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REVIEW OF THE HEALTH AND MORTALITY STUDY

The Health and Mortality Study was reviewed formally by five epidemiologists on November 20, 1972; all but one have been active in radiation epidemiology. Four of the five reviewers have submitted written reports. The fifth report ~~was~~ is delayed because of illness.

Opinions of the reviewers as to whether to continue the study and whether to retain the services of the contractor were solicited informally during executive sessions. The enclosures are directed in part to these questions.

The enclosures include the following:

1. Impressions regarding the study by the DBER technical representative with proposed alternative courses of action and a recommendation.
2. Summary of comments by the reviewers.
3. Letters submitted by the reviewers.
4. Semiannual brief report submitted by the contractor.

Sidney Marks, M.D.
Health Sciences Research
and Applications Branch
DBER

Enclosures:
As stated

REPOSITORY DOE - FORRESTAL
COLLECTION MARKEY FILES
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FOLDER Mancuso File 3/26/87

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IMPRESSIONS OF THE TECHNICAL REPRESENTATIVE (Dr. L. Marks)

1. Continuation of the study (see enclosure 2 for reviewers' comments)

The study should be continued in the following manner. There is need for continuous monitoring of the health and mortality of workers in the industry from the standpoint of operational safety, labor relations, workmen's compensation and public relations. The data accumulated for this purpose must be analyzed; the data collection and analysis should follow sound epidemiologic and statistical principles.

The observation of a human population exposed to relatively well documented doses of radiation is a potentially valuable scientific byproduct of this program. Contributions to occupational epidemiology may also be expected.

The position of DBER is that the collection of health data on workers is an operational responsibility. This principle has been accepted by operational divisions, and the costs of collecting current data are or will be assumed by the Divisions of Production, Reactor Development and Technology, and Military Applications. DBER should continue to be responsible for designing the format of data collection and for analyzing and publishing the scientific results. Expenditures by DBER for this purpose should decrease as development of the methodology allows much of the analysis to be performed as a routine operation.

2. Performance of the contractor (strengths)

a. Careful design of data collection

The data collection has been meticulous, and the contractor has exercised an extraordinary degree of quality control. Exhaustive efforts have been made to fill information gaps and to correct errors.

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b. Diligence in seeking biases instead of ascribing observed differences to radiation effects

The team has been conscientious in seeking explanations for observed differences between comparison groups that might have been ascribed improperly to radiation effects. In so doing, they have uncovered biases that might have been ignored by investigators who were less careful or who sought spectacular results.

c. Improved responsiveness

The team has been more responsive to AEC requests in the past year than previously. During this time they have produced analyses involving comparisons of Hanford employees with siblings for specific causes of death and are actively working on a grouping of workers based on their level of radiation exposure. A recently submitted, semiannual progress report is closer to the desired format than any previously prepared by the investigator (enclosure 4).

3. Performance of the contractor (weaknesses)

a. Unrealistic objectives

Drs. Mancuso and Sanders have repeatedly announced an objective of seeking very fine differences in longevity between worker and control groups. In so doing, they have ignored possible biases in the control groups that make such fine distinctions meaningless. Furthermore, they have used this objective as an argument for expansion of the population under study. Expansion of the population is a worthy consideration but would not guarantee achievement of their objective.

b. Poor progress and lack of initiative

The study has been conducted at an inordinately slow rate. A commendable concern with quality of data has been carried to an extreme that has seriously impeded progress of the study. Any analyses conducted to date have been made only in response to pressure from the DBER staff.

c. Evaluation of personnel

In spite of an established reputation in occupational epidemiology, which was the reason that he was approached by AEC to serve as contractor for the study, Dr. Mancuso is an ineffective principal investigator. A tendency to refer all questions concerning technical information to Dr. Sanders reflects an inadequate knowledge of the study. Dr. Mancuso does not function as a public expositor of the scientific aspects of the study but usually confines his remarks to questions of funding with emphasis on AEC deficiencies in this respect.

Dr. Sanders is a sincere and generally respected actuary with considerable experience in the Social Security Administration and in HEW along the lines of the work he is doing in the study. He is the moving force in the study despite his advanced age. Much of the work accomplished to date should be credited to him. His weakness stems from a lack of general statistical, epidemiologic and radiologic background. Dr. Sanders is an ineffective speaker but, nevertheless, functions as the scientific spokesman for the group. He is also the principal writer for the study but has produced only lengthy, rather poorly written reports and no scientific articles.

