ROCKETDYNE WORKER HEALTH STUDY

Appendix H

INTERNATIONAL EPIDEMIOLOGY INSTITUTE

Responses to Issues Raised by Science Committee (2001-2005)

July 13, 2005

RESPONSES TO SCIENCE COMMITTEE COMMENTS RECEIVED FEBRUARY 10, 2005 ON FINAL REPORT*

ROCKETDYNE WORKER HEALTH STUDY

INTERNATIONAL EPIDEMIOLOGY INSTITUTE

March 10, 2005

* Because of copyright restrictions, detailed tables of the study findings cannot at this time be posted on the website during the journal review process of four manuscripts submitted for publication. It is envisioned, however, that they will be made available sometime in the forseeable future.

Each of the 14 comments from the Science Committee is reproduced in bold and then followed by an IEI response. The additional tables requested are found in the attached Appendix.

1. **The SC continues to be impressed with the quantity and quality of work carried out in such a short time. The following comments are intended to improve on an already excellent product.**

   Response: Thank you.

2. **The SC appreciates the responsiveness of IEI to the various requests that we formulated over the past few months.**

   Response: Thank you. We will continue in our attempt to be responsive to the issues raised by the Science Committee.

3. **We recognize that IEI has added a large number of tables to these reports and that integrating them quickly with the text was not easy. Some of the tables are mentioned in the text and others are not. IEI might want to review the text and tables to see if there are any more tables that should be commented on, even if briefly. For example, Chem 2.2, 3.0, 6.2, 6.4 are not mentioned in the text but appear as part of the tables attached to the paper. One editorial comment from the SC is that the ordering of tables could be reversed, to respect the principle of going from the general to the particular. As an example, in the Radiation results paper, Table 3.2 would precede Table 3.1.**

   Response: Comments for the Tables mentioned above are included below. We will provide comments also for other Tables with missing comments as recommended. We will also integrate these comments into the appropriate manuscripts and documents. We will reorder the tables as recommended. Below we list the titles for the above mentioned tables followed by comments.

   Chem Table 2.2 Observed and Expected Numbers of Deaths and Standardized Mortality Ratios (SMR) for Rocketdyne Workers in the Chemical Cohort by Work Location (SSFL, Other Rocketdyne Facilities, Total) White Males Only. General Population of California Used to Compute Expected Numbers.

   Comment: Analyses were conducted for white male workers separately. Because white male workers make up the large majority of workers in the study population, there were no noticeable differences in the SMRs compared to analyses including all races and all genders. For example, for white male workers at SSFL, the SMR for all cancers was 0.87 (95% CI 0.89-0.95) based on 560 deaths (Table 2.2). For all SSFL workers, both men and women and both white and non-white workers, the SMR for all cancers was 0.89 (95% CI 0.82-0.96) based on 655 deaths (Table 2.1).

   Chem Table 3.0 Observed and Expected Numbers of Deaths and Standardized Mortality Ratios (SMR) for SSFL Workers by Time Since First Hire (Latency). General Population of California Used to Compute Expected Numbers.

Comment: Duration and latency SMR analyses were also conducted for 3 latency intervals and 3 duration of employment categories for 12 selected causes of death [Table 2.2; Appendix Table 2.2]. No cause of death, including lung cancer, was significantly elevated in any latency category. Risk for all cancers and lung cancer were higher among workers in the years 10 or more after first hire than in the first 10 years after hire, as typically seen in occupational studies where the low risk immediately after hire is attributed to factors that select healthy persons into the workforce. Such initial selection often decreases with increasing follow-up and there were no differences seen in years 10 to 29 (SMR all cancer 0.90) and in years 30+ (SMR all cancer 0.92). No cause of death, including lung cancer, was significantly elevated in any duration category and no clear patterns emerged, e.g., for duration of employment categories of < 5 yr, 5-9 yr, and 10+ yr the SMRs for lung cancer were 1.14, 1.25, and 1.03, respectively (Appendix Table 2.2).

Chem Table 6.2 Observed and Expected Numbers of Deaths and Standardized Mortality Ratios (SMR) for Male Hourly Test Stand Mechanics by Duration of Employment as a Test Stand Mechanic. General Population of the United States Used for Comparison.

Comment: Table 6.2 presents the SMRs for test stand mechanics by duration of employment using the general population of the United States for comparison. These SMR values are generally lower than those computed using the population of California for comparison (Table 6.1). Neither the US general population nor the California general population are ideal comparison groups because of differences between workers and the general population in potential confounding factors, and because of the selection factors of health associated with employment. As such, the internal cohort analyses are preferred in making inferences as to the possible effect of workplace employment on health (e.g., Tables 6.3 and 6.4 discussed below). Even the choice of California versus the United States for comparison is not entirely straightforward because at least 25% of the workers had left California after employment at Rocketdyne (based on information found on the death certificates for place of death). The use of the US population for comparison is often used in occupational studies because of availability of rates and because of the mobility of the workforce. The SMRs were lower when comparisons were made with the US population than the California general population. Thus the more accurate SMR values for this mobile population likely lies somewhere between those computed using US rates and those computed using California rates. Comparisons with the general population are useful for assessing patterns of risk that might be further analyzed within the cohort.

Chem Table 6.4 Internal Cohort Dose-Response and Relative Risk (RR) Computations for All Cancer Combined, Lung Cancer and Kidney Cancer for Test Stand Mechanics Over Categories of Years Worked as a Test Stand Mechanic. Other SSFL Workers Used as Referent.

Comment: Table 6.4 is similar to Table 6.3 except that only SSFL workers are used as the referent category whereas all Rocketdyne workers not monitored for radiation were used in Table 6.3. The distributions of risk over categories of years worked as a test stand mechanic were nearly identical as were the p-values for trend. For all cancers and lung cancer there was no evidence of increasing risk with increasing years worked as a test stand mechanic; and the RRs among the 474 mechanics who worked more than 5 years on a test stand were 0.99 (95% CI 0.72-1.35) and 0.96 (95% CI 0.58-1.59), respectively. There was a tendency for kidney cancer to be increased with increasing years worked but numbers were small and trend not significant (p=0.8).

4. **Trend tests play a large role in IEI's interpretation of findings. The methods used are sometimes ambiguous. For instance in a table like Rad 6.2, it is not stated whether the values tested are the individual values or group values. In a table like Chem 8.1, it is not clear what values were used for the independent variable. Nor is it clear whether a linear trend test is the best test of an association in a situation where there may be measurement error and non-linearity of effects. We believe the trend tests are informative, but so are point and interval estimates, especially in the face of exposure misclassification, which is inevitable in any retrospective investigation.**

Response: We will be more explicit with regard to the methods used in conducting the tests for trend. Trend tests for all internal cohort radiation dose-response analyses were conducted by entering the individual cumulative radiation dose as a continuous measure into a Cox proportional hazards model along with the exact same set of covariates used in the corresponding categorical dose analysis. This continuous measure of dose was the actual radiation dose value received by each individual worker (in units of rem). From the Cox model, a single estimate of risk was calculated for this continuous measure and the p-value from a Wald chi-square test was presented in the tables as the 'p for trend.' Thus, for Rad Table 6.2 the individual dose values and not group values are used to calculate the trend test.

Trend tests were conducted in similar manner described above for the internal cohort dose-response analyses with years worked taken as the continuous variable of exposure. However, there was one exception. For Chem Table 8.1 ordinal values were used for the independent variable, and we have now added a footnote to the table in this regard. The ordering was based on a logical ranking of the potential for hydrazine exposure among workers in each category.

We have used linear trend tests in most of the evaluations and agree that point and interval estimates are also important to present. Thus, we have presented point and interval estimates for each category in each interval dose-response table. In some of the tables we have also evaluated heterogeneity in the point estimates without any underlying assumption as to a monotonic increase in risk with measures of exposure (Rad Table 10). We also note that using a linear trend test in radiation studies is standard procedure, especially in studies of low dose exposures. We agree that measurement error and misclassification are important limitations in such studies as the one conducted and discuss this limitation in two paragraphs in the Discussion section of the chemical paper.

5. **There are some tables where sparse numbers mean that there is very little power to detect effects in subgroup analyses. In that case we would like an analysis that collapses subgroups. For Rad Tables 6.1 and 6.2 the SC requests estimates of RR with some collapsing of subgroups, for Dose > 5 (combined) and Dose > 10 combined, in addition to those already shown. The other table where we request an analysis collapsing categories is Chem Table 8.3, presenting data with all hydrazine combined compared to test stand mechanics without potential for hydrazine exposure.**

   Response: As requested, we have collapsed the dose data in Rad Table 6.1 and 6.2. Also, we combined the data in Chem Table 8.3 as requested. These new tables can be found in the appendices at the end of this response document. However, we do not believe the combination of hydrazine categories is appropriate. We perhaps have not been clear on the difference between the two categories. The "potential but unlikely" category meant that workers were employed at a large testing area where hydrazines had not been used except at a small sub-area which involved a few workers who we could not identify. For the majority of workers, potential exposure to hydrazine was not an issue because they worked on large engines where hydrazines were not used. However, because we could not distinguish the small number of workers potentially exposed to hydrazines from the larger number not potentially exposed, we created a category of "possible but unlikely" exposure potential. Chem Table 8.3 (also included in the Appendices) was recommended previously by the Scientific Committee and we believe is the scientifically appropriate one. This table separates the potential but unlikely exposure group from the potential exposure group. Nonetheless, the requested Table is found in the Appendix and there was no evidence of trend in years worked combining potential with unlikely exposure to hydrazines. The radiation re-categorization also had little effect on the observed patterns or on the point estimate for the high dose category. It is noted that the point estimates (RRs) for CLL tended to be larger than the point estimates for the non-CLL leukemias which is counter to expectation since CLL is not considered inducible by radiation.

