Health Studies at Santa Susana Field Laboratory

Expert Panel Review

June 20, 1999

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Table of Contents

Appendices

Health Studies at Santa Susana Field Laboratory
Expert Panel Review

Executive Summary

In response to Assemblywoman Kuehl's request, Governor Davis asked Cal/EPA to investigate the Department of Health Services (DHS) handling of the health studies at the Santa Susana Field Laboratory (SSFL). As part of that overall investigation, the Hazardous Materials Laboratory (HML) of the Department of Toxic Substances Control (DTSC) within Cal/EPA was asked to identify, review and evaluate the findings of the relevant health studies. Discussions with stakeholders helped narrow the focus of this review on three cancer incidence studies in the vicinity of SSFL. The first two studies were conducted by DHS and the third by Dr. Nasseri of the Tri-County Regional Cancer Registry. HML reviewed the reported health studies, convened an expert panel to obtain their independent opinions and summarized their findings in this report.

Whereas there were some differences in the geographic areas, time periods, case definitions and level of significance used in these three studies, the combined evidence from all three does not indicate an increased rate of cancer incidence in the regions examined. The extremely modest cancer incidence increases associated with known radiosensitive tumors could be easily explained by uncontrolled confounding or imprecision in the data. The results do not support the presence of any major environmental hazard.

Environmental questions involving very modest elevations in cancer incidence rates can not be resolved using surveillance systems. The California Cancer Registry (CCR) Guidelines need to be revised to provide clear guidance as to the need and extent of follow up when increased risk is suggested. Although Dr. Nasseri's report, in agreement with the previous two DHS studies, showed no significant risks, the information should have been shared with investigators studying health effects in the community. This information might have allowed studies to be refocused and prevent overlap in effort. Given the limitations discussed above, it would be very important that scientists be available to respond to inquiries from the community regarding interpretation of Dr. Nasseri's results.

A population based case control study focused on radiosensitive tumors that addresses occupational and environmental exposures to radiation, while controlling for all known risk factors, should be discussed. Alternatively, a study that includes socioeconomic data from the census, all types of cancer, all time periods for which data are available, and consistent epidemiologic methods over time, would improve confidence in the results of the three earlier studies. Further studies should only be embarked upon if the proposed protocol can provide improved exposure assessment and control for confounders, while substantially improving the precision of the estimates.

Introduction

In response to Assemblywoman Kuehl's request, Governor Davis asked Cal/EPA to investigate the Department of Health Services (DHS) handling of the health studies at the Santa Susana Field Laboratory (SSFL). As part of that overall investigation, the Hazardous Materials Laboratory (HML) of Cal/EPA was asked to identify, review and evaluate the findings of the relevant health studies. This report provides the background for the review, defines the review objectives, describes the approach used, and discusses the results of the review.

Background

The Santa Susana Field Laboratory (SSFL), located in Ventura County at the boundary of Los Angeles County, has served as a nuclear development facility for the US Department of Energy (DOE) operated by a series of contractors. Rocketdyne, currently part of Boeing, is the most recent contractor. Public concerns about possible radioactive releases to the nearby communities resulted in a series of investigations.

In 1990, a DHS study found a suggestive increased incidence of urinary bladder cancer (possibly radiosensitive tumor) in Los Angeles census tracts closest to SSFL. In response, the Legislature funded an occupational epidemiology study of SSFL workers to better assess potential health effects. If an association were found between occupational exposures and adverse health outcomes, a community study would be needed. The Legislature directed that the occupational study be conducted independently of DHS, DOE and Rocketdyne, and arranged for the formation of an Oversight Panel to select and oversee the contractor who would conduct the study.

In 1992, DHS released a study of cancer incidence in census tracts adjacent to the SSFL, in both Ventura and Los Angeles Counties. The study found an elevated incidence of lung (moderately radiosensitive) and bladder (possibly radiosensitive) cancers in men. The authors underlined inherent study limitations and recommended that these findings be considered in the context of the occupational study.

The first phase of the workers study (conducted by UCLA, School of Public Health) was released in 1997. The study found that SSFL workers exposed to radiation (internal or external) had a higher risk of dying of cancers of blood and lymph. Additionally, exposure to external radiation was associated with a higher risk of dying from lung cancer, while exposure to internal radiation was associated with a higher risk of dying from cancers of the oral cavity, pharynx, esophagus and stomach.

Upon release of the workers study (1997), Dr. Nasseri of the Tri-County Regional Cancer Registry calculated incidence rates for the Ventura County census tracts adjacent to SSFL. All "very radiosensitive" cancers appeared lower (40%) than expected in women and cancer of lung and bronchus appeared higher (17%) than expected in men and women combined. Dr. Nasseri emphasized the limitations of his study and suggested further follow-up.

In 1999 the second phase of the workers study was released. It found increased lung cancer mortality in workers exposed to hydrazine, but no association with asbestos exposure.

