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form, (3) the agency form number, if applicable, (4) how often the form must be filled out, (5) who will be required or asked to report, (6) an estimate of the number of responses, (7) an estimate of the total number of hours needed to fill out the form, and (8) an indication of whether section 3504(h) of Pub. L. 96-511 applies.

ADDRESSES: Copies of the form and supporting documents may be obtained from Patti Viers, Agency Clearance Officer (732), Veterans Administration, 810 Vermont Avenue, NW., Washington, DC 20420, (202) 233-2148. Comments and questions about the items on the list should be directed to the VA's OMB Desk Officer, Allison Heron, Office of Management and Budget, 726 Jackson Place, NW., Washington, DC 20503, (202) 395-7318.

DATES: Comments on the information collection should be directed to the OMB Desk Officer within 60 days of this notice.

DATED: March 5, 1987.

By direction of the Administrator.

David A. Cox,
Associate Deputy Administrator for
Management.

Extension

1. Department of Veterans Benefits
2. Report of Medical Examination for Disability Evaluation
3. VA Form 21-2545
4. On occasion
5. Individuals or households
6. 280,000 responses
7. 65,000 hours
8. Not applicable

Extension

1. Department of Veterans Benefits
2. Claim for One Sum Payment
3. VA Form 29-4125
4. On occasion
5. Individuals or households
6. 87,821 responses
7. 8,872 hours
8. Not applicable

[FR Doc. 87-5102 Filed 3-10-87; 8:45 am]

BILLING CODE 8320-01-M

Evaluations by the Veterans Administration of Scientific Studies Related to the Effects of Exposure to Herbicides Containing Dioxin or to Ionizing Radiation

AGENCY: Veterans Administration.

ACTION: Notice of evaluations.

SUMMARY: "Veterans Dioxin and Radiation Exposure Compensation Standards Act" (Pub. L. 96-542) and implementing regulations, 38 CFR 1.17,

require that there be published from time to time in the Federal Register evaluations by the Veterans Administration (VA) of scientific or medical studies relating to the adverse health effects of exposure to herbicides containing dioxin (specifically 2,3,7,8-Tetrachlorodibenzo-p-dioxin) or to ionizing radiation. This "Notice of Evaluations" contained in Appendix A is concerned with the scientific studies previously reviewed by the Scientific Council of the Veterans' Advisory Committee on Environmental Hazards, a committee established under the legislative authority of Pub. L. 96-542. A summary of the review of these studies by the Committee is provided as Appendix B.

FOR FURTHER INFORMATION CONTACT: Dr. Barclay M. Shepard, Director, Agent Orange Projects Office (10X2), Department of Medicine & Surgery, Veterans Administration, 810 Vermont Avenue, NW., Washington, DC 20420, (202) 653-5047.

SUPPLEMENTAL INFORMATION: A. The Studies reviewed in Appendix A are:

1. Hardell and Sandstrom, "Case-control study: Soft tissue sarcomas and exposure to phenoxyacetic acids or chlorophenols." *Br. J. Cancer* 39: 711-717, 1979
 2. Eriksson, Hardell, et al., "Soft tissue sarcomas and exposure to chemical substances: A case-referent study." *Br. J. Ind. Med.* 38: 27-33, 1981
 3. Smith et al., "Soft-tissue sarcoma and exposure to phenoxy herbicides and chlorophenols in New Zealand." (*Journal of National Cancer Institute*) *JNCI* 73: 1111-1117, 1984
 4. Greenwald et al., "Sarcomas of Soft Tissues after Vietnam Service." *JNCI* 73: 1107-1109, 1984
 5. Lawrence et al., "Mortality Patterns of New York State Vietnam Veterans." (*American Journal of Public Health*) *AJPH* 75: 277-279, 1985
 6. Kogan & Clapp, "Mortality Among Vietnam Veterans in Massachusetts, 1979-1983." 1985
 7. Holmes et al., "West Virginia Vietnam-era Veterans Mortality Study." 1986
 8. Anderson, et al., "Wisconsin Vietnam Veteran Mortality Study." 1985
 9. Wendt, "Iowa Agent Orange Survey of Vietnam Veterans." 1985
 10. Robinette, Jablon, & Preston, "Mortality of Nuclear Weapons Test Participants." National Research Council of the National Academy of Sciences, 1985
- B. The following evaluation factors were used:
- (1) Whether the study's findings are statistically significant and replicable,

(2) Whether the study and its findings have withstood peer review,

(3) Whether the study's methodology has been sufficiently described to permit replication,

(4) Whether the findings of the study are applicable to the veteran population of interest; and

(5) Views of the Veterans Advisory Committee on Environmental Hazards.

Dated: March 3, 1987.

Thomas K. Turnage,
Administrator.