6. **The SC needs to see Rad Table 3.1 broken down by hourly/salary.**

   Response: We provide Rad Table 3.1 broken down by hourly/salary in the attached Appendix. This in an external comparison with rates from the general population of California. We believe the internal cohort comparisons are the most appropriate ones (e.g., Rad Appendix Tables 1.3R and 1.4R also attached) where hourly workers are compared to hourly workers and salaried workers are compared to salaried workers; which minimizes the potential problem of differing characteristics such as smoking habits between the hourly and salaried worker population and the general population. See response to comments (3) and (9). Splitting the data (Table 3.1, included) into an additional two groups also increases the number of comparisons made (35 to 70) which could lead to statistically significant results due to chance rather than a real effect. There also is no reason to believe that hourly workers would respond differently to radiation than salaried workers. Further, Rad Table 3.1 involves only external exposure and not the internal dose contribution which hinders interpretation. Again, the internal cohort dose-response analyses are optimum for making inferences because the full range of doses are included, comparisons with the general population are avoided, and pay type can be adjusted for in the analyses. Such internal cohort analyses for major cancer sites and combinations are found in Rad Tables 5.1, 5.2, 5.3, 6.1, 6.2, 6.3, 7.0, 8.1, 8.2 and Rad Appendix Tables 1.3R, 1.4R, 2.2R, 2.3R, 3.1R, 3.2R, 4.1R, 4.2R, 5.1R, 5.2R.

Other comparisons with the general population for hourly and salaried workers can be found in Rad Appendix Tables 1.1R and 1.2R and Chem Tables 5.1, 5.2 and 6.1 as requested previously. It can be noted that there were few significant elevations in SMRs for hourly workers based on comparisons with California rates and no significant elevations when US rates are used. As described in (3), the more accurate SMR values must be between those computed from US rates and California rates for this mobile population.

7. **Initially, IEI intended to carry out some analyses using the Lockheed workers as a comparison population. Has this been done but not reported?**

Response: Initially, we had thought that it would be possible to make direct comparisons between the Lockheed Martin Worker Study and the Rocketdyne Worker Study, but we decided that the Canoga Park and De Soto Avenue workers would be an even more appropriate comparison group which could be followed for the same number of calendar years. The mortality follow-up of the Rocketdyne workers was up to the year 2000, whereas the Lockheed Martin Cohort stopped in 1996. The Canoga Park and De Soto workers also were similar in selection factor for employment, health care and local residence as SSFL workers.

8. **For many of the contrasts examined, statistical power to detect an effect was low and confidence intervals were wide. Such findings may be consistent with the null hypothesis but they don't prove it. The SC thinks the limitations of the data in detecting hazards (which were inherent in the study and not the fault of the investigators) need to be clearly stated alongside the interpretation of the results.**

Response: We agree. More can be added with regard to explicit statements about the limitations of the data to detect hazards. In the Discussion sections we will enhance this point regarding the ability to detect presumed risks in this worker population. We have also drafted a "text-box" to the lay summary (see below) and look forward to the SC comments on how best to portray these issues to workers and the retirees.

"Making causal inferences based on small numbers of cases. The number of cancer deaths can determine whether a study has the ability to detect a statistically significant increase. Studies involving small numbers are not as powerful as studies with large numbers. Small numbers result in estimates of risk that are very imprecise which means that chance often cannot be ruled out as an explanation for the findings. This does not mean that there was no increase in risk, just that the ability of the study to detect the risk was limited. Similarly, there were also tendencies for risk to decrease with increasing amounts of radiation such as for lung cancer and liver cancer. Again, the decrease was not statistically significant and chance could not be excluded as a possible explanation. Non-statistically significant decreasing trends or tendencies do not mean that radiation reduced the risk of cancer any more than non-statistically significant increases mean that radiation caused the increase. The study just wasn't large enough to provide clear results."

9. **The interpretation of lung cancer results is critical. The SC is concerned that the sentence included in the title of the several tables ("Caution in Interpretation… General Population") is an inappropriate flag. It is unorthodox to include such a disclaimer in a title and it might lead to inference that the results are uninformative. The SC does not necessarily disagree with the spirit of this statement but we feel that it would be preferable to deal with this particular issue in the text as with any other issue that affects the interpretation of results.**

Response: We have now removed the phrase in the table titles regarding concern over differences in smoking habits between hourly and salaried workers that might be responsible for some of the patterns observed. These issues had been discussed fully in the text, as well as in the sub-study recommended by the Science Committee regarding smoking habits between salaried and hourly workers.

10. **IEI states that their results "fail to confirm" the UCLA findings. The reader could interpret this in different ways. It may mean that the results differ or it may mean that IEI interprets the same results in a different way. It may be worthwhile to spell out what is meant by "fail to confirm", as noted above under (8).**

Response: At the request of the SC we had attempted to spell out differences between the UCLA study and the IEI study. An entire section had been added to the Final Report Appendix presenting the differences in the exposure categories and in the findings. We tried to match our categories to those presented by UCLA. Our general statement regarding "fail to confirm" was meant to imply that the statistically significant findings reported by UCLA and the patterns reported were not borne out with our additional follow-up. We will, however, try to use more explicit language in the Executive Summary, and papers, so as not to be misleading. We agree, also, that issues of statistical power are also important and will discuss more fully as done in our response to (8).

11. **The SC notes that there has not been an explicit discussion of the possibility of conducting nested case-control studies. IEI appears to think this would not be fruitful. The SC thinks it is important that IEI makes it clear what their recommendation is in this regard, and state explicitly why they have reached this conclusion.**

Response: In the Executive Summary, section 10 on Recommendations we state "Because there were no significant increases seen in the cohort internal dose-response evaluations, there seems little justification to consider nested case-control studies at this time. The additional number of cancer deaths that would accrue in a further follow-up, however, would be informative with regard to the health evaluation of Rocketdyne Workers."

Our conclusion is based upon several observations, including the absence of any significant or consistent excesses. As the SC mentions in (5) and (8) the study in general has limited statistical power to detect effects (whether using a cohort approach or a case-control approach). The radiation dose distribution is very low and much lower than in other studies were effects are clearly evident. The numbers exposed to “high” doses of radiation are small, as are the numbers of workers “potentially” exposed to hazardous chemicals. The exposure assessment problem for the chemicals is recognized by the SC as above, which includes having to use “years worked” as a surrogate for actual exposure and to the fact that the exposures occur outdoors and not in enclosed spaces where concentrations are necessarily diluted. Attempts to improve the exposure assessment to radiation or to chemicals are unlikely to yield an appreciable improvement. Additional investigation of potential confounding influences, such as tobacco use, would not be recommended because of the absence of any significant increases over categories of radiation dose to lung or over categories of years worked as a test stand mechanic. Obtaining accurate and valid smoking information would be difficult, also, for those who have died, where surrogate responses from spouses or children many years after the fact would have to be obtained. Finally, the number of cancers for some sites of potential interest, such as kidney, are small and generally less than 10 and not amenable for meaningful case-control evaluation.

Thus, the small numbers of workers in the study, the relatively low exposures to radiation and chemicals, and the absence of any significant or consistent excesses argues at this time against the need for a nested case-control investigation.

12. **In judging the results of this study, one has to break it down by outcome. Is there an excess risk of lung cancer? Is there an excess risk of leukemia? Is there an excess risk of kidney cancer? At present it is quite difficult to form a clear opinion because the results for a given outcome (e.g. lung cancer) are spread over scores of tables. It would help the SC and other readers if all the findings on the three cancers of concern (lung, leukemia, and kidney) are retrieved and presented in a single (long) table. Such a table should include information on the exposure group, the comparison population, whether external or internal, the table of origin, and other critical variables that define the contrast.**

Response: The Science Committee is asking for a table that summarizes the findings on lung cancer, leukemia and kidney cancer. It is requesting that all exposure groups and comparison populations and analyses be put together in one long format. We have made an attempt and include 5 tables in the Appendix summarizing the internal cohort analyses for lung cancer, kidney cancer and leukemia for the radiation cohort and the chemical cohort. We have not had the time to do a similar tabulation for the SMR analyses but note that the information is available in the tables in the Final Report. The SMR analyses are also more limited than the internal cohort dose-response analyses presented, as discussed in (6), for making inferences.

13. **IEI has done an excellent job. Because of various administrative and logistical exigencies, it is necessary to produce a report quickly on this study. Nevertheless the**

database remains one which could potentially be further analyzed and exploited to elucidate possible health risks among the workers at Boeing. This could take the form of new analyses with the data available, or nested case-control studies, or tracing in incidence tumor registries, or additional mortality follow-up. Boeing and UAW must establish guidelines for the storage and maintenance of the data that were collected in this enterprise, and develop a system for allowing access to the data so that useful analyses can be conducted in the future by others.

Response: Boeing has already agreed that the edited datasets (without personal identifiers) are to be placed on the DoE website (CEDR, Comprehensive Epidemiologic Data Resource). This will be done as soon as manuscripts and other contract work are complete. Other issues regarding the database are to be decided by Boeing and UAW.