Disagreements between some members of the Oversight Panel and DHS staff over distribution of information, led to a request by Assemblywoman Sheila Kuehl for an investigation of DHS practices. Governor Davis asked Cal/EPA to head such an investigation. As part of that investigation, HML identified and reviewed the reported health studies, convened an expert panel to obtain their independent opinions and summarized the findings in this report.

Objectives of this Report

The objective of this review was to focus on the scientific merit of the health studies at SSFL.

The specific objectives of the review were to:

- Identify all health studies related to SSFL;
- Obtain input from stakeholders to focus on pertinent issues;
- Evaluate and summarize the findings of each study;
- Identify ambiguous or contested issues;
- Recruit an independent expert panel;
- Send relevant material to the panel and obtain the panel's responses;
- Discuss issues with panel and reach conclusions.

Approach

Focus of this review

To ensure that all relevant studies had been identified, discussions were held with key staff from DHS, Ms. Kuehl's office, the Tri-County Regional Cancer Registry, and the Committee to Bridge the Gap. All provided information and material for review. Discussions with these key staff helped narrow the focus of this review on the three community cancer incidence studies; no concerns were expressed regarding the occupational study and the conclusions of the radiation or the chemical phases of that study.

Expert Panel

All identified studies were summarized for review by DTSC Management. A decision was then made to invite an independent panel with expertise in cancer registries, and no affiliation with DHS, to review the original cancer incidence studies. The two panel members selected were Dr. James Beaumont, Associate Professor at the Department of Epidemiology and Preventive Medicine, at UC Davis School of Medicine, and Dr. Faith Davis, Professor and Director, Division of Epidemiology and Biostatistics, School of Public Health at the University of Illinois, Chicago. Their curricula vitae are in Appendix A of this report.

Expert Panel Review Procedure

Each member of the panel received a package with the original studies, and was asked a series of structured questions to facilitate and focus the review. (The entire package is in Appendix B).

The panelists provided written responses to those questions (Appendix C) and participated in a 3-way conference call with HML where these questions were further discussed and additional issues raised. The combined responses and comments of the panelists were summarized in a draft report, which the panelists were asked to review and edit. This Final Report incorporates all reviews and summarizes the panelists' opinions.

Discussion

Elements required to indicate an increase in cancer incidence

Statistically significant increases in cancer rates often happen because of random variation in temporal and spatial case occurrence. Evidence that there might be a causal relationship between an environmental risk factor and cancer in a community is provided under one or more of the following circumstances:

- There is no change in the reporting/recording requirements.
- The increase is consistent across multiple time periods.
- The increase is consistent across genders.
- The increase is consistent across race/ethnicity groups.
- The increase is elevated compared to other regions.
- The increase is highly significant (i.e., $p<0.01$).
- The magnitude of the increase is greater than the "noise" caused by common biases.
- The increase is temporally correct with regard to the type of cancer and time since exposure (e.g. a latent period of 5+ years for leukemia and 10+ years for lung and bladder cancer).
- A causal relationship between the particular type of cancer and the suspected risk factor has been shown in human or animal studies.
- Exposure to the suspected risk factor has been documented in the community.
- When the suspected risk factor is known to cause more than one type of cancer (e.g. smoking), the proper constellation of increased rates is seen.

These elements should be taken into account when results from the three cancer incidence studies are evaluated.

Strengths and weaknesses of cancer registry data for studying environmental risk factors

Cancer risk is influenced by many factors, including genetics, infections, occupational and environmental exposures, diet and lifestyles. As data on risk factors are not recorded in cancer registries, they cannot be addressed in analysis. In addition to the lack of information on these factors, cancer registries have no record of length of residency within the community, population estimates between census counts are uncertain, and reporting of cancer cases to the registry usually lags behind diagnosis.

Cancer registries are population based, allowing rates to be calculated using census data. The strength of cancer registry data lies in the ability to document elevated cancer incidence rates and identify changes in patterns of rates which, in turn, raise questions as to the reasons for these

changes. These questions can be addressed in more rigorous and focused special studies, providing that the magnitude of the increases and statistical power warrant such studies.

DHS Cancer incidence studies conducted in the community in 1990 and 1992

The 1990 study found suggestive increased rates of bladder cancer in the community, as compared to Los Angeles (LA) County. Over the two time periods studied, one census tract out of the five examined showed statistically higher rates than the LA County rate for "all sites", "bladder" and "acute non-lymphocytic leukemia". These increases, however, were temporally and spatially inconsistent. The concern raised about bladder cancer rests on the observation that rates from three census tracts in the 1983-87 period ranked in the highest quartile of LA County rates. Whereas this observation warrants further investigation, in and of itself should not be interpreted as an established elevation in incidence. A substantial drop in rates in the remaining two census tracts raises the question of whether a population shift took place in the region that might explain this observation. As noted by the authors, the increased bladder rates may be explained by demographic or smoking differences, or by random variation.