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Dr. Brodsky is a young health physicist with a voluminous curriculum vitae and a recent D.Sc. in biostatistics. Reviewers have judged his statistical input to the study to be atrocious; however, his statistical role has diminished. Dr. Brodsky's health physics reputation is good, but he has not imparted any aura of radiologic sophistication to the study.

Dr. Elston is a recent addition to the team as a statistical consultant. He is a sound biostatistician from the University of North Carolina and has improved the statistical methodology. The reviewers expressed regret that Dr. Elston or someone else of his stature is not more extensively involved in the study.

d. Geographic dispersion

The project suffers from undue physical separation of the principals in the conduct of the study. The central office is located at the University of Pittsburgh; Dr. Sanders directs the detailed operation of the team from San Diego; the computer center is located in Oak Ridge. At the very least, the individual responsible for analyses (Dr. Sanders) and the computer should be in the same location.

e. Publications

Several lengthy annual reports and a recent, long, unrefereed report in a Health Physics Society Symposium Proceedings are the only publications produced thus far. No articles of reasonable size have been submitted to scientific journals. The investigators are apparently waiting until the analyses are completed to make their submissions to journals.

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Alternative courses of action

1. Retention of the contractor

Retention of the contractor without change would be an unsatisfactory solution. Although increasing progress is being made in the analysis of data and production of results, the unrealistic goals and weaknesses in their understanding of radiobiologic considerations and in their capacity for publication remain.

2. Early replacement of contractor

Such a move, although justified on the basis of performance, may have undesirable consequences.

Unless an immediate replacement is found, a public charge may be made that the AEC is stopping this program out of fear that positive findings will emerge.

Finding a suitable replacement under existing conditions is handicapped by general knowledge that this is Dr. Mancuso's project and that any new principal investigator will be replacing Mancuso (and, by implication, putting him out of a job). Overtures to possible candidates must be carried out now in a clandestine atmosphere. Under these conditions, potential candidates will be unable to learn enough about the study to develop carefully prepared proposals that may be judged fairly to arrive at a proper choice of a contractor. Furthermore, the large amount of work performed to date using Dr. Mancuso's methodology, may be jeopardized by a new investigator's lack of familiarity with that methodology or by poor cooperation of the Social Security Administration with a new investigator.

3. Orderly disengagement

This is a proposal to retain Dr. Mancuso as contractor for the

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completion of two specific projects -- the Hanford and Oak Ridge analyses and the master file of employment in AEC plants. A time limit of two to three years can be set for the completion of these activities with a diminishing budget projected as different parts of the work are completed. Completion of these projects by Dr. Mancuso's team will require continuation of the recently increasing surveillance of the study by DBER personnel. We will exert a major effort to make Dr. Mancuso's completion of the Hanford and Oak Ridge Studies productive of results useful to AEC.

In the meantime, information can be disseminated to the effect that (a) the study will be extended to other AEC plants on a prospective basis; (b) contract proposals from other investigators incorporating alternative methodologies will be considered along with a new proposal from Dr. Mancuso; and (c) that consideration will be given to splitting the current single into multiple contracts involving distinct spheres of expertise such as epidemiology and health physics. Implicit in all of this will be termination of the open-ended, exclusive character of Dr. Mancuso's contract. The latter point can be made explicit.

Recommendation:

The third alternative (orderly disengagement) is recommended for the following reasons:

a. It will continue the involvement of Dr. Mancuso in the study, at least temporarily, and thereby secure a measure of cooperation from him during a transitional period.

b. It will obviate potential adverse criticism that might follow an abrupt termination of the contract.

c. Provision will be made for completion of the projects cited above in which a large investment has been made.

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d. Time and favorable conditions will be gained for a careful consideration of alternative approaches to the further conduct of this long-term study so that it may be pursued with greater effectiveness in the future.

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ENCLOSURE 2

SUMMARY OF COMMENTS OF REVIEWERS

The review team consisted of three epidemiologists from various universities and an epidemiologist and a statistical epidemiologist from government agencies.