APPENDIX A—"Analysis of Studies" Relating to the Effects of Exposure to Herbicides Containing Dioxin or to Ionizing Radiation

1. Hardell and Sandstrom, "Case-control study: Soft tissue sarcomas and exposure to phenoxyacetic acids or chlorophenols." *Br. J. Cancer* 39: 711-717, 1979

Description of Study

In this report the authors present a case-control study in an effort to determine the association between exposure to phenoxyacetic acid herbicides and/or chlorophenols and the appearance of soft tissue sarcoma (STS). The study consists of 52 males cases (21 living, 31 deceased) between 28 and 80 years of age who were admitted to the University Hospital in Umea, Sweden, during 1970-1977. The controls, also males (4 for each case for a total 208) were selected from the general population and matched for age and place of residence. Deceased controls were selected for deceased cases. Exposure to the chemicals of interest was determined by a variety of methods including self-administered questionnaires, follow-up interviews and employers' responses to letters requesting exposure data. Time and duration of exposure among the cases and controls varied from 2 days in a 10-year period to 49 months in a 13-year period of time. Similarly the time interval between initial exposure and the time of diagnosis ranged up to 27 years. In the total group of those exposed to phenoxy herbicides and/or chlorophenols the relative risk for STS was 5.7 and in those believed to be exposed to phenoxy herbicides alone the relative risk was 5.3. From these data the authors concluded that occupational exposure to these chemical compounds and/or their contaminants, such as 2,3,7,8-TCDD, significantly increases the risk of developing soft tissue sarcoma.

Commentary

The case-control study methodology is appropriate in evaluating the risk for rare and unusual diseases and the selection of cases and controls is in accordance with scientifically accepted standards. The study design has been described in sufficient detail to permit replication. Studies by other investigators using a similar design, however, have not resulted in similar findings. In examining the conduct and conclusions of this study, several serious questions are raised:

(a) It appears that there exists considerable opportunity for recall bias in that study subjects (or their next of kin in the case of deceased subjects) having a serious illness such as a life-threatening malignancy (cases) are more likely to recall exposure to a perceived or potentially cancer-causing chemical than are study subjects who are free of such a disease (controls). The precise details and use of the questionnaire as well as the criteria for follow-up interviews are not carefully described and consequently add to the concerns related to recall bias.

(b) The criteria for assigning exposure lacks precision and there is no discussion of an analysis of data to determine the presence of a dose-response relationship.

(c) Among the study subjects categorized as being exposed to phenoxy herbicides alone, there were only 13 cases and 14 controls who were deemed to have been exposed to these compounds. In this group there was a total of only 46 cases of STS. These are relatively small numbers, and consequently, study conclusions must be drawn with caution.

(d) For the most part, the outcome of interest, soft tissue sarcoma was treated as though it were a single entity. It is well-known that soft tissue sarcomas represent a wide variety of tumors arising from many different types of tissue and having a wide variation in biological behavior. There is no evidence to suggest that these tumors have a common etiology. The authors do not indicate the distribution of the various types of soft tissue sarcomas in the case group in order to check for any deviation of such a distribution from what is seen in the general population. Although the histology was reviewed by a single pathologist, the details and results of this review are not mentioned. Furthermore, if there is a causal relationship between phenoxyacetic acid exposure and soft tissue sarcomas, it is highly unlikely that this relationship exists equally for each of the many cell types in this group of cancers. Therefore,

if a casual relationship exists for any of the cell types, it should manifest itself by revealing a variation from the usual distribution of such tumor types. Failure to describe and compare this distribution among the exposed and unexposed cases represents a serious omission on the part of the authors.

(e) This study, which should be considered more of a hypothesis-seeking than a hypothesis-testing effort certainly raises the possibility of a casual connection between phenoxy herbicide exposure among males and one or more of the soft tissue sarcomas. Although the overall age range of the study subjects is given, the ages of the individual subjects or even their age distribution are unfortunately omitted from the table describing the various exposure features for each of the exposed cases and controls. This represents an unfortunate omission of information which would have been easy to provide. The applicability of this study to the Vietnam veteran population is remote since the age range of the subjects, the mode and duration of exposure and the time interval between exposure and onset of disease are not comparable in many instances.

2. Eriksson, Hardell, et al., "Soft tissue sarcomas and exposure to chemical substances: A case-referent study," *Br. J. Ind. Med.* 38: 27-33. 1981.

Description of Study

This study, similar in design and purpose to the Hardell report described above, is also a case-control study. It consists of 110 cases and 220 controls, presumably males, although the sex of the subjects is not given. Also missing in the description are the age ranges of cases and controls as well as the details relating to duration of exposure and time interval between initial exposure and time of diagnosis for the cases. In this study the authors report a relative risk for STS of 5.1 for the overall exposed group and 6.8 for those deemed to be exposed to phenoxy herbicides alone.