14. **The documents presented represent the work and opinions of IEI. The SC intends to produce its own brief document summarizing its interpretations of the results. This should be done in March 2005.**

Response: IEI looks forward to receiving a copy of your document summarizing interpretation of the results. I'm confident that we can converge on a single summary that would be helpful to Boeing and UAW when describing the study results to workers and retirees.

INTERNATIONAL
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INSTITUTE, LTD.

January 14, 2005

To: Steve Lafflam, Division Director, Safety, Health and Environmental Affairs
From: John Boice, Scientific Director, IEI
Subject: Final Report for Rocketdyne Worker Health Study

Enclosed is the revised Final Report taking into account the recommendations made during the 6 December 2004 meeting of the Science Committee. The components are:

- Executive Summary
  - Index of Radiation Tables and Figures
  - Index of Chemical Tables and Figures
  - Index of Tables and Items in the Detailed Appendices
- Radiation Study
  - Radiation Tables and Figures
- Chemical Study
  - Chemical Tables and Figures
  - Index and Tables of Chemical Cohort Excluding Radiation Workers
- Radiation Dosimetry Paper
- Uranium Aluminide Paper
- Detailed Appendices

A detailed summary of recent work as well as a summary of the revisions made in response to the recommendations received during the December meetings also are attached.

We are working on a draft "Lay Summary" and should be able to send to you shortly.

Enclosures (as above)

cc: Scientific Advisors for Rocketdyne Worker Health Study
Frank Mirer

1455 RESEARCH BOULEVARD SUITE 550 ROCKVILLE, MARYLAND 20850 USA TELEPHONE 301-517-4060 FAX 301-517-4063

Responses to the Recommendations Made During the December 2004 Meetings
January 15, 2005

New Items and General Comments:

1. *Figures.* Figures have now been added to the Radiation and Chemical Sections for selected internal cohort dose-response analyses.

2. *Multiple Comparison Groups.* For many of the analyses, different comparison groups are now presented. For SMR analyses, comparisons are made with California and with the U.S. general populations and occasionally with the Los Angeles + Ventura county populations.

For internal cohort analyses for the Chemical Cohort (test stand mechanics for example), comparisons are presented with Rocketdyne workers, SSFL workers, and with “zero exposed” test stand mechanics (for hydrazines and TCE analyses) as referent.

3. *White Males.* Analyses restricted only to white males are presented.

4. *Early Years after Hire.* Tables are presented which exclude the first 10 years of follow-up after hire.

5. *Latency and Duration.* Several tables are presented by latency intervals (time since hire) within categories of duration of employment.

6. *Lagging.* Radiation tables are presented with a 2-year lag for leukemia analyses and a 10-year lag for analyses of solid cancers.

7. *UCLA Comparisons.* Detailed comparisons with the previous investigation by UCLA are now presented in the Appendices, Section D. The key summary tables from the UCLA investigation are reproduced and then the data corresponding to the current investigation are presented for comparisons.

8. *Smoking.* The results of the Smoking Survey have been tabulated and are presented in the Appendices, Section C.

9. *Dosimetry Paper.* Was submitted to Health Physics and received a favorable review (tentative acceptance).

10. *Reformatting and Restructuring Tables*. As recommended, detailed listings of tables and detailed titles have been prepared. Further, all tables pertaining to the Radiation Study now follow the Radiation Paper in the format of detailed index (listing), text tables, appendices tables and figures. All tables pertaining to the Chemical Study follow the Chemical Paper in format: index, text tables, appendices tables, figures. The appendices radiation and chemical tables mainly are those “auxiliary” tables that support statements made throughout the texts.

11. *Appendices.* As before, the appendices include an eclectic group of items pertaining to (A) a few additional analyses and summary tables that include “all” (radiation and chemical) Rocketdyne workers studied, (B) study topics such as asbestos, (C) detailed smoking survey results, (D) tabular comparisons with UCLA study, (E) databases used during the study, (F) glossary of terms, (G) study documents (essentially volume 7A distributed 6 December 2004 which included IRB approvals, quarterly reports, etc).

12. *Executive Summary.* This provides an overview of the study conduct and results. Brief paragraphs then follow summarizing the (1) IRB approvals, (2) identification of study population, (3) tracing of population, (4) cause of death determination, (5) assessment of radiation doses, (6) chemical exposure assessment, (7) study findings, (8) auxiliary analyses, (9) comparisons with the UCLA study, (10) recommendations for future study, (11) manuscript drafts.

Responses to each of the 20 items distributed after the 6 December meeting of the Science Committee are made below in *italics*.

1. Revise table titles to be more specific. Longer titles as needed.

   All table titles have now been revised to be as explicit as possible with regard to content. Footnotes also have been added to aid understanding.

2. Provide a list of all tables.

   Two detailed listings of the tables and figures have been provided, one for the Radiation Study and the other for the Chemical Study. These index listings are found after the Executive Summary and also reproduced after the respective Radiation and Chemical papers.

3. Conduct analyses that include the radiation exposed workers who were test stand mechanics in the SSFL cohort.

   The 182 test stand mechanics, who also had been monitored for radiation, have now been included in all Chemical tables. We have kept the previous tables that do not include the radiation workers as an additional appendix in the Radiation Section with each title including the letters NR for "no radiation". UCLA did not include the workers monitored for radiation.

4. Place Appendices Analyses after the Appropriate Paper and not in separate Appendices.

   All the chemical-specific and radiation-specific analyses and tables have now been placed after the appropriate paper. The are referred to as "radiation appendix tables" or "chemical appendix tables". The only analytical tables that remain in the Appendices are a few overview tables that include all Rocketdyne workers studied, i.e., combining the radiation and chemical cohorts.

5. Be more consistent in description of results. Use "statistical significance" as appropriate. More uniformity and care in describing risks that are not "statistically significant" risks.

   We have attempted to be more uniform in describing results, but some inconsistencies may remain. We will continue to review and revise for consistency and clarity.

6. Radiation paper. Latency analysis, Table 3a. 2-year latency for leukemia and perhaps 10-year latency for solid cancer. Conduct dose response with internal referent with lags also.

   Analyses have now been conducted and tables presented with 2-year latency periods for leukemia and 10-year latency periods for solid cancers. Internal cohort dose-response analyses have also been conducted with 2-year lags for leukemia and 10-year lags for solid cancers. [see Radiation Tables 2.3, 3.1, 4.1, 5.1, 5.3, 6.1, 6.3, 8.1, Appendix Tables 1.3R, 1.4R, 2.2R, 3.1R, 4.1R, 5.1R; Chemical Tables 2.3, Appendix Tables 2.2C, 3.0C] Analyses without latency considerations and lags are also presented.

7. More evaluation of Hydrazine. Analyses using "no hydrazine exposure as the referent". Little is known about hydrazine, but exposure is outdoors (Simi = windy) and not in confined environment. Anomalies in SMR analyses. But be careful in reading too much in the SMRs since hydrazine workers all hourly, non-administrative and general population contains salaried workers and not optimum comparison. More confidence in the radiation findings since doses low, and little excess expected and little seen, and body of literature to support finding. Not so for hydrazine. Little human literature. But number exposed also low.

   Internal cohort dose-response analyses for hydrazine (and TCE) have now been conducted using three different comparison groups: All Rocketdyne workers, SSFL workers, and test stand mechanics with no years of work with hydrazine (or, correspondingly, with TCE). [See Tables 8.1-8.3 and 9.1-9.3].

8. Non-SSFL hourly workers have significant excess risk compared with some general population

comparisons. Hourly, non-administrative workers likely select on smoking but could be chemical/other worker environment. Conduct internal analyses by years worked at non-SSFL facilities. Conduct duration and latency analyses also. Perhaps force of mortality is in the long latency but short duration group. Perhaps health related termination.

Internal dose-response analyses have been conducted for the non-SSFL workers over years worked for all cancers taken together, lung cancer and kidney cancer using two different referent cateogies: SSFL workers who were not test stand mechanics and non-SSFL who had worked less than 2 years [Chemical Appendix Tables 4.1, 4.2]. No trends or subcategories were statistically significant.

Duration and latency SMR analyses were also conducted for 3 latency intervals and 3 duration of employment categories for 12 selected causes of death [Appendix Table 3.0]. As stressed throughout the report, hourly workers are know to use tobacco to a greater extent than salaried workers and the general populations and care is necessary when evaluating SMR analyses. Lung cancer was significantly elevated in several categories but no clear patterns emerged, e.g., for duration of employment categories of < 5 yr, 5-9 yr, and 10+ yr the SMRs were 1.25, 1.15, and 1.15 respectively.

9. Conduct similar latency (years since first hire), duration analyses for SSFL workers also as above.

Duration and latency SMR analyses were also conducted for 3 latency intervals and 3 duration of employment categories for 12 selected causes of death [Appendix Table 2.2]. No cause of death, including lung cancer, was significantly elevated in any categories and no clear patterns emerged, e.g., for duration of employment categories of < 5 yr, 5-9 yr, and 10+ yr the SMRs for lung cancer were 1.14, 1.25, and 1.03, respectively.