The 1992 study was a follow up to the 1990 study. Although the methodology is more elegant, comparison with the 1990 study is difficult. The study period was extended by one year, the study area was expanded to more census tracts, the study population was limited to non-Hispanic Whites, and the case definition was changed to invasive cancers only. Bladder cancer was elevated in some census tracts, but the increase was inconsistent between genders (elevated in males only) and across geographic areas (increase only in LA County tracts, but not in Ventura County). Similarly, lung cancer rates were increased in some census tracts, but the increase was again inconsistent between genders (males only) and geographic areas (increase in Ventura County tracts only). Considering this evidence, and the criteria discussed above, the 1992 study does not indicate increased cancer incidence.

Dr. Nasseri's report (1997)

Dr. Nasseri states that he based his calculations on the 1992 DHS study. It is not clear, however, if he restricted his analysis to non-Hispanic whites. Additionally, only Ventura County tracts were examined, and a 99% confidence level was used (consistent with California Cancer Registry Criteria) as opposed to the 95% used in the two earlier DHS studies.

Dr. Nasseri used the Standardized Incidence Ratios (SIR) statistic, where the ratio of the observed number of cases over the expected number of cases is computed (as %), and where normal risk is indicated by a SIR of 100. Dr. Nasseri's report has the usual limitations encountered when registry data are used to search for an association with environmental risk factors: There are no exposure data and no data on education or income. Additionally, there are uncertainties resulting from data limitations, such as the use of the unadjusted 1990 census to calculate expected number of cases, and incomplete (88%) reporting of observed cases for one of the years studied. The report does not present data on cancer sites not considered to be radiosensitive. This is consistent with Dr. Nasseri's intention to model his calculations on the 1992 DHS study. However, information on cancers (other than lung) caused by tobacco would have been helpful to evaluate smoking as a contributing factor.

Bladder cancer was of concern based on the previous DHS reports. In this study this tumor is separated into two categories: urinary bladder and other urinary system. The SIR for the former was 102 and the latter was 130 in males, and 71 and 50 respectively for females. The SIR of 130 is roughly equivalent in magnitude to the SIRs of 128.6 and 132.6 from 1978-82 and 1983-88 respectively, reported in the earlier DHS studies.

Dr. Nasseri's calculations show a statistically significant (but modest) increase only for lung cancer. Since tobacco smoke is a strong carcinogen for the lung, the causal factor may be higher historical cigarette consumption among the residents. Other types of cancer, such as laryngeal cancer, bladder cancer, and pancreatic cancer are also caused by smoking. Of these, only bladder cancer was examined, and its observed rate was slightly less than expected, which is some evidence that cigarettes may not be responsible for the higher incidence of lung cancer. However, cigarettes are a more powerful carcinogen for the lung than for other organ sites, and the increase in lung cancer was small (17%). Thus if cigarettes were responsible for a small lung cancer increase, it would be difficult to detect an increase in bladder or other cancers related to smoking.

The extremely modest cancer incidence rate increases associated with known radiosensitive tumors could be easily explained by uncontrolled confounding or imprecision in the data. The results do not support the presence of any major environmental hazard.

Follow-up to Dr. Nasseri's report

Dr. Nasseri used the best available data, and further analysis of the limited cancer registry data is unlikely to change the primary results. However, reassurance that these estimates are correct and consistent with the LA County rates may be gained by conducting an analysis of all the years for which data are available from LA County and Ventura County. Using the same criteria, extending the estimates to all cancers and noting site specific trends as feasible, may increase the confidence in the patterns of incidence across all three reports.

The California Cancer Registry (CCR) Guidelines provide no recommendations for scientific follow-up when increased risk is suggested in an assessment of observed vs. expected number of cases. This is a serious deficiency of the CCR Guidelines and should be addressed by DHS. The Guidelines do provide recommendations for communication, as follows (in the section titled Communicating the Results): "If the cancers are elevated or otherwise unusual, future actions planned, e.g., consultation with other agencies, or monitoring, or both, should be described. County health officials should be notified."

Dr. Nasseri's report, along with the two earlier DHS studies did not show "elevated or otherwise unusual" cancer rates in the areas studied. However, given that on-going investigations at SSFL were under way and a community study was being planned, Dr. Nasseri's report should have been shared with investigators studying health effects in the community. This information might have allowed studies to be refocused and prevent overlap in effort. Given the limitations discussed above, it would be very important that scientists be available to respond to inquiries from the community regarding interpretation of Dr. Nasseri's results.

Suggestions for future studies

Two types of community studies would be helpful:

1. An ecological epidemiology study that is similar to the previous studies, but that includes socioeconomic (SES) data from the census, all types of cancer (not just the "radiosensitive cancers"), all time periods for which data are available, and consistent epidemiologic methods over time. This would provide consistency across the three earlier studies and increase confidence in the results. This would be an easy and economical study to carry out, however, environmental questions which involve very modest elevations in rates cannot be resolved using data systems set up to conduct surveillance.