Commentary

Since this study's methodology is essentially the same as the Hardell study, most of the same concerns and criticisms apply. In addition to those described above, the following should be noted:

(a) Unlike the Hardell study, the Eriksson study provides the distribution of the various cell types of the 110 case tumors. It is most unfortunate, however, that the authors fail to show the same distribution for the exposed and unexposed groups, in other words, to

show how many of each cell type were seen among the exposed and the unexposed subjects. Surely the information was available, and it would have been a simple matter to add two more columns in Table I to show if the increased risk was attributable to any one of the 13 cell types shown. Failure to provide this information seems a serious omission on the part of the authors.

(b) Unlike the Hardell study, the Eriksson study addresses the dose-response issue, as seen in Table IV. Thirty days of exposure is taken as the dividing point and the number of cases above and below this exposure time is the same, suggesting that there is no dose-response relationship. This in turn raises serious doubt as to the likelihood of any causal relationship between exposure to these chemicals and soft tissue sarcomas.

As in the Hardell study and for many of the same reasons this study cannot be considered directly applicable to the Vietnam veteran population.

3. Smith et al., "Soft-tissue sarcoma and exposure to phenoxy herbicides and chlorophenols in New Zealand." *JNCI* 73: 1111-1117. 1984.

Description of Study

This is a case-control study to examine the association between soft tissue sarcomas and occupational exposure to phenoxy herbicides in New Zealand where these chemicals have been used extensively since the late 1940's. The 82 cases of soft tissue sarcoma were all males selected from a National Cancer Registry and had all been reported from public hospitals between 1976 and 1980 inclusive. The histology was confirmed by a single pathologist. The 92 controls, also males, were selected from the same source and had another type of cancer. The use of cancer controls is thought to significantly reduce the likelihood of recall bias. The authors found that among the study subjects who were deemed to be probably or definitely exposed for more than 1 day and more than 5 years prior to entry into the cancer registry (17 cases vs. 13 controls) the relative risk for soft tissue sarcoma was 1.6. These were the same exposure criteria used in the Swedish studies, but unlike the Swedish studies, the increased risk in this study was not statistically significant. In a second analysis of subjects classified as probably or definitely exposed for at least 5 days and 10 or more years prior to entry into the cancer registry, the relative risk fell to 1.3, again not statistically significant. This suggests

the absence of a dose-response relationship and is contrary to what one would expect if there is a causal relationship between exposure to these chemicals and soft tissue sarcomas.

Commentary

The design, methodology, and findings of this study are clearly outlined and can be readily compared to other studies of this type. This study does not support the conclusions reached in the Swedish studies described previously. The failure to show a dose-response effect and the use of cancer controls to minimize recall bias are seen as strengths of this study. There are, however, some aspects of the study which should be noted:

(a) The numbers of exposed and unexposed cases and controls are relatively small and therefore conclusions must be drawn cautiously.

(b) The cases and controls were selected from among individuals reported to the National Cancer Registry from public hospitals only. The authors suggest that reporting from other hospitals was more recent and/or less complete. There is no discussion, however, as to how representative the public hospital patient population is with regard to the population of exposed workers and whether or not limiting the selection of study subjects to this group alone introduces any bias.

(c) There was no distribution of cancers by cell type to determine any variation from the usual distribution in the general population. The authors thereby seem to treat soft tissue sarcomas as a single entity. Concerns related to this issue are previously described.

(d) The exposure criteria are somewhat imprecise. This may in part be due to the intention of the authors to mimic the Swedish studies for the purpose of comparison.

(e) This study does not examine a population analogous in age to Vietnam veterans. For this reason and the lack of similarity of exposure characteristics, the study cannot be considered directly applicable to the Vietnam veteran population.

4. Greenwald et al., "Sarcomas of Soft Tissues after Vietnam Service." *JNCI* 73: 1107-1109, 1984

Description of Study

The authors present a case-control study to examine the relationship between military service in Vietnam and the occurrence of soft tissue sarcoma among male residents of New York State (excluding New York City) who were of draftable age during the

Vietnam conflict. The study consists of 281 cases (151 living and 130 deceased) of soft tissue sarcomas selected from the New York State Cancer Registry diagnosed between 1962 and 1980 and between the ages of 18 and 29 during the years 1962 to 1971. Two control groups were chosen as follows:

(a) 281 live male controls selected from drivers' license registration files from the New York State Department of Motor Vehicles matched by age (within 5 years of birth date), race and place of residence;

(b) 130 deceased males selected from New York State death certificates and similarly matched to deceased cases. No cancer deaths were included among the controls. Of the 281 cases, 10 had military service in Vietnam as compared to 18 of 281 live controls and 9 of 129 deceased controls. From these data the authors concluded that military service in Vietnam does not increase the risk of developing soft tissue sarcoma. This same conclusion applies to military service in general. In addition to questions relating to military service, considerable data relating to non-military occupations and exposure to herbicides were obtained. Analyses of these data showed no statistically significant association between soft tissue sarcomas and occupational exposure to herbicides or other pesticides.