10. Consider moderate upgrade of conclusion of the Chemical paper regarding findings for TCE.

The conclusion has been slightly modified. *The discussion of the association between TCE and kidney cancer is as follows. "Arguments favoring a causal interpretation in our series include the magnitude of the increase risk, over two-fold, the suggestion of a dose response and the consistency with animal evidence. Arguments against a causal interpretation include the small numbers of observed cases, i.e., no association was statistically significant, the absence of any increased risk for the other cancers, such as lymphomas, thought to be inducible by TCE, the role of chance due to multiple comparisons, and exposure assessment inaccuracies. Nonetheless, the finding should be evaluated further in any additional follow-up of the Rocketdyne population.*

11. Dose response analyses separate for hourly and salary workers.

Radiation internal cohort dose-response analyses have been conducted separately for hourly and salaried workers for all cancer taken together, all cancers excluding leukemia, and lung cancer [Appendix Tables 1.3R, 1.4R]. Analyses with and without 10-year lagging of dose are presented.

Internal cohort dose-response analyses have been conducted separately for hourly and salaried workers for all cancers and lung cancer for workers in the Chemical cohort over years of employment at SSFL [Chemical Table 10.2]

12. Stomach cancer data missing in Appendix Table C6.

The stomach cancer data have now been included. It was missing in previous Appendix Table C2, not C6. This table has been modified and is now Chemical Table 10.1.

13. Consider preparing a Lexicon or Glossary of terms/definitions used throughout. Monitored, hourly, salaried, administrative, etc.

A five page glossary of terms used throughout the report has now been included as Section F in the Appendices.

14. Revisions to be made by IEI by January 15, 2005.

    Revisions complete on January 14, 2005 and placed in Federal Express envelops for next business day delivery.

15. Advisory Committee to have Conference Call, January 26, 2005, 11 am EST.

    We understand that the conference call has been changed to January 31, 2005. It has been set up by Nina Mattera and is scheduled for 10 a.m. (Pacific Time). The phone line is scheduled for 2 hours in the event extra time is needed. (866) 350-0777 then Pass Code - 83605#

16. Don't wait to send all revisions at once. Send radiation first. Send the lay summary for radiation at that time also (with the general information that pertains to both rad and chemical).

    We decided not to send the Radiation pieces first but to send everything 2 weeks in advance of the January 31st telephone conference call.

17. Smoking Survey. Complete details as survey questionnaires come in. Add write up of the abstraction done of medical records. Include national survey data and add California data if it exists.

    Detailed results of the Smoking Survey are now presented in Section C of the Appendices. A discussion of the Smoking Survey results, abstraction of medical records and comparisons with national and California data can be found in the Appendices Section C as well as in the Discussion Section of the Chemical Paper. The conclusions are that hourly workers use tobacco products to a greater extent than salaried workers, and that hourly workers have used tobacco products to a greater extent than the general population, including the general population of California which has lower prevalences of smoking than practically all other states. [See also: Centers for Disease Control and Prevention (CDC). Cigarette smoking among adults – United States, 2002. MMWR Morb Mortal Wkly Rep 53:427-431, 2004a. And Centers for Disease Control and Prevention (CDC). State - specific prevalence of current cigarette smoking among adults – United States, 2002. MMWR Morb Mortal Wkly Rep 52:1277-1280, 2004b.]

18. Roll Out, communication plan tentative for April 6-8. April 6 for travel and perhaps practice. April 7 and April 8 for 2 presentations to workers and one presentation to retirees. Be ready for press inquiries but don't make press release. Be able to respond to public questions.

    A lay summary is being drafted for distribution for review shortly. Presentations will be made as discussed.

19. Provide specific exposure information for workers who are still alive and may wish to know their Rocketdyne radiation dose.

    Specific radiation exposure information will be provided for workers still alive regarding their exposure while working at Rocketdyne.

20. Steve Lafflam asks that these "rough" notes be sent to him, Frank Mirer and the Advisory Committee.

    The notes were sent as requested around 7 p.m. after the meeting had concluded on 6 December 2004.

ROCKETDYNE WORKER STUDY (11 MAY 01)

Responses to Requests of the Scientific Advisory Committee at 1 Feb 2001 Meeting

Table of Contents

I. **Provide a more specific approach to the study conduct based on new knowledge gained from visits and data evaluation.**

The numbers in the various figures will change somewhat as the study progresses. Best estimates are presented.

A. Population Identification

1. Radiation Workforce (see Figure 1).

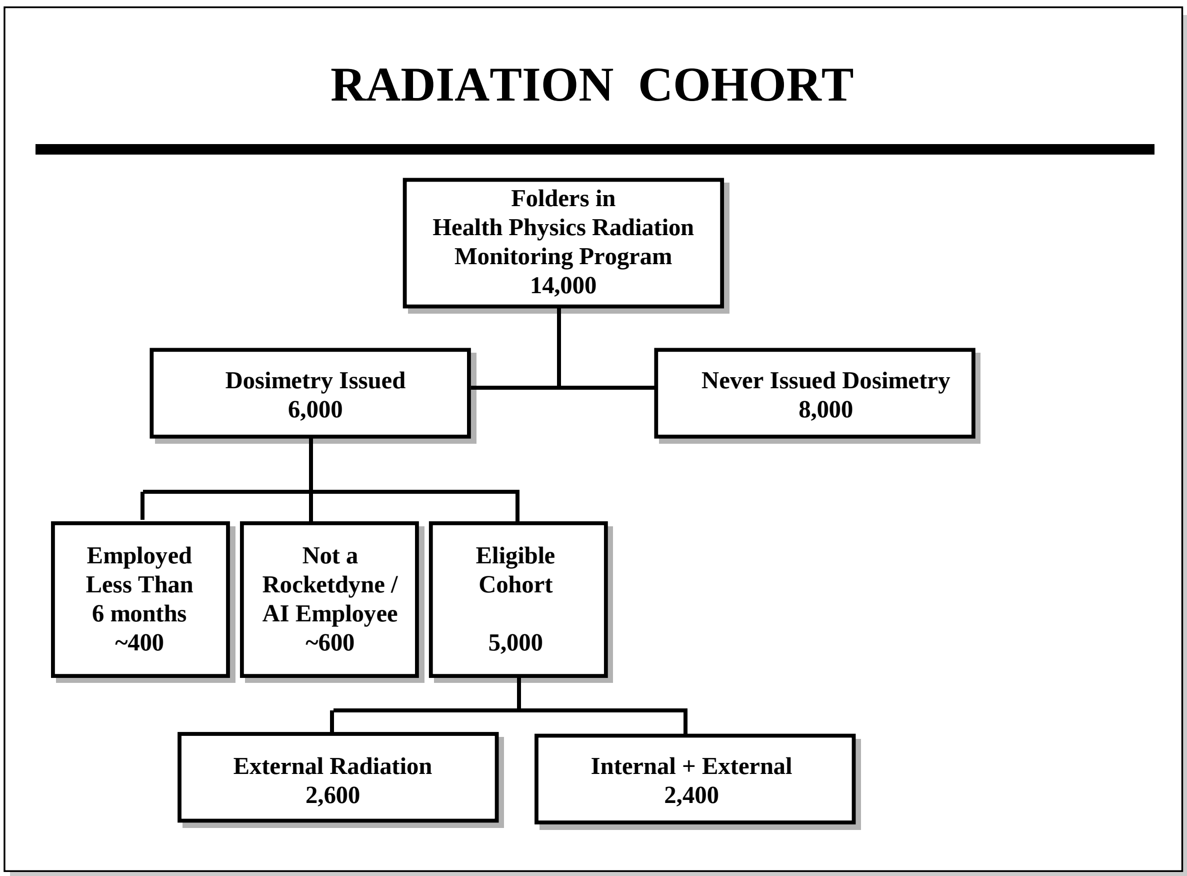

Figure 1 - Radiation Cohort, numbers are approximate

The radiation workforce will be identified from the 14,000 personnel folders within the Health Physics Radiation Monitoring Program (HPRMP). All records will be imaged and evaluated for eligibility, i.e., the workers must have been issued dosimetry, worked for at least 6 months at Rocketdyne/Atomics International (AI), and been an employee at

Rocketdyne/AI. Radiographers employed prior to 1984 will be included. Workers will be classified as to whether they were exposed to external sources of radiation (gamma rays, x-rays, neutrons) or had the potential for inhalation or ingestion of radionuclides such as uranium, plutonium, strontium, cesium, tritium or others. Over 8,000 of the 14,000 folders in the HPRMP belonged to individuals who were never issued dosimetry badges because they never worked in a radiation area. Also the folders included visitors and contractors and others who were not employed at Rocketdyne/AI. Thus, the radiation worker population will consist of about 5,000 workers exposed to external and/or internal radiation sources. All 14,000 records are being scanned, each file will be evaluated for eligibility, and then the radiation measurements will be computerized. Thus, numbers are still approximate. Approximately 1,600 of the radiation workers apparently worked at facilities other than SSFL (Figure 2).