2. A population based case control study that addresses occupational and environmental exposures to radiation while controlling for all known risk factors focused on radiosensitive tumors should be discussed. This seems to be the only study design that may be able to separate out the effects of exposures from different sources. Research on molecular markers associated with radiation exposures has progressed and should be explored as a tool to aid in this situation. An assessment of the type and magnitude of the potential environmental doses involved may also help to clarify the utility of further investigations. While the elevated rates reported are very modest and not statistically significant, the exposure of concern is a known carcinogen and should be considered carefully. Further studies should only be embarked upon if the proposed protocol can provide improved exposure assessment and control for confounders, while substantially improving the precision of the estimates. Some consideration should also be given to minimizing any potential current exposures.

Conclusions

Three studies of cancer incidence in the vicinity of SSFL were reviewed. Whereas there were some differences in the geographic areas, time periods, case definitions and level of significance used in these studies, the combined evidence from all three does not indicate an increased rate of cancer incidence in the regions of interest. The extremely modest increases in cancer incidence rates associated with known radiosensitive tumors could be easily explained by uncontrolled confounding or imprecision in the data. The results do not support the presence of any major environmental hazard.

Environmental questions involving very modest elevations in rates can not be resolved using surveillance systems. A population based case control study that addresses occupational and environmental exposures to radiation while controlling for all known risk factors focused on radiosensitive tumors should be discussed. Alternatively, an ecological epidemiology study that includes socioeconomic data from the census, all types of cancer, all time periods for which data are available, and consistent epidemiologic methods over time, would improve confidence in the data provided in the three earlier studies.

The California Cancer Registry (CCR) Guidelines need to be revised to provide clear guidance as to the need and extend of follow up when increased risk is suggested.

Appendix B

Material sent to panel

Department of Toxic Substances Control

Edwin F. Lowry, Director
Hazardous Materials Laboratory
2151 Berkeley Way, Room 515
Berkeley, California 94704

Winston H. Hickox
Secretary for
Environmental
Protection

Gray Davis
Governor

May 19, 1999

James Beaumont, Ph.D.
Department of Epidemiology
UC Davis
1 Shield Ave.
Davis CA 95616

Dear Dr. Beaumont,

Thank you for agreeing to serve on the expert panel assisting Cal/EPA in a review of cancer incidence in the vicinity of the Santa Susana Field Laboratory (SSFL) in Southern California. As you may know, Cal/EPA was asked by the Governor to review this information and the way it was handled by the Department of Health Services (DHS). Cal/EPA is willing to compensate you for your efforts upon completion of this report.

I have enclosed the following material for your review:

1. "Cancer incidence rates in five Los Angeles County census tracts". DHS Report, 1990
2. "Cancer incidence near the Santa Susana Field Laboratory". DHS Report, 1992
3. Letter from Dr. Nasseri to Mr. Lorenz, 1997
4. "Fact Sheet". Tri-County RCR. Santa Barbara County Public Health Department
5. "Guidelines to address citizen concerns about cancer in their communities". CCR, 1998

Please review this material and try to answer the following questions:

a. In your experience with cancer registries, what are the necessary elements that would alert you to significant increases in incidence?
b. Does either of the first two studies (items 1 and 2 above) indicate an increased cancer incidence in the community during the periods studied?
c. Do Dr. Nasseri's calculations (items 3 and 4) indicate an increased cancer incidence in the community during the periods studied?
d. Given the CCR Guidelines (item 5 above), should Dr. Nasseri's calculations have been followed up with a more intensive study?

e. Should Dr. Nasseri's calculations have been disseminated to community representatives?

f. Would Dr. Nasseri's calculations be of interest to investigators studying health effects in the community near SSFL?

g. Briefly summarize the strengths and weaknesses of using cancer registry data to study environmental risk factors

h. Given that an occupational study showed increased cancer mortality (lung cancer and leukemias) for SSFL workers exposed to radiation, how would you have used cancer registries to investigate cancer incidence in the community surrounding SSFL?

i. Any other suggestions for a community study?

I would like your written comments by June 4th, 1999, or sooner, if possible. I am planning to hold a meeting of the expert panel during the week of June 7th to discuss and summarize all comments. The consensus opinion will be incorporated in the Cal/EPA report and all written comments will be referenced and included in an appendix.

Please contact me if you need additional information at (510) 540-3624 or at mpetreas@dtsc.ca.gov.

Sincerely,

Myrto Petreas, Ph.D., MPH
Hazardous Materials Laboratory
Cal/EPA

Appendix C

Written comments from panel

Review of documents related to cancer incidence in the vicinity of the Santa Susana Field Laboratory (SSFL) in Southern California

Submitted to the California EPA on June 14, 1999

This report addresses the questions posed by the California Environmental Protection Agency in a letter from Dr. Myrto Petreas dated May 21, 1999. The questions and my responses are outlined below.

a. In your experience with cancer registries, what are the necessary elements that would alert you to significant increases in incidence?