Commentary

This study is described with sufficient clarity and detail to be readily replicated given the availability of comparable data bases. The relatively large number of cases and the two groups of carefully matched controls make this a strong study. A moderate-sized sample (108 of 281 cases) of pathology specimens were reviewed by a single pathologist who was "blinded" as to the military service status of these cases. In reviewing this study, the following concerns are raised:

(a) The reason for reviewing only 108 pathology specimens is not given, and the accuracy of this review relative to the coded diagnoses in the cancer registry is not described. These are unfortunately omissions especially in view of the difficulty in classifying these tumors. The distribution by cell type among the cases is not provided in sufficient detail to make comparisons between the various subsets of study subjects.

(b) The results of the interviews are not provided in sufficient detail as to be readily understood, although the outcome of the analyses of these data are stated as not showing a statistically

significant association with a number of occupational exposures as noted above.

(c) As stated by the authors, the average latency period is only about 12 years, which is relatively short for chemical carcinogens but approximates what is claimed by concerned individuals.

This is primarily a study to determine the risk for soft tissue sarcoma among Vietnam veterans and other veterans of the Vietnam era. It is therefore directly applicable to the Vietnam veteran population and makes a strong case for the lack of such an increased risk. There is less adequate data, however, to make an equally strong statement as regards the risk of developing soft tissue sarcoma among veterans exposed to Agent Orange, other herbicides and contaminants such as 2,3,7,8-TCDD.

5. Lawrence et al., "Mortality Patterns of New York State Vietnam Veterans." *AJPH* 75: 277-279, 1985

Description of Study

This is a mortality study comparing case of death patterns among various groups of males of the age group eligible for military duty during the Vietnam conflict and whose deaths were recorded in the New York State Vital Records. The selection of subjects included males between the ages of 18 and 29 inclusive during the time period 1965 to 1971 who had died during 1965 to 1967 and 1970 to 1980 in New York State, excluding New York City. There were 22,494 deaths which included 4,558 Vietnam era veterans. Veteran status and Vietnam service status were more accurately determined using a combination of Defense Department and Veterans Administration data files which when matched with New York State files resulted in a total of 1,498 deceased Vietnam era veterans of whom 555 had served in Vietnam. In comparing the two groups, the authors found no remarkable disease differences between Vietnam veterans and other veterans of the Vietnam era. There was, however, an increase in deaths due to non-motor vehicular injuries of transport.

Commentary

This study was based on linkage of data files and therefore conclusions must be drawn cautiously since the accuracy of the records was not checked in detail. As pointed out by the authors, this type of study is most useful in seeking hypotheses to be tested by other epidemiological techniques. In addition, this study has no ability to determine the health risks of exposure to phenoxy herbicides or other chemicals of concern

in military or other occupational settings. Being a study of New York State Veterans of the Vietnam era, this has direct applicability to this group of veterans as a whole.

6. Kogan & Clapp, "Mortality Among Vietnam Veterans in Massachusetts, 1979-1983." 1985.

Description of Study

This is a state report of a mortality study of white males of the Vietnam veteran age group who died in Massachusetts between 1972 and 1983 and whose death certificate information was recorded in a data base compiled by the Massachusetts Department of Public Health. This was linked to a data base of veterans awarded a state bonus which consisted of \$300 for service in Vietnam and \$200 for service elsewhere between 1958 and 1973. This linkage provided 840 deceased veterans presumed to have served in Vietnam and 2,515 veterans classified as non-Vietnam veterans. Among the more striking conclusions were an approximately 9-fold increased risk for connective tissue cancers and a slightly less than 2-fold increased risk of kidney cancer when comparing Vietnam veterans to non-Vietnam veterans. When comparing these two groups, there was a moderately increased risk of "estimated suicides" which included unknown causes of death and poisonings in addition to recorded suicides. Deaths from all external causes including motor vehicle accidents were also moderately increased.

Commentary

This study utilizes an interesting and imaginative technique of data base linking which has the advantage of producing rapid results. Its principal value lies in seeking out hypotheses to be tested through the use of more precise epidemiological techniques. These factors are well described by the authors who point out the limitations and cautions which should be applied to such a study. Of particular concern are the following:

(a) Death certificate information needs validation especially when dealing with a diagnosis of the complexity of connective tissue (soft tissue) cancers. These diagnoses need confirmation by a pathologist expert in this field.

(b) Any Vietnam veterans' bonus list needs validation particularly with regard to actual in-country service. Many of the state bonuses were awarded on the basis of information on the veteran's discharge certificate which

usually does not discriminate between in-country service and service in the general vicinity of Southeast Asia during the time of the Vietnam conflict.