2. SSFL Chemical Workers - Test Stand Workers (see Figure 2)

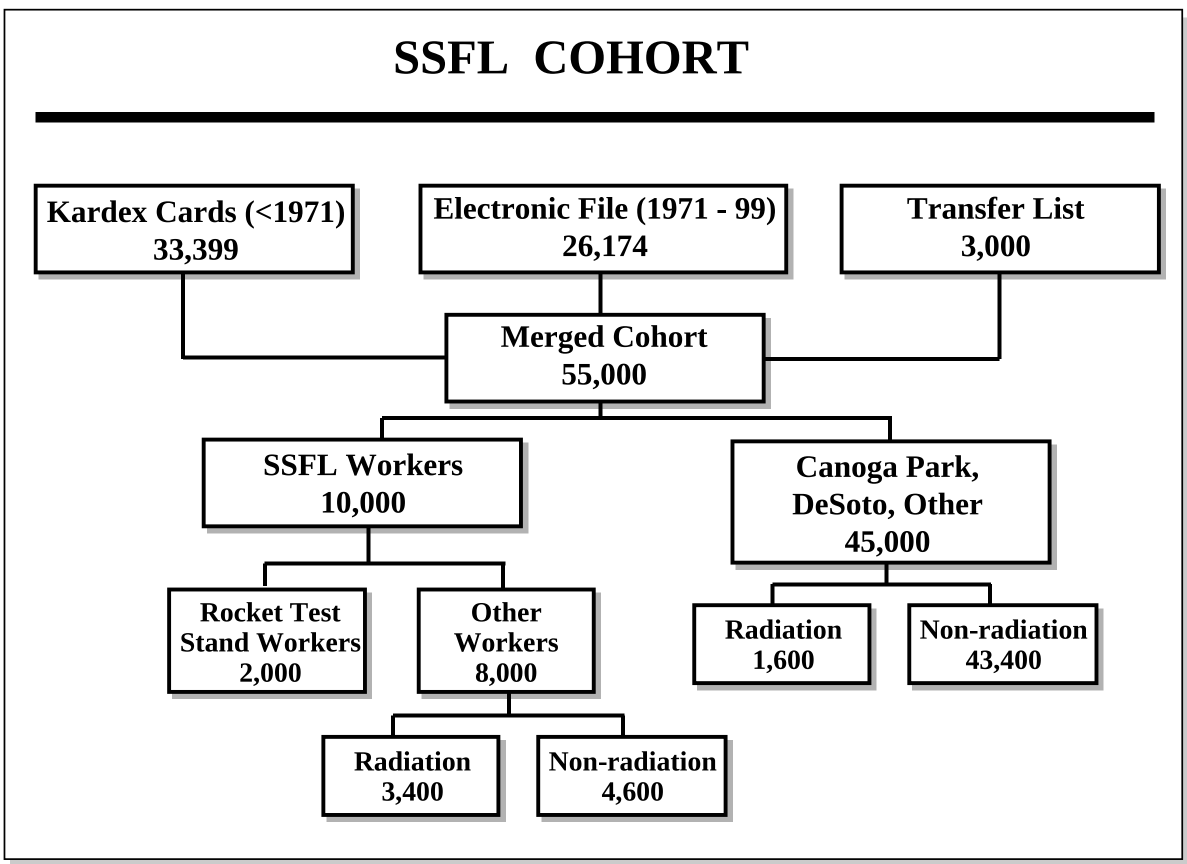

Figure 2 - SSFL Cohort, numbers are approximate

The SSFL workforce will be identified from the scanned Kardex cards, the electronic personnel files and the transfer list. Based on single, double or triple letter location codes, the SSFL workforce will be identified. Eligible workers must have worked at least 6 months at SSFL. The key group potentially exposed to chemicals will be the rocket test stand workers who will be identified from job titles and interviews (discussed below). Currently it is estimated that about 2,000 were involved with rocket engine testing with potential for exposure to fuels, solvents and other chemicals. Approximately 4,600 other SSFL workers will also be evaluated for exposure to chemicals used in the course of laboratory or other work.

3. Comparison Workers

There will be two potential sources of non-exposed or minimally exposed workers, those at SSFL and those at other facilities such as Canoga Park. It is estimated that approximately 48,000 Rocketdyne workers will be available for comparison purposes with the radiation and chemical workers. They will be followed for mortality and basic job histories will be determined. Comparison workers must have been employed by Rocketdyne/AI for at least 6 months.

B. Radiation Exposure Assessment

1. Radiation Records

The radiation exposure data will be extracted from the scanned dosimetry files of the HPRMP (Figure 1). Although there are over 14,000 folders in the HPRMP, fewer than 6,000 workers were issued dosimetry badges and thus eligible for study and data abstraction.

10. PERIOD OF EXPOSURE FROM MO	DAY	YR	TO MO	DAY	YR	11 X OR GAMMA DOSE FOR THE PERIOD (rem)	12. BETA DOSE FOR THE PERIOD (rem)	13. NEUTRON DOSE FOR THE PERIOD (rem)	TOTAL DOSE FOR THE PERIOD (rem)
23		27	28		32	33 DECIMAL 38	39 DECIMAL 44	45 DECIMAL 50	DECIMAL
1	01	4	3	31	4	030			030
4	01	4	6	30	4	050			050
7	01	4	9	30	4	060			060
10	01	4	12	31	4	050			050

Figure 3 – Example of External Radiation Record (1964)

Information abstracted for external exposures (for example, Figure 3) will include:

Name
Social Security Number
Year of radiation record
Period of Exposure
Penetrating dose such as X or Gamma (Units)
Non-penetrating dose such as Beta (Units)
Beta Dose
Neutron Dose
Number of Badges Reported

The abstracted dose will be checked against the computerized files of the Landauer dosimetry company which provided dosimetry services during most of the calendar years of study.

DATE	TYPE	ANALYSIS	METHOD	RESULTS	REFERENCE
18 Sept 67	Urine	UR	ID	78 d/m/sample	U.S. Testing
25 Sept 67	Urine	UR	ID	90	U.S. Testing
2 Oct 67	Urine	UR	ID	78	"
9 Oct. 67	Urine	UR	ID	116	"
16 Oct 67	Urine	UR	ID	175	"
23 Oct. 67	Urine	UR	ID	40	"
28 Oct. 67	Fecal	UR UF	ID IA	58 d/m/48g 9.2 d/m/48g	U.S. Testing
30 Oct. 67	Urine	UR	ID	60	U.S. Testing
6 Nov 67	Urine	UR	ID	66	U.S. Testing
17 Nov 67	TBC	U^{235} for U^{234}		0.0089 μCi U^{234}	UCLA
24 Nov 67	TBC	"		0.0087 μCi U^{234}	ORNL
20 Nov 67	Urine	UR	ID	47	US Testing
21 Nov 67	TBC	U^{235} for U^{234}		0.0086 μCi U^{234}	UCLA
27 Nov 67	Urine	UR	ID	54	US Testing

MFP | Gβ | H3 | Po | Pu | Th | Gα | ISO | Hg | Pb | Be

Figure 4 – Example of Bioassay Data (1967)

Information abstracted from bioassay data are more complex (Figure 4) and will require individual assessments. Important information to capture will include, in addition to the personal identifiers, specific radionuclides, urine, fecal, and whole body radionuclide count results. Information on acute versus chronic uptakes, solubility and particle size will be captured to the extent available. Air sampling information will be evaluated as available.

2. Lifetime doses

Lifetime occupational exposure to radiation will be captured to the extent available. Sources will include:

Rocketdyne/AI records as above
Rocketdyne/AI records of pre-Rocketdyne dose
Linkages with the following data sets for post-Rocketdyne dose:
- REIRS, Nuclear Regulatory Commission
- REMS, Department of Energy (DOE)
- CEDR, Comprehensive Epidemiological Data Resource, DOE
- Landauer Dosimetry Company Files

