A) is commercially available at the Sierra Vista Municipal Airport. The fuel is stored in underground fuel storage tanks that have proper safety and vapor prevention devices. In addition, Fort Huachuca stores jet aviation fuel (JP 8) in underground storage facilities at Libby Army Airfield. All of the aviation fuel used at Libby Air Field is delivered by truck and dispensed according to the current industry standard methods.

Fort Huachuca Soil Contamination

Fort Huachuca is an Army post near Sierra Vista that has been in continuous operation since its establishment in 1877. There are 4 hazardous waste sites and 18 former underground storage tanks that have leaked into soil or groundwater. In addition, there are 20 sites at Fort Huachuca that the ADEQ classifies as solid waste sites. The principal contaminants at the various sites are petroleum hydrocarbons. All identified contaminants are below the Arizona Soil Remediation Levels. These include organochlorine pesticides, primary metals, and VOCs detected at South Range Landfill and East Range Mine Shaft.

In general, contaminated soils at Fort Huachuca are limited to protected areas and are a safe distance from the nearest residences. Fort workers may have contacted low-levels of contaminated soil during their routine work, but exposure, if any, probably occurred infrequently and for only short periods of time. No current or future exposures are likely to occur because of successful cleanups at the airfield and because of institutional controls preventing contact with on site contaminants.

Summary

Based on a review of all available information, detected chemical concentrations in both the public drinking water systems and other environmental media are not likely to have contributed to an increase in childhood leukemia rates at Sierra Vista. ADHS will continue to review additional environmental information as it becomes available.

Appendix

Figure 8. ICD-O-3 codes used in classifying child leukemia. We do not show the comparable ICD-O-2 codes, which are available upon request.

Leukemia		
Lymphocytic leukemia		
Acute lymphocytic leukemia		9826, 9835-9837
Chronic lymphocytic leukemia	C420, C421, C424	9823
Other lymphocytic leukemia		9820, 9832-9834, 9940
Myeloid and monocytic leukemia		
Acute myeloid leukemia		9840, 9861, 9866, 9867, 9871-9874, 9895-9897, 9910, 9920
Acute monocytic leukemia		9891
Chronic myeloid leukemia		9863, 9875, 9876, 9945, 9946
Other myeloid/monocytic leukemia		9860, 9930
Other leukemia		
Other acute leukemia		9801, 9805, 9931
Aleukemic, subleukemic, and NOS		9733, 9742, 9800, 9831, 9870, 9948, 9963, 9964
	C420, C421, C424	9827

SEER Incidence - AA Rates for 13 Registries, 1992-2003

Results:

Selections:

Statistic type = Age-adjusted rate;
Standard population = 2000 U.S.;
SEER registry = Total (registries depend on race/ethnicity);
Site = Leukemia;
Race/ethnicity = All races;
Sex = Male and female;
Age at diagnosis = 00-14;

Citation:

Surveillance, Epidemiology, and End Results (SEER) Program
 (www.seer.cancer.gov) SEER*Stat
 Database: Incidence - SEER 13 Regs
 Public-Use, Nov 2005 Sub (1992-
 2003), National Cancer Institute,
 DCCPS, Surveillance Research
 Program, Cancer Statistics Branch,
 released April 2006, based on the
 November 2005 submission.

1992	4.5
1993	4.6
1994	4.3
1995	4.7
1996	4.9
1997	4.7
1998	5.2
1999	4.7
2000	4.7
2001	4.8
2002	5.0
2003	4.2

Table Variable:

Row = Year of diagnosis

Figure 9. Single age rates (per 100,000 population) of leukemia, 1992-2003, 13 SEER registries in the United States. Source: SEER*stat, query of Oct 26, 2006.