In the following summary prepared by the DBER technical representative an attempt is made to collate the attitudes of the reviewers relative to specific issues. The four reviewers considered here are those who have submitted written reports. The letters of the reviewers are available in enclosure 3.

1. Continuation of the study

   Three reviewers enthusiastically recommended continuation of the study; two of the three favored expansion to include other AEC installations. A fourth reviewer did not consider this matter.

2. Continued use of ~~the principal~~ a contractor

   One reviewer recommended retention of this contractor and his team but expressed some reservations about Dr. Brodsky. Another provided contradictory comments in that he cited agreement by the review team "that the University of Pittsburgh should continue as the contractor" but then offered several personal reservations "which may well be cause for considering an alternate contractor." His specific reservations included such comments as "no overall direction" of the study, "minimal involvement in this project by the P.I." and "paucity of the results." He finally asked whether it is possible for the AEC to alter the open-ended character of the current contract. A third reviewer recommended that another contractor, preferably from a university Department of Epidemiology, be found to serve as the principal investigator. A fourth reviewer did not consider the matter of retention of replacement

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of the contractor.

3. Progress of the study

Three reviewers deplored lack of progress commensurate with the duration of the study. They criticized excessive preoccupation of the investigators with details and with unavoidable deficiencies in the data. A fourth did not address himself to this issue.

4. Publication

All reviewers criticized the publication record of the investigators. One recommended editorial assistance to improve the quality of writing exhibited in the reports of the contractor. Two stated that methodological articles could have been published already.

5. Personnel

One reviewer expressed approval of the investigator and his team except for Dr. Brodsky's contributions to the statistical analyses. Two reviewers endorsed Dr. Elston's statistical participation in the program and expressed hope that his limited role can be increased. Two reviewers criticized the limited involvement of the P.I. in the study as manifested by his lack of familiarity with relevant technical information. One of these two expressed concern about a seeming lack of knowledge of radiation effects by the team of investigators.

6. Methodology

The consensus of the reviewers was that in-plant, unirradiated control groups would be of greater interest than the external controls (siblings, nonstarts and Social Security Administration matched). However, the use of siblings was considered desirable. The nonstarts were regarded as trivial by all, including the investigators. The matched controls

were regarded as potentially interesting, especially if the matching procedure could be improved to include socioeconomic factors. One reviewer suggested an approach to the inclusion of socioeconomic factors in the matching process. Comparison of the cancer mortality of workers with U. S. life table values was suggested by two reviewers.

The use of unorthodox methodology was criticized by two reviewers. They felt that the primary methodology should be relatively standard so that results could be compared with those of other studies. Thereafter, innovative methods could be introduced without impairing comprehension and comparison of results.

7. General attitudes of the reviewers

The tenor of one reviewer's letter was quite strongly favorable to the contractor and his team. The second reviewer was noncommital as to the conduct of the study; he confined his remarks to substantive comments and suggestions. The tenor of the third letter was critical of the conduct of the study. The fourth reviewer registered strong disapproval of the team of investigators and recommended a change of contractors.

December 28, 1972

Enclosure 4

University of Pitts
CH AT(11-1)-3428
Thomas F. Mancuso, M.
Barkev S. Sanders, Ph.
Allen Brodsky, Sc. D.

Study of the Lifetime Health and Mortality Experience of Employees of AEC Contractors

Progress to Date

To date, even though we have essentially completed the basic personnel information for some 170,000 present and former employees of AEC contractors, our findings are restricted to relative frequency of deaths reported by the Social Security Administration (SSA) among 32,000 Hanford employees, 2,400 job applicants who turned down the job when it was offered to them (nonstarts), and 14,0 identified siblings of Hanford employees. Of the 32,000 employees only about 3 percent have one or more identified siblings of the same sex.

When the mortality of Hanford employees is compared with that of nonstart for male employees the mortality is significantly lower; for females the mortali is somewhat higher among employees, though this difference is not statistically significant.

The mortality of male Hanford employees with one or more identified sibli shows no significant difference compared with that of their siblings. When the mortality of all male Hanford employees is compared with that for identified si lings the employees show a somewhat higher mortality. This excess, however, is contributed almost exclusively by the earliest two or three cohorts (those hire in 1945 or earlier). Such differences could be the result of selective factors particularly since only 16 percent of the employees in these cohorts have any tified siblings, in contrast to 32 percent for the remaining cohorts.