Incidence rates that are elevated compared to other regions or are increased over a several year period.
The increase is not limited to one subgroup if an environmental exposure is at issue.
The magnitude of the increase is statistically significant.
There is no change in reporting/recording requirements that may explain a change.

b. Does either of the first two studies indicate an increased cancer incidence in the community during the periods studied?

Wright and Perkins. This study compares incidence rates during one decade across census tracts. This is really too short of a time period to address trends and because of the small numbers of rare tumors in small geographic regions the time was appropriately grouped into two five-year periods. As such this analysis cannot adequately address whether or not there is a trend in rates. It can however, document if the rate in one region may be different than the rate in another region and the authors chose to compare site–specific incidence rates in each census track to the incidence rate for LA County. As the percentage of LA county population in these census tracks is small, this comparison seems reasonable. Unfortunately, there is no way of knowing if the pattern of rates observed in this decade (1978-87) is similar or different from previous time periods.

This study showed no excess of cancer by census track for lung, bone, thyroid, hodgkins, non-hodgkins, acute lymphocytic leukemia, chronic lymphocytic leukemia or chronic myelogenous leukemia. One in ten of the census rates compared were statistically significantly higher than the county rate for all sites, bladder and acute non lymphocytic leukemia. However, these increases were not consistent by region and time period.

The concern raised about bladder cancer rests on the observation that rates from 3 census tracks in the 1983-87 period ranked in the highest quartile of LA County rates. This observation does warrant further consideration, but in and of itself should not be interpreted as an established

elevation in incidence. Oddly, there is a substantial drop in rates in the remaining two census tracks studied (20.5 to 10.0 for 1351 and 18.1 to 13.0 for 1352). I wonder whether there was some natural population shift from one region to the other (a new retirement community or a major new subdivision opening for instance) that may explain this phenomenon. This shift would be reflected in the numerator of the rate, but not the estimated denominator.

Coye and Goldman. This report is a follow-up study to the Wright and Perkins report. Unfortunately it was conceived and executed in a manner which makes it difficult to put the results in the context of the previous report. The rationale for these refinements are understandable but not well presented.

The methods in this report are more elegant and while they appear to be appropriate, the results are presented in such a manner as to make comparisons within this report and to the previous report difficult. It adds one year of cancer incidence data, limits the disease definition to invasive cancers, refines and extends the census track areas included, limits the focus to non Hispanic whites and regroups tumors into categories of radiosensitivity. Given that this analysis only extends the previous report by a year, on the face of it, the overall results should be similar – with the value of this analysis in the gender subgroup results. Limiting the analysis to non-Hispanic whites (which they indicate is the major population group near the SSFL) reduces the number of bone cancers in 1978-82 from 4 to 1 (25%), thyroid cancer from 18 to 17 (94%), lung cancers from 175 to 163 (93%) and bladder cancers from 73 to 59 (80%). These numbers are based on both Table 1s. The disproportionate decline in the percent of bladder cancers reflects the redefinition of cases from the earlier report from all cancers to invasive cancers. It is this change in disease definition that drives the results. The regroupings based on the known radiosensitivity of tumors is nice, although the absence of all cancer sites limits the interpretation of smoking related tumors.

The rate of bladder cancer is elevated in both time periods, although this reaches statistical significance only among males in the 1983-88 time period. The rate of lung cancer was not statistically significantly elevated in males or females in the 1978-88 data. The sparseness of data in 88-89 from Ventura County combined with the use of proportionate ratios makes these results extremely difficult to interpret.

The combined evidence from these two studies do not indicate an increased rate of cancer incidence in the regions of interest.

c. Do Dr. Nasseri's calculations indicate an increased cancer incidence in the community during the periods studied?

Dr. Nasseri's calculations appear to be based on the same criteria as Coye and Goldman for the 1988-94 time period. Its not clear if he restricted his estimates to non Hispanic whites but he indicates estimates were race adjusted. His analytic technique involves counting cases in the SSFL region

and estimating the number of expected values in the same region. The expected values are based on population census from 1990 and incidence rates from the Tri-county region. Increasing the statistical cutoff to 99% from 95% is consistent with the CCR guidelines.

Bladder cancer is the site of concern based on the previous reports. In this study this tumor is separated into two categories: urinary bladder and other urinary system. The SMR for the former is 102 and the latter is 130 in males and 71 and 50 respectively for females. The SIR of 130 is roughly equivalent in magnitude to the SIRs of 128.6 and 132.6 from 78-82 and 83-88 respectively. The statistically significant lung cancer estimate is a modest SIR of 114 and leukemia is 114. The extremely modest estimates associated with known radiogenic tumors could easily be explained by uncontrolled confounding of imprecision in the data. These results are reassuring that no major environmental hazard is present.

d. Given the CCR guidelines should Dr. Nasseri's calculations have been followed up with a more intensive study?