(c) There exists a number of opportunities for bias being introduced with the use of the Massachusetts bonus list. Such bias may result from excluding Vietnam veterans who failed to apply for the bonus or who were ineligible for the bonus by virtue of the six-month residence requirement or a less than honorable discharge.

As in the other studies using Vietnam veterans as study subjects, the Massachusetts mortality study is considered directly applicable to this veteran population as a whole. The results, however, must be interpreted with caution, and since no attempt was made to analyze for Agent Orange exposure, no conclusions can be drawn with regard to the possible effects of such exposure.

7. Holmes et al., "West Virginia Vietnam-era Veterans Mortality Study." 1986.

Description of Study

This is a report by the West Virginia Department of Health of a mortality study of veterans of the Vietnam era who died in that state between 1968 and 1983 inclusive. This study is similar in design to the Massachusetts study, i.e., subjects were identified by linking a state death records data file with a computer file containing the names of all applicants for a state military service bonus given to veterans who were on active duty between 1964 and 1973. There was a differential payment based on in-country vs. non-in-country service, and to be eligible the veteran must have been a resident of West Virginia for at least six months prior to entry into active duty and have received an honorable discharge. The study subjects included 615 deceased in-country Vietnam veterans and 610 deceased Vietnam era veterans who had not served in the Southeast Asia theatre of operations. Results of a detailed series of analyses comparing causes of death among the Vietnam and non-Vietnam veterans as well as all veterans and non-veterans are presented clearly and in a manner which would permit replication given the availability of comparable data bases. Among the more striking results were the following:

(a) When comparing Vietnam to non-Vietnam veterans, statistically significant increases were found in three groups of malignancies: lymphoma, including Hodgkin's disease (7 cases); testicular cancer (3 cases); and soft tissue sarcoma (3 cases). In each

instance, however, the numbers of cases were small and interpretation of results must be made with caution.

(b) In comparing all Vietnam era veterans to non-veterans, there was a relatively small but statistically significant increase in the overall category of deaths due to accidents, poisoning, and violence. In the specific subcategories of motor vehicle and non-motor vehicle fatalities, suicides, and all other external causes, however, there were no statistically significant increases.

Commentary

This study closely resembles the Massachusetts study and consequently many of the same observations apply to both studies, in particular, the need for caution in drawing conclusions from the results of the statistical analyses and the possibility of selection bias with regard to actual in-country service. Also, as noted previously, there was no attempt to analyze for herbicide exposure and, consequently, no conclusions can be drawn from this study regarding the effects of exposure to Agent Orange or its dioxin contaminant. This study also has direct applicability to the Vietnam veteran population, but as pointed out by the authors, interpretations and conclusions must be made with caution.

8. Anderson, et al., "Wisconsin Vietnam Veteran Mortality Study." 1985.

Description of Study

This is a detailed report of a very extensive mortality study which was conducted in three phases, each of which makes comparisons of mortality patterns among different groups of veterans in the State of Wisconsin. It is the fourth state mortality study included in this review. The three phases provide comparisons among the following groups:

Phase 1—All Wisconsin veteran deaths for the years 1960 through 1979 were compared to non-veteran deaths.

Phase 2—All Wisconsin Vietnam and non-Vietnam veteran deaths for the years 1964 through July 1983 were compared to each other and to non-veteran.

Phase 3—A large cohort mortality study based on 122,238 Vietnam era veterans of whom 2,698 had died and for whom 2,590 (98%) death records were obtained. Of these 927 (35.8%) had served in Vietnam (Vietnam veterans) and 1,663 had served elsewhere (non-Vietnam veterans). The distribution of Vietnam versus non-Vietnam veterans among deceased veterans was almost

identical to the same distribution in the entire cohort.

Since Phase 1 did not focus specifically on Vietnam veterans, this review will deal with Phases 2 and 3 which are directly applicable to the Vietnam veteran population as a whole.

Study Conclusions

When comparing causes of death among Vietnam versus non-Vietnam veterans, significant findings in Phase 2 include the following:

(a) Cancer of the pancreas, diseases of the genito-urinary system when combined, and all pneumonias were the only conditions for which there was a statistical significant increased risk.

(b) There was a small excess of soft tissue sarcoma and cancer of the digestive organs and peritoneum but these were not statistically significant.

(c) There was no increased risk for any other malignancy. In comparing cause of death patterns among Vietnam and non-Vietnam veterans, Phase 3 findings included the following:

(a) There were statistically significant increased rates of death due to motor vehicle accidents, all accidents and all external causes.

(b) There was a small, not statistically significant increase in deaths recorded as suicide.

(c) There were no statistically significant increases in deaths due to any malignancy including soft tissue sarcoma.