For females in general the mortality of Hanford employees is somewhat hig than for the identified siblings. These differences are nevertheless small an could be the result of selective factors.

Analyses of Hanford data for employees and siblings by cause of death giv

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indication that certain causes, such as cancers, occur with greater frequency amo employees--this is true both for males and females. This initial analysis of causes of death indicated certain deficiencies. To correct these dificiencies 4,000 or so death certificates were re-coded by a highly qualified nosologist though no analysis based on these is as yet available. It is believed, however, that the findings of no significant difference in causes of death between employees and siblings would not be altered by the recoding. The analyses by cause of death is restricted to 91.1 percent of employee deaths, and 88.1 percent of sibling deaths for which death certificates were at hand.

These comparisons of causes of death between employees and identified siblings based on some 4,000 deaths with over 7,000 separate diagnoses as causes of death, give no indication of any higher rate of cancers or other diseases among employees as compared with siblings--this in spite of the fact that Hanford emplo ees have a mean annual exposure to occupational radiation of 220 m rem per persor when employed at Hanford.

The comparative analyses of mortality and causes of death for Hanford emplo ees and siblings include each cohort from 1943-44 through 1969 for the observatic period beginning with the date of employment at Hanford and running to the date c death of the employee or the sibling or to the cutoff date, 6/30/70. SSA has jus completed reprocessing some additional identified siblings for Hanford employees, and all Hanford employees and their previously identified siblings through a more recent cutoff date, 9/30/72. This updating increases appreciably the sibling cor trols and the number of known deaths when the data becomes available for analysis in 1973. SSA has also completed recently the identification of siblings for Oak Ridge. The proportion of identified siblings for Oak Ridge (Union Carbide) repre sents 57 percent of known siblings; the corresponding percentage for Hanford employees in the analyses on which our preliminary findings are based represents 3 percent of the known siblings.

Radiation exposure data for Hanford has just come to hand; so far we have no comparative mortality rates for employees with known radiation exposures of variou degrees and those without any. Such comparisons should become available in 1973. We expect to have, for employees of each cohort (year of hire), the mean occupatio exposure to radiation for each year for those living at the end of that year and those who died within the year. Also, we anticipate obtaining the mean occupatio radiation of deaths from specified causes, after proper adjustment for the age at death, and years subject to potential radiation exposure, to ascertain whether the is any indication that for the employee population certain causes of death, such a cancers, are more apt to be associated with occupational radiation.

Our findings to date, based on relative mortality and causes of deat. for employees and siblings with death certificates located, can still be expressed by what we stated in our monograph:

> "if there are any harmful effects from employment at Hanford, they could not be gross in character, nor could they affect large numbers of workers. However, it would be premature with the information we have now and findings surfaced so far, to conclude that radiation, within permissible limits, has had no adverse effects at all. In closing, we wish to emphasize again that even if our study of Hanford were to prove conclusively no adverse effects, it would be unwarranted with presently available insights to generalize such findings to apply to all forms of ionizing radiation in all the other AEC plants."*

We have indicated the need for further work to reach firm conclusions by 1) adding other criteria, such as incapacity as a measure of health, which manifests itself much earlier than death; 2) the selection of A and B matched controls to overcome many of the limitations inherent in identified siblings used as the o controls so far; 3) extending the study to Oak Ridge and other contractors, the p sonnel rosters for which are essentially completed; and 4) extending the scope of

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* Mancuso, T.F., Sanders, B.S., Brodsky, A., "Study of the Lifetime Health and Mortality Experience of Employees of AEC Contractors, Part I.: Methodology and Some Preliminary Findings Limited to Mortality for Hanford Employees", AEC Contract No. AT(30-1)-3394 and No. CH AT(11-1)-3428, Proceedings, Sixth Annual Health Physics Society Topical Symposium, Vol. III, p. 15.

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the study to employees of plants not so far included in the study, such as Rocky Flats, Los Alamos, etc., not merely to enlarge the sample and vary the circumstances of exposure to occupational radiation, but even more to fill the gaps in obtaining the cumulative lifetime exposure for employees who have worked for many AEC contractors. It is essential that the study be continued for some years to come until the findings are conclusive and irrefutable.

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