Possibly. The data on which these estimates have been made are the best available and further analysis of the limited cancer registry data is unlikely to change the primary results. The very modest non statistically significant elevations in males could simply reflect the occupationally exposed segment of the population. However, reassurance that these estimates are correct and consistent with the LA county rates may be gained by doing an analysis of all the years for which data are available from LA county and Ventura county. Using the same criteria, extending the estimates to all cancers and noting site specific trends as feasible, may increase the confidence in the patterns of incidence.

e. Should Dr. Nasseri's calculations have been disseminated to community representatives?

Yes. They appear to be competently compiled and nothing is to be gained by withholding data from a community. The one major limitation of these estimates, that they maybe underestimated because not all cases from the last year were included, would need to be addressed/communicated in some way. It is very important that scientists be available to respond to inquiries from the community regarding interpreting the results.

f. Would Dr. Nasseri's calculations be of interest to investigators studying health effects in the community near SSFL?

Yes – this information may allow current studies to be refocused and prevent overlap in effort.

g. Briefly summarize the strengths and weaknesses of using cancer registry data to study environmental risk factors.

There are many factors that influence cancer risk: including genetics, diet, occupation, various lifestyles and infections. As data on risk factors are not collected in a cancer registry they cannot be addressed in analysis. As such, registry studies are useful to document elevated or changing cancer rates, but not useful in identifying specific causes for those observations. Special studies are required to test hypothesis regarding underlying patterns of rates.

In studying an environmental exposure the most persuasive indirect evidence that may come from registry data would be a dose response relationship by distance from the exposure (rates decreasing as the exposures from a point source decreased allowing an appropriate latency interval). Even data like this would need to be supplemented to ensure that other correlated factors did not explain the dose response. An effort like this would require a great deal more information on the environmental exposures in these communities.

The strength of cancer registry data lies in the ability to identify the magnitude and trends in rates which raise questions about why changes are taking place. These questions can then be addressed in more rigorous special studies, providing the magnitude of the increase in the rates and the statistical power of the protocol warrant it.

h. Given that an occupational study showed increased cancer mortality (lung and leukermia) for SSFL workers exposed to radiation, how would you have used cancer registries to investigate cancer incidence in the community surrounding SSFL?

I would have done studies similar to those reported in an effort to rule out large increases in incidence in the communities surrounding the facility and gathered information on the type and magnitude of the potential environmental exposures to radiation. The current data consistently show no elevation in leukemia, a very modest non statistically significant elevation in lung cancer and bladder cancer. As all of these elevations are specific to males, one would want to consider the gender of the occupational workforce. If primarily male, then these modest elevations in the population based data may reflect occupational exposures. As the methodology to study environmental exposures in regional populations is inherently imprecise surveillance should be continued to rule out larger effects which may emerge over time.

We know that leukemia is a radiogenic cancer, with the exception of cll, with a latency period as short as three to five years reported in some radiation exposed populations. We suspect that lung cancer is also a radiogenic tumor (data from the Southern Urals suggest an elevated risk of lung cancer in

plutonium exposed workers), although the data on this point are less clear with respect to the type and dose levels required to induce tumors and the latency appears to be quite long (20 or more years). The results of the occupational study are biologically plausible and consistent with what we know about radiogenic tumors. As the plant has been operating since 1948 and the incidence data appears to be available since 1978 (30 years later), it is impossible to assess incidence rate patterns with these latency intervals in mind.

It also seems impractical to use cancer incidence data alone to separate the effects of occupational exposures from environmental exposures. One would need a mechanism to remove all past workers residing in the region from both the numerator and the denominator to obtain an estimate of the cancer rates involving the environmental component of this equation.

i. Any other suggestions for a community study?

Environmental questions which involve very modest elevations in rates are really unresolvable using data systems set up to conduct surveillance. A population based case control study that addresses occupational and environmental exposures to radiation while controlling for all known risk factors focused on radiogenic tumors should be discussed. This seems to be the only study design that may be able to separate out the effects of exposures from different sources. Research on molecular markers associated with radiation exposures has progressed and should be explored as a tool to aid in this situation. An assessment of the type and magnitude of the potential environmental doses involved may also help to clarify the utility of further investigations. While the elevated rates reported are very modest and not statistically significant, the exposure of concern is a known carcinogen and should be considered carefully. Further studies should only be embarked upon if the protocol proposed can provide improved exposure assessment and control for confounders while substantially improving the precision of the estimates. Some consideration should also be given to minimizing any current exposures should they warrant it.