3. Bioassay and external dose determination as discussed in the original proposal (Figure 5).

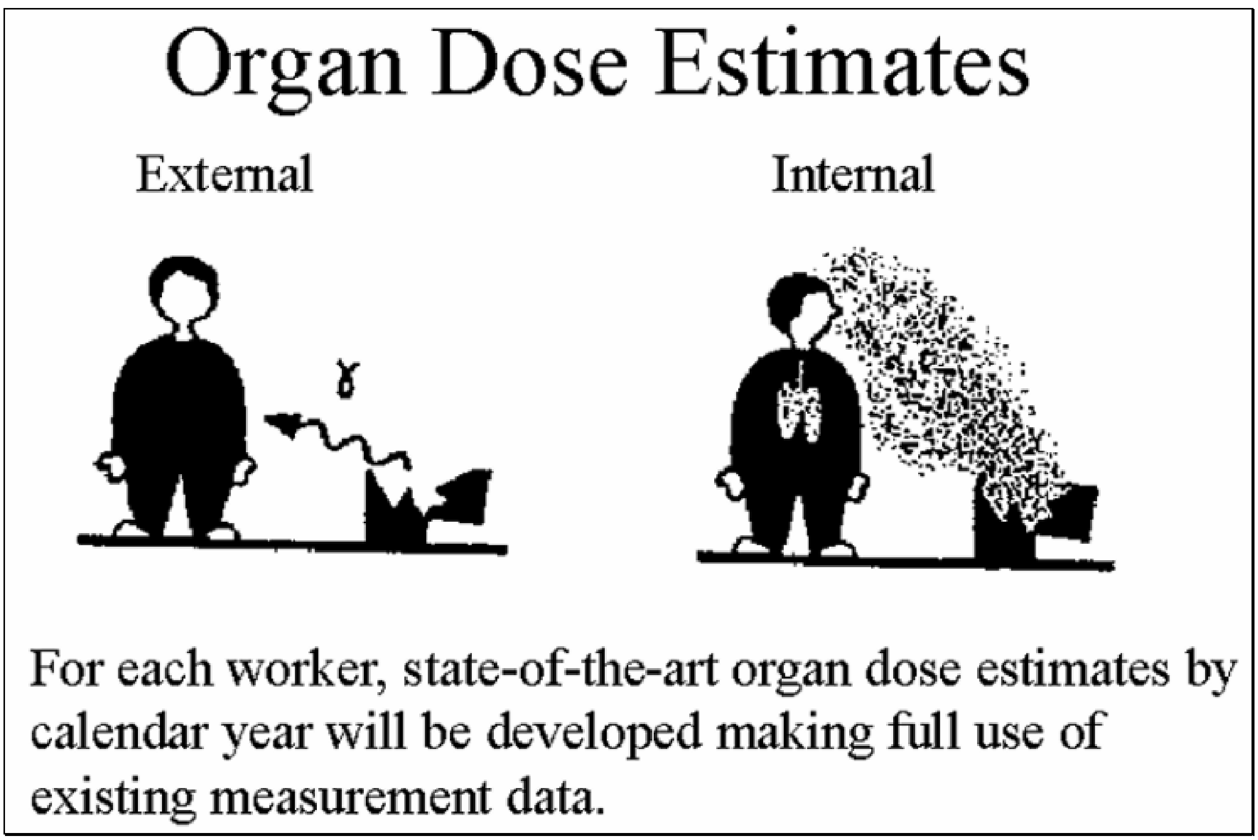

Figure 5 - Organ Dose Estimation

We reviewed the folders for 22 current or former Rocketdyne workers with potential internal exposures to radionuclides. Some of these workers were chosen at random, and some were chosen because bioassay records indicated elevated intakes for at least short periods. The review had two main purposes: (1) to familiarize ourselves with the type of exposure information available in the files, so that we could begin to modify our computer codes to address the types of exposures received at Rocketdyne, and (2) to help determine the type of information that could be computerized by ORAU to facilitate our calculation of internal dose for the large number of cases to be addressed. It appears from these records that exposures often were acute, but in some cases elevated exposures may have continued for several months. The assignment of exposure scenarios is complicated by indications that inhaled material may have been insoluble in some cases and either soluble or a mixture of soluble and insoluble in other cases. It appears that reasonably good estimates of organ doses can be made in most cases.

We recently received scans of the radiation dosimetry records for 100 workers with elevated bioassay measurements and have begun to examine those records in a continued effort to develop a suitable methodology for back-calculating organ doses from the Rocketdyne data. Although generic bioassay models and codes are already available, it is necessary to adapt these to the specific types of information available for the Rocketdyne workers.

C. Chemical Exposure Assessment

Workers will be evaluated for their potential for chemical exposure using a variety of means. Job histories will be important for identifying specific job titles that will require further evaluation. Interviews with workers will be selected based on job titles. Personnel assignment lists, purchasing records, test stand operation records and other records will be incorporated into the exposure assessment scheme.

1. Job Histories (see Figure 6)

Date	Job Title	Location / Plant
1-08-58	MEC ENG PRO T	S
5-17-59	MEC–PROP TST	SH
1-23-61	MEC-PROP TST L/O REINST	SL
3-18-62	MEC-TST S	SL
4-21-63	TEC ENG TST	SL
.	.	.
.	.	.
.	.	.
3-13-66	TEC ENG TST	SH
8-27-67	MEC-TST S	SL
1-02-69	MEC-TST S	SE
12-27-70	MEC-TST S	SL
7-27-75	TEC-ENG TST	TBD

Figure 6 – Example of Job History from Kardex Personnel Cards

For SSFL workers, job histories will be abstracted from the Kardex images or obtained from the electronic personnel files. Jobs with potential for chemical exposure will be identified from job titles, such as engine test mechanics and certain laboratory personnel and equipment handlers. Detailed job histories for radiation workers with chemical exposures will also be abstracted.

2. Test Stand Historical Database

A test stand historical database will be developed (Figure 7). Program, engine, fuels, oxidizers and other chemicals will be enumerated. This database will help in assessing the potential for chemical exposures over calendar years and test sites for specific workers.

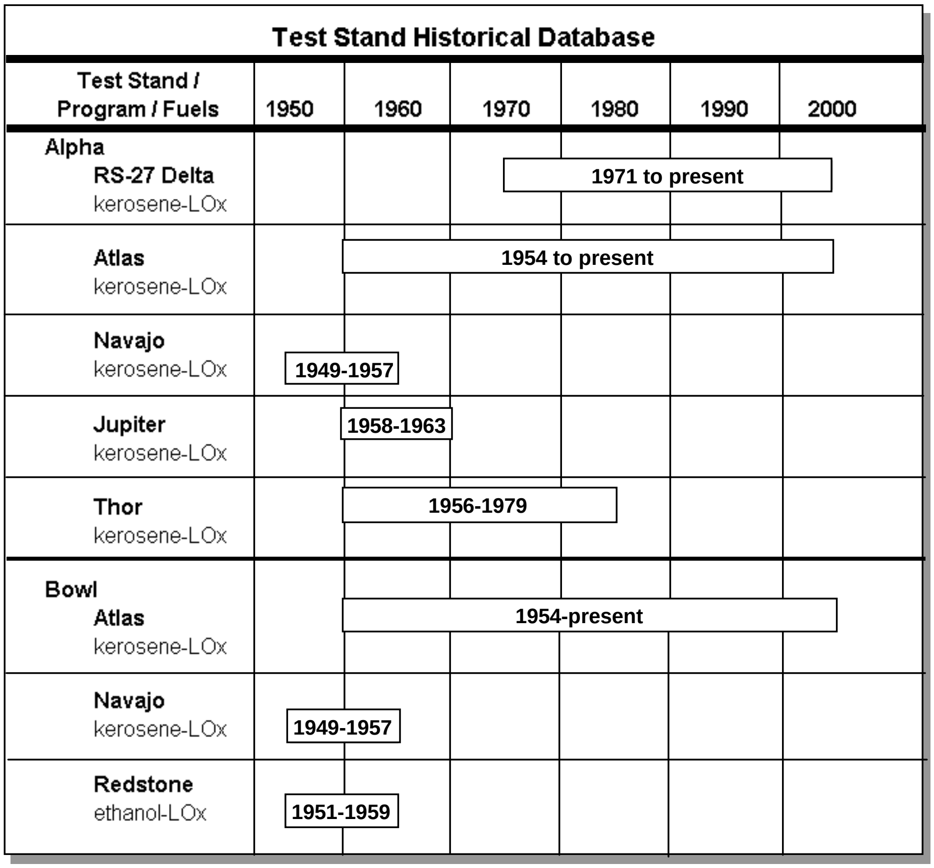

Figure 7 - Schematic of Test Stand Historical Database

3. Personnel Assignment Lists

One challenging aspect of the exposure assessment will be to assign workers to specific engine test sites. The location and use of Personnel Assignment Lists (Figure 8) will be helpful in this regard. The Personnel Assignment Lists look similar to phone books and list individual workers in various occupations at specific test sites.

J-2 Engine Test, D/096-213-Zone 11
Santa Susana Field Laboratory, Dept 096, Group 213

Delta Engineering		Delta Firing Unit	
First Shift		Second Shift	
Jackson, J.C.	5416-5419	Doe, F.L.	5701-5703
Jackson, C.F.	5416-5419	Doe, V.E.	5701-5703
.	.	.	.
.	.	.	.
.	.	.	.
Delta Pre-Test Mechanics		**Bowl Area Mechanics**	
Third Shift		First Shift	
Jones, C.M.	5701-5703	Smith, G.V.	5301-5304
Jones, L.A.	5701-5703	Smith, E.D.	5301-5304
.	.	.	.
.	.	.	.
.	.	.	.

Figure 8 - Abstract of Rocketdyne Engineering Personnel Assignment List (Jan 1965)

4. Worker Interviews

Over 300 interviews are planned. Test stand work and other chemical exposures of the SSFL workforce will be determined. Each worker who consents to be interviewed will be sent a copy of his work history (Figure 6) and, if a test stand worker, asked to recall the corresponding test stand using a prompt as in Figure 7. Groups of workers of the same era are planned to be interviewed together. Others with similar jobs who cannot be interviewed will be assigned to test stands if their co-workers can recall working with them. We plan to discuss this approach at union, retirement and other worker meetings to ask for their advice and support. All occupations with potential exposure to chemicals will be evaluated.

The Interviews will be conducted over a time period of approximately one year.

There are three objectives for the interviews:

- To gain a clear understanding of the chemicals, work practices, engineering controls and respiratory protection used at the various engine test stands and other work locations throughout the years at Santa Susanna;

- To help fill in gaps in the Test Stand History Database that is being developed to detail the chronological history of various engine test programs, fuels and chemicals used;

- To identify specific individuals who worked at specific test stands during specific years.

To better fulfill these objectives, certain tasks must be completed before the interviews begin. Emphasis is on the test stand workers who likely had the greatest potential for chemical exposures but all occupations will be evaluated. The Test Stand History Database should be populated with all existing information so that we have a framework and starting point to support the discussions. Individual work histories should be provided to each employee to facilitate recall. Work histories will need to be abstracted from the 33,400 Kardex images in this regard. In addition, lists of all test mechanics that worked during specific time periods should be available so that the interviews will assist in placing specific individuals at specific test stands. It will likely be 6 to 9 months before this information will be completely available.