Commentary

Of the four state mortality studies presented in this review, the Wisconsin study is the most detailed and most comprehensive. In addition it encompasses the two most widely accepted analytical techniques used in conducting mortality studies, i.e., a proportional mortality ratio (Phases 1 and 2) and a calculation of actual death rates derived from a cohort of Vietnam and a cohort of non-Vietnam veterans (Phase 3). The latter provides the basis for a standardized mortality ratio analysis. As with the other Vietnam veteran mortality studies, the Wisconsin study has direct applicability to the Vietnam veteran population and again as in the other mortality studies, no attempt was made to analyze for herbicide exposure.

It is of interest that these four studies failed to demonstrate any consistent pattern for Vietnam veterans having an increased risk for a particular disease or category of disease as a cause of death which compared to non-Vietnam veterans. There is, however, a suggestion of an increase in deaths due to motor vehicle and non-motor vehicle

accidents as well as deaths due to external causes such as trauma and poisoning. Deaths recorded as suicides are not consistently elevated, but some of the deaths due to external causes may result from suicide, which, is often under-reported as a cause of death.

9. Wendt, "Iowa Agent Orange Survey of Vietnam Veterans." 1985.

Description of Study

The Iowa Agent Orange Survey is a state report which includes a very detailed description of the whole Agent Orange issue including an historical overview of the military use of herbicides by U.S. Armed Forces in Vietnam and highlights of a variety of subsequent events. It focuses primarily on the concerns of Vietnam veterans and the response to these concerns on the part of the Congress, various federal agencies and state governments.

A central purpose of the report is to present the results of a survey of Iowa Vietnam veterans as mandated by the State Legislature in May 1983. The survey was initiated by mailing a questionnaire to 45,181 Iowa Vietnam veterans. 10,846 responses met the criteria and formed the basis of the survey. The report gives a detailed listing and analysis of the responses in a number of areas including military and post-military occupations as well as personal and family health-related questions. The final section of the report includes a statement that "no definitive evidence exists to establish any link between exposure to Agent Orange and subsequent long-term adverse health effects. At present, there is no convincing evidence that the rates of birth abnormalities, physical disorders, and mortality are significantly increased among Vietnam veterans."

Commentary

This report represents a very responsible and comprehensive effort on the part of the Iowa State Department of Health, to provide a most useful guide and source of information for Vietnam veterans concerned about the possible adverse health effects of exposure to Agent Orange. The survey instrument is well designed and the information derived from it is carefully analyzed and clearly depicted. The findings and conclusions, as noted above should provide some measure of reassurance to Vietnam veterans in the State of Iowa as well as to all Vietnam veterans and their families. Unlike the studies described above, there was no intent to compare the results of the survey with data derived from a non-Vietnam veteran group and therefore does not constitute

an "epidemiological study" in the usual sense of the term. It does, however, as with other carefully designed and conducted health surveys, provide a basis for seeking possible adverse health effects for further study.

10. Robinette, Jablon, & Preston, "Mortality of Nuclear Weapons Test Participants." National Research Council of the National Academy of Sciences, 1985.

Description of Study

This is a cohort mortality study of the 46,106 active duty military participants of a series of five nuclear weapons tests conducted between 1951 and 1957 at either the Nevada Test Site or the Pacific Proving Ground. The study included an analysis of the cause of death pattern among 5,113 deceased veterans compared to cause and age-specific mortality rates in the U.S. population. The overall death rate was somewhat less than expected in the general population reflecting the commonly observed "healthy veteran" effect. When comparing the rates for deaths due to accidents, acts of war and other external causes, there was a small (6%) increase among the veterans. On the other hand, there were fewer than expected deaths from all malignancies combined, including leukemia. When analyzing the deaths among the participants in the test named SMOKY, there were 10 deaths due to leukemia, 2.5 times greater than the expected number. The analysis revealed that this was a statistically significant increase in this group. When analyzing the leukemia deaths among all other test participants, however, there were slightly fewer than expected deaths (not statistically significant).

Commentary

A statistically significant elevation of deaths due to a disease process was seen for leukemia in only one of the tests. This was based on only 10 deaths from this cause, a relatively small number. As stated by the authors, these results can neither confirm nor deny that the increase in leukemia was due to radiation exposure. This is especially so since there was no increase in leukemia or other malignant disease among the nuclear test participants when the data from all tests were combined.

Summary Conclusions of the Research Studies Reviewed to Date

Based on the reviews of the research studies noted above, there does not appear to be sufficient evidence to establish a causal relationship between possible exposure of veterans to

phenoxy herbicides in Vietnam and adverse health effects, including soft tissue sarcomas, other cancers or other systemic diseases. It should be noted, however, that among the studies of veterans noted above, none has attempted to correlate the degree or intensity of exposure to herbicides/dioxins, with adverse health effects. Rather, the correlation has been with military service in Vietnam. Even in this matter actual "in-country" service has not been conclusively established in each instance. Furthermore, it should be noted that verified "in-country" service in Vietnam cannot be equated to herbicide/dioxin exposure for the purpose of drawing scientifically valid conclusions regarding the possible adverse health effects of such exposure. Many veterans with actual service in Vietnam had little or no opportunity for herbicide/dioxin exposure.