Review of documents related to cancer incidence in the vicinity of Rocketdyne's Santa Susana Field Laboratory

Submitted to California EPA on June 15, 1999

by

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Introduction

This report addresses questions posed by the California Environmental Protection Agency in a letter dated May 19, 1999, from Dr. Myrto Petreas of the Hazardous Materials Laboratory (Appendix 1). The questions refer to the following documents:

1. "Cancer incidence rates in five Los Angeles County census tracts." CDHS Report, 1990
2. "Cancer incidence near the Santa Susana Field Laboratory. CDHS Report, 1992
3. Letter from Dr. Nasseri of the Tri-County Regional Cancer Registry to Mr. Lorenz of the Santa Barbara County Public Health Department, 1997
4. "Fact Sheet." Frequently asked questions and answers about item #3. From the Tri-County Regional Cancer Registry of the Santa Barbara County Public Health Department
5. "Guidelines to address citizen concerns about cancer in their communities." From the California Cancer Registry, 1998.

General Comments

- The studies (items 1-3) were surveillance studies (ecological epidemiology) that had little ability to detect environmental carcinogens such as those that may have been released from the Santa Susana Field Laboratory (SSFL). The problem with surveillance studies is that they lack data on important variables such as length of residence, socioeconomic conditions, population size changes, and likelihood of exposure to environmental, occupational, and lifestyle carcinogens. Because of their limitations, surveillance studies can only detect very large risks and they tend to be hypothesis-generating in usefulness. On the other hand, analytic epidemiologic studies (case-control and cohort studies) collect data of all kinds on individual subjects and they tend to be hypothesis-testing in usefulness. Unfortunately, analytic studies are much more expensive and should only be done if there is a good reason to suspect an excessive risk of cancer.

Review of documents related to cancer incidence in the vicinity of Rocketdyne's Santa Susana Field Laboratory

Submitted to California EPA on June 15, 1999

by

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This report addresses questions posed by the California Environmental Protection Agency in a letter dated May 19, 1999, from Dr. Myrto Petreas of the Hazardous Materials Laboratory (Appendix 1). The questions refer to the following documents:

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5. "Guidelines to address citizen concerns about cancer in their communities." From the California Cancer Registry, 1998.

General Comments

- The studies (items 1-3) were surveillance studies (ecological epidemiology) that had little ability to detect environmental carcinogens such as those that may have been released from the Santa Susana Field Laboratory (SSFL). The problem with surveillance studies is that they lack data on important variables such as length of residence, socioeconomic conditions, population size changes, and likelihood of exposure to environmental, occupational, and lifestyle carcinogens. Because of their limitations, surveillance studies can only detect very large risks and they tend to be hypothesis-generating in usefulness. On the other hand, analytic epidemiologic studies (case-control and cohort studies) collect data of all kinds on individual subjects and they tend to be hypothesis-testing in usefulness. Unfortunately, analytic studies are much more expensive and should only be done if there is a good reason to suspect an excessive risk of cancer.

- The studies did not discuss evidence of potential exposure to residents from SSFL. I recommended that the Guidelines (item 5) be amended to address this deficiency (also see Question _).

Question A. *What are the necessary elements that would alert me to significant increases in cancer incidence?*

Statistically significant increases in cancer rates happen often due to random variation in case occurrence across time periods and geographical areas. Thus, most statistically significant increases in community cancer rates are not caused by environmental factors.

Suspicion that there might be a causal factor is raised in my mind under one or more of the following circumstances:

- The increase is consistent over multiple time periods.
- The increase is consistent across genders.
- The increase is consistent across race-ethnicity groups.
- The increase is highly statistically significant (e.g., $p < 0.01$).
- The magnitude of the increase is outside the "noise" range caused by common biases.
- The increase is specific to one histologic type of cancer (sometimes the case for environmental carcinogens)
- The type of cancer with the increased rate has been previously associated in animal or human studies with an exposure that has been documented in the community.
- The increase is temporally correct with regard to the type of cancer and time since first environmental exposure in the community (e.g., a latent period of 5+ years for leukemia and 10+ years for lung and bladder cancers).
- When the suspected exposure is known to cause more than one type of cancer (e.g., cigarettes), that the expected constellation of increased organ site-specific rates is seen.

Question B. *Do either of the first two studies indicate increased cancer incidence in the community during the periods studied?*

The first study (released in 1990) found suggestive increased rates of bladder cancer in the study region compared to L.A. County in general. However, as noted by the authors, the increase in rates might easily be explained by ethnic or smoking differences, or by random variation. There was no increased risk of lung cancer, which argues against the smoking explanation. The study had many limitations (e.g., no SES or gender in analysis), and the bladder cancer association was inconsistent geographically and over the two time periods. On balance, I conclude that the 1990 report does not indicate increased cancer incidence.

The second study (released in 1992) verified the bladder cancer increase reported for 1983-1987 in the 1990 report (but extended the study period by one year to 1988). The increase was inconsistent between genders (only increased in males) and across geographic areas (increase only occurred in L.A. County). Similarly, lung cancer rates were increased in some census tracts, but the increase was inconsistent between genders (only increased in males) and across geographic areas (the increase only occurred in Ventura County). This study was of better quality than the first study, but it also had many limitations. Considering all of the evidence, I conclude that 1992 report does not indicate increased cancer incidence.