The information should be assembled and sent out to each interviewee prior to conducting the interview to give the interviewee time to review the materials, refer to historical documents that they may have or talk to other former workers who may help refresh their memories. Historical photographs will be available as an additional memory help. The interviews should be structured and focused on a specific test stand or area. For example, an interview could focus on the Alpha test stand and the interviewees would all have worked at Alpha sometime during their career. Some will have worked at other locations also and we will gather information about these other sites during the interview. The interview should be conducted in-groups of 4 to 6 individuals that have similar work histories and last 2 to 4 hours.

Various technology resources will be considered to best facilitate the discussions. For example, a digital projector (LCD) attached to a portable computer could be used to project the Test Stand History Database so that additions and changes could be made in real time, in front of all participants. Thus, consensus could be reached by the group on any changes made while the group is still assembled.

5. Estimate Potential For Exposure

Estimates will take into account calendar years worked, program, engine, fuels, job title and all other relevant information as described previously. Reliance will be on job histories, interviews, and historical data available on chemical use.

We have learned that hydrazines were not used by all Propulsion Test Mechanics/Technicians. Hydrazines apparently were not used in great quantity or uniformly, and only at a few test stands. Hydrazines were used mostly on small rocket engines, although not exclusively. Direct hydrazine exposures may have been limited to periodic tasks, i.e., sampling.

Trichloroethylene (TCE) was used in much greater quantity and more extensively to flush engines at a number of test stands and as a parts cleaner and to wash hands. TCE exposure levels may have changed over time due to process change and use of respiratory protection.

Job titles alone are not adequate to characterize exposure and thus assignments to test stands will be essential. Construction of a Job/Exposure Matrix will be challenging, but we believe that we will be able to reliably reconstruct what chemicals were used at which test stand during specific time periods. The interviews, phone books and other sources of information will be used to place individual workers at specific test stands in specific years as described above.

6. Size of “chemical workers” cohort

There were approximately 6,600 non-radiation workers at SSFL, including an estimated 2,000 who worked with engine tests. These engine test personnel would have the highest potential for exposures to fuels, such as hydrazine, and solvents, such as TCE. The other 4,600 SSFL workers will also be evaluated, however, for their potential chemical exposure.

D. Smoking Assessment

Medical records contain information on smoking of various levels of completeness over the years. Smoking was routinely collected only for certain years, but some special surveys were conducted and notations occasionally appeared in the medical notes. From 1963 to about 1967, it appears that the fact of cigarette smoking was recorded in the worker's preemployment self-administered medical form. Medical records from later years seem to have more detailed information, although not on all employees. These data will be abstracted from the medical records on the eligible workforce and on a sample of the non-exposed comparison group. Confounding will be assessed by looking for variations in smoking patterns by job title, and within categories of estimated chemical or radiation dose. In addition, contrasts can be made with smoking prevalence data for the general population. Although adjustment for smoking at an individual level may not be possible, we plan to perform qualitative evaluations of smoking (e.g., compare smoking habits of rocket engine test mechanics to other occupational groups at Rocketdyne) and can evaluate the extent to which smoking will be an important confounding factor to be adjusted for in subsequent mortality analyses.

E. Tracing

A comprehensive approach to tracing includes use of company records, California death tapes and microfiche, NDI+, Social Security Administration, Health Care Financing Administration, TransUnion credit bureau, Departments of Motor Vehicles, and state Departments of Vital Statistics (Figure 9). All deaths will be coded for cause of death. Alive status will be confirmed. The shaded boxes represent current evaluations.

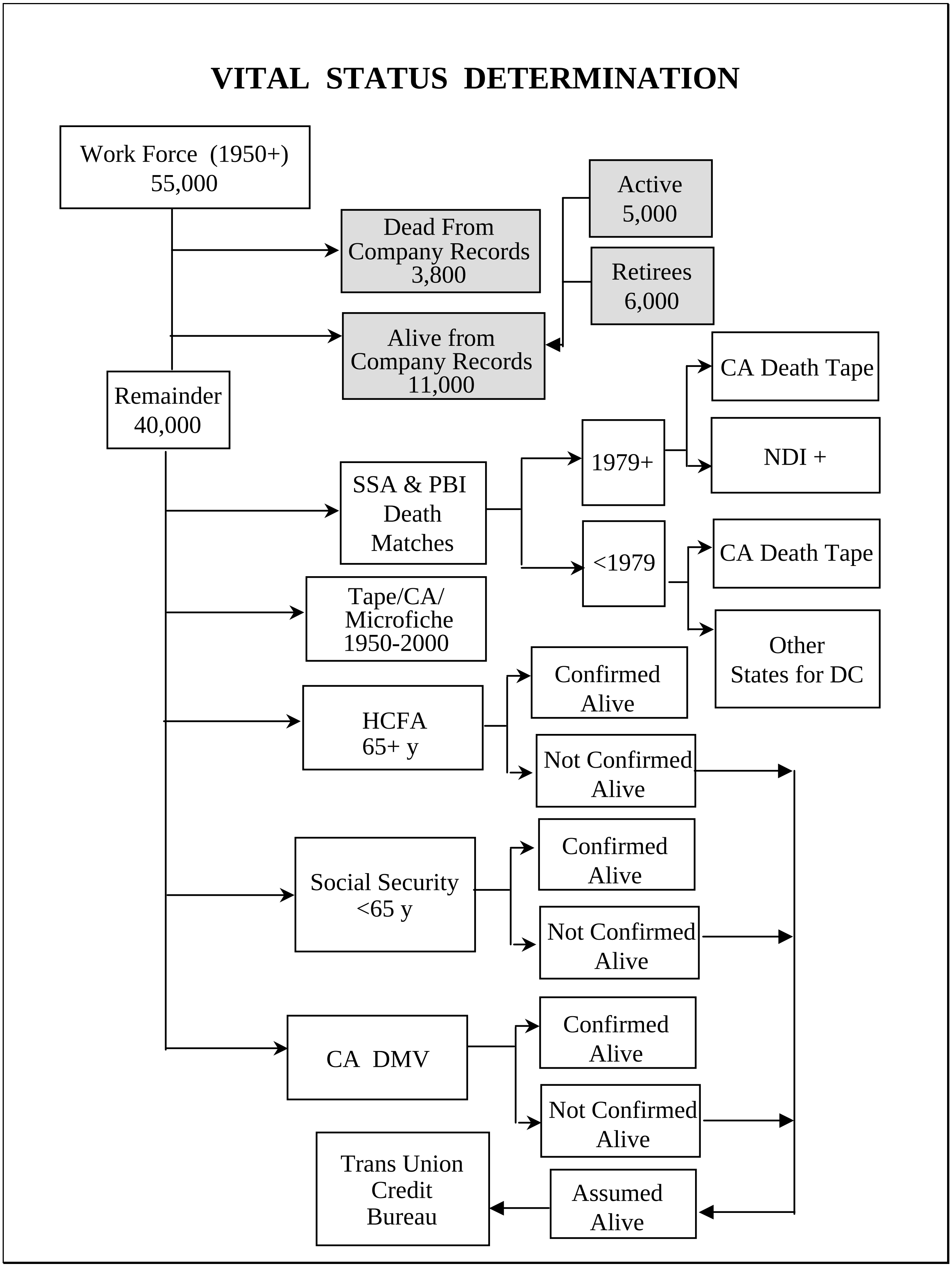

Figure 9 – Schematic of Vital Status Determination

F. Summary

There are approximately 55,000 workers available for study since 1950. Recognizing the need for an efficient allocation of resources in order to maximize the information in this followup study, we will:

- Trace all eligible 55,000 workers at the level of mortality and vital status

- Conduct comprehensive exposure assessment on the 10,000 SSFL workers, i.e., the radiation workers and the 6,600 test stand or other workers.

- Radiation, external. This assessment is straightforward and cumulative dose can be obtained on the entire radiation cohort from existing records. There are about 5,000 radiation workers from SSFL, De Soto and Canoga Park facilities. We are imaging all worker folders in the HPRMP filing cabinets to facilitate selection of all eligible workers.

- Radiation, internal. There are 2300 workers monitored for internally received radionuclides (U, Pu, Cs, Sr, fission products).

  - We are imaging all worker bioassay records

  - ORNL will evaluate the images of the worker records and select those for whom detailed computerization is required (currently estimated to be several hundred). Not all those monitored had positive bioassays so that this approach is reasonable and cost effective.

  - The comprehensive internal radiation dosimetry would be conducted for all organs, including lung, bone marrow, kidney, bladder, lymph system, and esophagus.

- Chemical. The approximately 6,600 SSFL workers would be characterized as to the potential for exposure to hydrazine and TCE, as well as to other fuels and chemicals. This would be done mainly by assigning workers to specific test stands over time, but all occupations with potential for chemical exposure will be evaluated. We believe we'll be able to do this in a cost effective manner by use of a test stand "questionnaire", by identifying "phone books" or "Personnel Assignment Listings" of years past which place individual workers at specific test stands, by interviewing workers themselves as well as long term employees familiar with the workforce of years past, and by using information in organizational charts and Kardex work histories. For those workers with job classifications involving rocket engine testing, we would send a listing of each worker's work history, including job title and dates, and ask him to list to the best of his recollection which test stand (alpha, bravo, caco, delta, bowl, tree, STL4, etc) he was working at during this period. This information would supplement the interview responses and assist in assigning the potential for certain chemical exposures (hydrazine, kerosene, LOx FLOx, TCE, alcohols, etc.). To enhance the response rate would discuss the approach at union, retirement and other worker meetings and ask their advice and support.

