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Deputy Director
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From: Myrto Petreas, Ph.D., MPH
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Re: Health Studies at Santa Susana Field Laboratory- Expert Panel Review

Date: June 20, 1999

Attached please find the Final Report entitled "Health Studies at Santa Susana Field Laboratory-Expert Panel Review".

The Final Report provides the background for the review, defines the review objectives, describes the approach used, and discusses the conclusions reached by the two independent reviewers, Dr. James Beaumont of UC Davis, and Dr. Faith Davis of the University of Illinois, Chicago.

This Final Report is independent of my own evaluation and recommendations described in my May 12, 1999 Progress Report to you. The conclusions reached by the panel members upon review of the original material, however, are practically the same.

Health Studies at Santa Susana Field Laboratory

Expert Panel Review

June 20, 1999

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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. Nasserri 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. Nasserri'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. Nasserri'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.