Question C. *Do Dr. Nasseri's calculation (items 3 and 4) indicate an increased cancer incidence in the community during the periods studied?*

Dr. Nasseri's calculations show increased risk only for lung cancer. He does not assess the lung cancer increase for statistical significance, but I would guess that the increase is real. Since tobacco smoke is a strong carcinogen for the lung, the causal factor may be higher historical cigarette consumption among the residents.

Types of cancer other than lung are also caused by smoking, including laryngeal cancer, bladder cancer, and pancreatic cancer. Of these, only bladder cancer was reported, and its observed rate was slightly less than expected, which is some evidence that cigarettes may not be responsible for the higher incidence of lung cancer. However, cigarettes are a more powerful carcinogen for the lung than for other organ sites, and the increase in lung cancer was small (17%). Thus if cigarettes were responsible for a small lung cancer increase, it would be difficult to detect an increase in bladder or other cancers related to smoking.

Several potential biases are mentioned in Dr. Nasseri's letter and in the fact sheet distributed by the Santa Barbara department of public health. However, those documents do not discuss the direction of effect that could be caused by the potential biases. The potential biases are listed here:

<u>Potential biases discussed in documents</u>

- Lack of SES data
- Study area population rates (1988-1995) and control population rates (1988-1992) covered slightly different time periods.
- Rate denominators from the census were for 1990 only. This was OK for the control population rates because 1990 was in the center of their 1988-1992 time period, but it may have caused bias in the study area rates (1988-1995) that were not centered around 1990.
- Cancer data ware incomplete for the study population in 1995. While the completeness was estimated to be 88% for all types of cancers combined, the completeness for specific types of cancer probably varied considerably. Cancers are not reported at the time of diagnosis as stated in the fact sheet; in fact they are

reported after the first course of treatment is completed, which depends on the type and stage of cancer. The bias that might occur is that the rates in the study area may be artificially low, which could partly explain decreased risks such as that seen for leukemia in women.

Other limitations

- No exposure data.
- No data on cancer sites not considered to be radiosensitive, which is a problem when information is need for cancers caused by environmental factors other than ionizing radiation. For example, data on other cancers (other than lung) caused by tobacco smoke would have been very helpful.

Question D. *Given the CCR Guidelines, should Dr. Nasseri's calculations have been followed up with more intensive study?*

No. The CCR Guidelines provide no recommendations for scientific follow-up when increased risk is suggested in an observed/expected assessment. This is a serious deficiency of the guidelines. The Guidelines do provide recommendations for communication, as follows (in the section titled Communicating the Results): "If the cancers are elevated or otherwise unusual, future actions planned, e.g., consultation with other agencies, or monitoring, or both, should be described. County health officials should be notified."

Question E. *Should Dr. Nasseri's calculations have been disseminated to community representatives?*

Yes, in my opinion and according to the CCR guidelines (in the section on Communicating the Results), the calculations should have been disseminated.

Question F. *Would Dr. Nasseri's calculations be of interest to investigators studying health effects in the community near SSFL?*

Yes. All relevant and valid data would be of interest, including Dr. Nasseri's calculations.

Question G. *Summarize the strengths and weaknesses of cancer registry data for studying environmental risk factors.*

There are many strengths and weakness of cancer registry data for studying environmental risk factors, but some the more important ones for this situation are as follows:

Strengths

- Incident cases (as opposed to mortality cases).

- Population based, which allows rates to be calculated using census data.

Weaknesses

- Long reporting time after diagnosis (average 8 months).
- No exposure data.
- No length of residence data.
- No smoking data.
- Weak occupational data.
- Population sizes uncertain in years between census counts.

Question H. *Given that an occupational study at SSFL showed increased cancer lung and leukemia mortality in persons exposed to radiation, how would I have used the cancer registries to investigate cancer incidence in the community?*

I would have performed a study similar to Dr. Nasseri's, but would have additionally included (and statistically modeled) census data on education and income (both associated with cigarette smoking) and cell type data from the registry if certain cell types were implicated in the worker study.

Question I. *Suggestions for a community study?*

Two types of community studies would be helpful:

- An ecological epidemiology study that is similar to the previous studies, but that includes SES data from the census, all types of cancer (not just the "radiosensitive cancers"), all time periods for which data are available, and consistent epidemiologic methods over time. The epidemiologic methods that are inconsistent between the three community studies (items 1-3)) include: use of invasive versus all cancers, use of population based rates versus proportions of cancer types, and organization of cancer type categories (International Classification of Diseases codes).
- A population-based case-control study that provides data on residential history, smoking history, occupational history, and estimates of environmental exposures from SSFL . This type of study would take longer and cost more than a surveillance study, but it would be more powerful and more conclusive.