Several additional studies dealing with health effects of Vietnam service and/or herbicide exposure are currently underway and nearing completion. The conclusions drawn from these studies will be the subject of future notices in the Federal Register.

As regards the effects of veterans' exposure to ionizing radiation, the single study in this area as noted above suggests the possibility of an increased risk of leukemia in one group and prostate cancer in another group. These findings were limited to one nuclear test in each case and hence must be viewed as inconclusive. Further research in this area is being contemplated.

Future Scientific Evaluations

In accordance with the provisions of Pub. L. 98-542 and implementing regulations, additional evaluations will be published from time to time in the Federal Register. The nature of such evaluations and the scope of research to be reviewed is contingent on the number of completed research studies published following the date of this notice. A number of such studies are currently in progress and will be the subject of future reports.

Appendix B—Summary of Review of Studies by the Scientific Council of the Veterans' Advisory Committee on Environmental Hazard

Studies:

1. Hardell and Sandstorm, "Case-control study: Soft tissue sarcoma and exposure to phenoxyacetic acids or

chlorophenols," *Br. J. Cancer* 39: 711-717. 1979.

This is a retrospective case-control study which attempted to determine a causal relationship between phenoxyacetic acids or other chlorine-containing organic compounds and the development of soft tissue sarcoma. The study's authors calculated the relative risk of developing a soft tissue sarcoma as 5.3 times greater in the "phenoxyacetic exposed" population and concluded that their investigation showed an increased risk.

2. Erikson, Hardell, et al., "Soft tissue sarcomas and exposure to chemical substances: a case-referent study," *Br. J. Ind. Med.* 38: 27-33. 1981.

This study utilized the same design as the 1979 Hardell study. A relative risk of 8.8 for soft tissue sarcoma was calculated for persons exposed to phenoxyacetic acids.

3. Smith et al., "Soft-tissue sarcoma and exposure to phenoxy herbicides and chlorophenols in New Zealand." *JNCI* 73: 1111-1117. 1984.

The data in this case-control study showed no relationship of soft tissue sarcoma with occupational exposure to phenoxy herbicides and chlorophenols. The relative risk was 1.3, and was not statistically significant.

4. Greenwald et al., "Sarcomas of Soft Tissue After Vietnam Service." *JNCI* 73: 1107-1109. 1984.

This case-control study looked at the Vietnam service and military service experiences of men with soft tissue sarcomas and compared them to a control group matched on the basis of dates of birth and places of residence. The study failed to show an association of soft tissue sarcoma with exposure to Agent Orange or with service in Vietnam. The study also compared those or with service in Vietnam. The study also compared those who died with a second control group derived from death certificates. No relationship to service in Vietnam was detected.

Commentary: The Committee noted that the methods of the Hardell and Erikson studies had been criticized as to the statistical methods employed. Criticism had also been expressed about the possibility of selective recall in answering the mail and telephone questionnaires.

Specifically, the observation was made that a person reporting an illness

would be more likely to recall the supposed causal event than would a well person to recall the same type of event. Concern was also expressed about the reliance upon the Ninth Revision of the International Classification of Disease (ICD 9) code 171 for the selection of the soft tissue sarcoma cases in the New Zealand study as this would not include a variety of other soft tissue sarcomas involving various organ sites. The Committee expressed its conclusion that these studies did not resolve the issue in either direction. The early positive studies were considered to have had such serious methodological flaws that the evidence linking soft tissue sarcoma to herbicide exposure is not credible.

5. Lawrence et al., "Mortality Patterns of New York State Vietnam Veterans." *AJPH* 75: 277-279. 1985.

This cohort study compared deceased New York State veterans with Vietnam service to veterans of the Vietnam era with no Vietnam service and found no remarkable disease differences between the two groups. To the extent that Vietnam service was indicative of dioxin-contaminated herbicide exposure, no association of it with cause of death was found.

6. Kogan & Clapp, "Mortality Among Vietnam Veterans in Massachusetts, 1979-1983." 1985.

This study analyzed the mortality patterns of Vietnam veterans compared to non-Vietnam veterans and to other male who died during the period 1972 to 1983. The study found elevated risks of death due to motor vehicle accidents and suicide and excess cancers of the connective tissue and kidney.

Commentary: The committee believed that these two studies were well-conducted and that the authors properly stated their limitations. With respect to the Massachusetts study, it was noted that there was no attempt to correlate the findings with the amount of exposure to Agent Orange a veteran may have had in Vietnam and that the number of cases identified was low, although statistically significant. Concerning the New York study, it was thought that the study may have been conducted too soon to reveal any conditions which may have a long latent period.