- Other chemical. To the extent possible, other chemicals would be evaluated from the job titles, building and work history information. This would include asbestos potential (which seems small), beryllium (which also seems to involve small numbers), chromates, and other.

- Other factors. Information available on pre-employment forms and medical records would be assessed, such as cigarette smoking, and prior work histories.

- Comparison Group. It appears feasible to assemble a comparison group from the 48,000 workers at SSFL, Canoga, De Soto and other facilities not included in the exposed cohorts.

II. Reconsider whether an incidence component to the study might be worthwhile.

A. Previous Comments

Previously, in response to a request from Boeing whether to include an incidence study or justify why not, we wrote for distribution at the February 2001 meeting:

"We have enhanced our proposal and "scope of work" to address the issue of adding a cancer incidence component, which is discussed below:

> Cancer incidence. Adding a cancer incidence component was considered but decided against for the following reasons. Cancer registration during the calendar years of study is incomplete in California and the U.S. as a whole and the results would not differ materially from a comprehensive and complete mortality study. Prior to 1988, the cancer registration in California is spotty and doesn't exist at all prior to 1972 for the LA area.
>
> A comprehensive cancer incidence study would be prohibitively expensive. Since the U.S. does not have a national cancer registration system, we would have to contact all workers or their next of kin and inquire about cancer diagnoses. We would then have to validate the self-reported cancers through review of hospital records. The statewide California cancer registry began in 1988 and the Los Angeles county registry in 1972. A geographically limited cancer incidence study, restricted to cancer occurring in the 1990s among residents of California, for example, would also be problematic because of its incomplete coverage, the need for complete residential histories (to know the proper denominator), and the likely small numbers of anticipated incident cancer cases. A limited cancer incidence study would require knowledge of the number of workers continually residing in the California and/or the Los Angeles catchment area. Linkage with the cancer registries could determine observed numbers of cases, but computing the expected number would require an intense effort to learn these residential histories. We have not included a budgetary item for the expense needed for the residential history determination.
>
> The *a priori* cancers of interest are lung cancer, leukemia and lymphoma. Survival for lung cancer is poor, hence mortality data would be a good reflection of incidence. Similarly, survival for the myelogenous leukemias and certain lymphomas are also poor. For example, the 5-year relative risk survival rate for lung cancer in 1950-54 was 5% and in 1989-95 was only 13%. Thus, a comprehensive and complete mortality study of the worker population would be a better indicator of possible health effects than the incomplete and potentially biased evaluation of cancer incidence in limited areas and over restricted calendar years.

Computer linkage of data files available from the Los Angeles Cancer Registry and the California Cancer Registry, however, could be used to validate a sample of the cancer deaths of workers who died in California. If a nested case-control study of a particular cancer is launched after the cohort study is completed, the registry may be used to obtain detailed information on histologic type of the malignancies.

Assistance in the validation and assessment of cancer diagnoses made within the Rocketdyne workers residing in Los Angeles County is available from the Cancer Surveillance Program of Los Angeles County (LA-CSP). Operated by the University of Southern California (USC), the LA-CSP has a complete repository of pathology reports for all histologically confirmed cases of cancer occurring in the County since 1972. In 1992, LA-CSP was designated a Surveillance, Epidemiology and End Results (SEER) Registry by the National Cancer Institute."

B. Further discussion on limitations of an incidence component.

We continue to believe that an incidence component would provide only minimal scientific gain, and would require a substantial increase in cost. The key issues are:

1. Incomplete coverage

There is uncertainty and difficulty in identifying workers who lived in the catchment areas during the periods when cancer incidence would be recorded. We know that we are dealing with a mobile population. Based on our initial tabulation of over 3,000 deaths among Rocketdyne employees, we find that 27% of all deaths occurred in states other than California. Based on our tabulations of over 26,000 zip codes, we find that about 30% of the population lives/lived outside of California and a much larger percentage lives/lived outside of Los Angeles county. Furthermore, even for lifetime Los Angeles residents, all cancer incidences in 1950-1970s would be missed. Los Angeles County Registry coverage began in 1972 but LA-CSP became a SEER Registry (National Cancer Institute) only in 1992. The California Registry began in 1988 and consists of regional population-based registries.

2. High Mortality for Cancers of Interest

The mortality study will detect the large majority of lung cancers, the cancer of *a priori* interest because of possible radiation and chemical etiology. The 5-year relative survival rate for lung cancer was 5% for cases diagnosed 1950-54 and 13% in 1989-95 (SEER, NIH Publ 99-2789, p.17, p. 53).

For leukemia, the 5-year relative survival rate was 10% for cases diagnosed in 1950-54 and 44% in 1989-95 (SEER, NIH Publ 99-2789, p. 17, p. 53). For acute myeloid leukemia the most radiosensitive cell type, 5-year survival during 1989-95 was only 12%.

For NHL the 5-year relative survival rate for cases of NHL was 33% for cases diagnosed in 1950-54 and 52% in 1989-95 (SEER, p. 17, p.53).

For cancer of the esophagus the 5-year relative survival rate was 4% in 1950-54 and 13% in 1989-95 (SEER, p. 17, p. 53).

The relatively poor survival rates for these cancers mean that only a small percentage of incident cases will be missed by the proposed mortality analyses.

3. Comprehensive Mortality Coverage

The mortality coverage will be 99% complete over the entire followup period, based on our experience with the Lockheed Martin aerospace worker cohort. While there are recognized limitations associated with death certificate coding, cancers, and especially those of *a priori* interest, are more accurately recorded than other diseases (Percy C, Stanek E, Gloeckler L. Accuracy of cancer death certificates and its effect on cancer mortality statistics. Am J Public Health 1981;71:242-50). Hence, it is unlikely that our mortality searches will miss fatal cancers that would have been detected from cancer incidence searches.

4. Interpreting Living / Dead Subject Information

Including the small number of non-fatal cancers of *a priori* interest who would have been diagnosed in the catchment areas covered by cancer incidence during limited number of calendar years would not provide an incremental gain in knowledge commensurate with the effort involved. Further, this hybrid design would not be straight forward because of the absence of residence histories for Rocketdyne workers, hampering interpretation. We have serious reservations related to potential biases associated with a study of cancer incidence in a select subset of the cohort. Differential effects may be involved in that persons of higher SES might be more likely to leave California than remain, and exposure doses appear related to SES (i.e., pay grade). A limited incidence component combining living and dead cases and comparing less precise (because of the limited coverage) incidence data with the more stable mortality data is not a straightforward maneuver.

C. Conclusion.

We are sympathetic to the suggestions to incorporate an incidence component into the study. At the end of the day, however, we believe that the potential benefits would not outweigh the very real costs and complexities. Today, cancers are recorded with high precision on death certificates, so 1990s cancer registry data will be adding non-fatal tumors, but the cancers of interest, and in particular lung cancer, have a high fatality rate. Because of incomplete cancer incidence registrations over the years and in various counties, the large majority of cancers diagnosed between 1950 and the 1980s would be missed in an incidence survey. Furthermore, the absence of residential histories for Rocketdyne workers would hamper interpretation of an incident component that combines living and dead cases, increasing the likelihood that biases might creep in. Finally, we performed an incidence substudy within the Lockheed cohort and learned that the additional cases identified were too few to be informative with regard to the comprehensive mortality investigation.

III. Reassess rationale for contacting workers via mail questionnaire and requesting information on other jobs and health habits.

We have carefully considered the request of the Science Committee and now agree that there would be little marginal gain in information or study quality by contacting those who are living, even with a brief questionnaire on job history and lifestyle factors. Thus, we no longer plan to send such a questionnaire.

IV. Consider comparisons with the previous UCLA study to classify why there might be differences in results.

We agreed to make comparisons at the end of the study with the UCLA cohort to the extent possible. However, as we have acquired knowledge on both the UCLA cohort and the Rocketdyne workforce, we believe such a comparison will be problematic for the following reasons listed below and would like to bring this to the attention of the Scientific Committee.

1. Our definition of the radiation-exposed workforce is not the same.

   Unlike UCLA, we will not include radiation workers who were employed less than 6 months, nor will we include visitors or non-Rocketdyne/AI personnel. We will not exclude workers who also tested rocket engines.

2. Our assessment of external and internal doses will be substantially different.

   Unlike UCLA, we will not use committed dose to the lung as a surrogate for all organ-specific doses from internal sources, but we will compute individual organ doses up to the time of cancer death with appropriate lag intervals. We will include lifetime radiation doses obtained before and after Rocketdyne employment.

3. Our definition of the eligible workers with potential for chemical exposures is not the same.

   For the chemical cohort, we will require that each worker be employed for at least 6 months at SSFL. We will not exclude a worker because he was at one time monitored for radiation by the HPRMP, and we will include women.

4. Our assessment of the potential for chemical exposure will be substantially different.

   Unlike UCLA we will not assume that any job title involving rocket tests meant hydrazine exposure. We will assign workers to specific test stands for specific calendar years and assess the potential for exposure to specific fuels, solvents and other chemicals. We will conduct over 300 interviews to assist in the chemical exposure assessment of test stand, laboratory and other workers.

These differences will make it difficult for us to make meaningful comparisons. For example, our preliminary evaluation of the radiation workers' files suggests that we might include more than 500 additional workers in the radiation cohort.