7. Holmes et al., "West Virginia Vietnam-era Veterans Mortality Study." 1986.

This study compared the causes of death among Vietnam veterans, Vietnam-era veterans who did not serve in Vietnam, and male non-veterans and found no difference for all causes of death but did note higher incidences of Lymphoma (Hodgkins Disease), testicular cancer, and soft tissue sarcoma among Vietnam veterans. The Study's authors noted that the findings must be interpreted cautiously and set forth the basis for this caution.

8. Anderson, et al., "Wisconsin Vietnam Veteran Mortality Study." 1985.

This proportionate mortality study compared the causes of deaths among Vietnam veterans, Vietnam-era veterans, non-veterans and all other veterans (phases 1 and 2; phase 3 compared the death rates of Wisconsin Vietnam veterans to a cohort of non-Vietnam veterans). The study found statistically significant increases in pancreatic cancer, all diseases of the genito-urinary system and all pneumonias.

Commentary: The Committee agreed with the West Virginia study's authors as to the limitations of the study. Among these were that there was no basis for determining the completeness of the data based used and that there had not been a verification of the service data to prevent possible misclassification. Neither study presented any information concerning significant confounding factors such as smoking and alcohol consumption. Also, these studies were relatively small with few deaths being studies. The Committee believed that the findings left open the question of whether soft tissue sarcoma may be associated with Vietnam Service.

9. Wendt, "Iowa Agent Orange Survey of Vietnam Veterans." 1985.

The data were collected from a self-administered questionnaire. The results found no definitive evidence to establish any link between exposure to Agent Orange and subsequent long-term

adverse health effects. The study also concluded that there was no convincing evidence that the rates of birth abnormalities, physical disorders, and mortality were significantly increased among Vietnam veterans.

Commentary: The Committee noted with interest the study's findings but cautioned that they were based upon a self-administered, uncorroborated questionnaire. The weaknesses of such a study, the Committee noted, are many and well-known.

10. Robinette, Jablon, & Preston, "Mortality of Nuclear Weapons Test Participants." National Research Council of the National Academy of Sciences. 1985

This investigation involved a review of the death certificates of the approximately 46,200 veterans who participated in one or more of five series of atonic weapons tests in Nevada or the Pacific Islands. About 5,000 of these men were known to have increased deaths from cancer or other diseases for the veterans overall. The study did, however, confirm an excess of leukemia among veterans of one nuclear test (Shot SMOKY) and a slight increase in the number of prostate cancers among veterans of another test. The lack of consistent evidence of increased cancer incidence led the study's authors to proffer two explanations: that the observed high incidence of leukemia among the Shot SMOKY participants is simply a "chance aberration" or the actual radiation exposure of these men was several times the dose recorded at the time.

Commentary: The Committee believed that this study was well designed and executed. The Committee agreed with the study's investigators' description of the study's findings and limitations.

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Cooperative Studies Evaluation Committee Notice of Meeting

The Veterans Administration gives notice under Pub. L. 92-463 that a

meeting of the Cooperative Studies Evaluation Committee, authorized by 38 U.S.C. 4101, will be held at the The Children's Inn, 342 Longwood Avenue, Boston, Massachusetts 02115 on April 8, 1987. The meeting will be for the purpose of reviewing proposed cooperative studies and advising the Veterans Administration on the relevance and feasibility of the studies, the adequacy of the protocols, and the scientific validity and propriety of technical details, including protection of human subjects. The Committee advises the Director, Medical Research Service, through the Chief of the Cooperative Studies Program, on its findings.

The meeting will be open to the public up to the seating capacity of the room from 7:30 to 8:00 a.m., on April 8, to discuss the general status of the program. To assure adequate accommodations, those who plan to attend should contact Dr. Ping C. Huang, Coordinator, Cooperative Studies Evaluation Committee, Veterans Administration Central Office, Washington, DC (202-233-2861), prior to March 20, 1987.

The meeting will be closed from 8:00 a.m. to 3:30 p.m. on April 8, for consideration of specific proposals in accordance with provisions set forth in section 10(d) of Pub. L. 92-463, as amended by section 5(c) of Pub. L. 94-409, and subsection (c)(6) and (c)(9)(B) of section 552b, title 5, United States Code. During this portion of the meeting, discussions and decisions will deal with qualifications of personnel conducting the studies and the medical records of patients who are study subjects, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy. Additionally, premature disclosure of the Committee's recommendations would likely frustrate implementation of final proposed actions.

Dated: February 28, 1987.

By direction of the Administrator:
Rosa Maria Fontanez,
Committee Management Officer.

[FR Doc. 87-5141 Filed 3-10-87; 8:45 am]

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