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**TO:**

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**SUBJECT:** Air Force Surgeon General's Statement on the Air Force Health Study (Ranch Hand)

Statement with questions and answers in response to recent news media coverage are attached for your information.

*Priscilla,*

*Here is the Ranch Hand response.*

*Nick*

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Total Number of Pages, Including Cover Sheet: 8

Air Force Surgeon General's Statement on  
Air Force Health Study (Ranch Hand) Issues  
Nov. 18, 1998

The Air Force Health Study (AFHS), is a 20-year prospective epidemiologic study of veterans of Operation Ranch Hand, the unit responsible for the aerial spraying of Agent Orange and other herbicides in Vietnam from 1961 to 1971.

An article, "Fatal Flaws," appeared Nov. 1, 1998, in the *San Diego Union Tribune*. This article heavily criticized the conduct of the Air Force Health Study (AFHS). Many statements in the article are misleading and others are incorrect. The four main criticisms presented by the reporter were:

- The study is flawed and tainted
- Management interfered in the study
- The AFHS withheld and altered 1984 birth defects and cancer findings
- Diabetes findings were not released for five years

The first three criticisms were given to the reporter by a former principal investigator who left the study in 1984. These criticisms were previously raised in 1988 and resulted in congressional hearings at that time.

The study is not flawed; it has been carried out according to its protocol, under the review of a non-governmental oversight committee – the Ranch Hand Advisory Committee, and all results are published in peer-reviewed scientific journals. Study investigators report progress and results annually to Congress and all results are further reviewed and summarized bi-annually by the National Academy of Sciences (NAS).

This study has been free of management interference. All decisions regarding the technical aspects of the study have been made on the basis of their scientific merit. Additionally, there is no institutional bias in this study. Although bias is a concern when an organization investigates itself, the authors of the protocol knew this and wrote safeguards into the study design to prevent inappropriate influence. Those safeguards include an oversight committee of non-governmental experts in medicine, toxicology and statistics with some members nominated by veterans advocacy organizations; peer review of our reports; and, more recently, annual reports to Congress, bi-annual review by the National Academy of Sciences; and publication of results in peer-reviewed scientific journals. Finally, we protect ourselves from bias by seeking outside opinion from expert researchers from institutions such as the Centers for Disease Control and Prevention (CDC) and universities.

Because the birth defects data in the baseline report was not yet verified, the principal investigators presented a guarded interpretation rather than use a stronger interpretation as advocated by one of the principal investigators. Subsequently, a preliminary follow-up birth defect report reanalyzed the data after children with reported defects were verified by medical records but prior to the verification of all children. The oversight committee was critical of the preliminary follow-up report and recommended that it not be released and that we should verify all of our data before writing another

report. The principal investigators agreed with the committee and began verifying the birth defect status of ALL children in 1984. This five-year effort represents the verification of over 10,000 reproductive outcomes. The AFHS collaborated with CDC to write a reproductive outcome report based on verified data. Articles were published in a peer-reviewed journal; two were co-authored with CDC. The research found little or no relation between paternal dioxin body burden and birth defects or any of the other outcomes studied. However, small numbers of children with spina bifida fathered by veterans with high dioxin levels were found. The numbers were too small for statistical analysis. The NAS interpreted this data as suggestive, and Congress, wanting to give the "benefit of the doubt" to veterans, responded by enacting compensation legislation for these children.

It was suspected in 1984 that dioxin might cause or promote certain cancers and inhibit or prevent others. So to some scientists, combining skin and systemic cancers into a single analysis did not make biological sense, a view shared by the committee. Skin cancer was not an expected outcome of dioxin exposure. This, together with the lack of adjustment for sun exposure and skin reaction to the sun, motivated a guarded interpretation. The numbers in the baseline report can be added to produce a combined analysis. However, such an analysis, while statistically more powerful, is, to some reviewers, more difficult to interpret because it includes etiologically dissimilar malignancies, as pointed out by our committee. The emphasis on skin cancer was a misinterpretation, as pointed out in an Aug. 25, 1987, letter to Senator Thomas Daschle. It was not true that most cancers were of the skin since a nonsignificant increase in internal cancers was also seen at baseline. The same analyses were repeated in subsequent reports and the increase in skin cancer was found in 1987, but not in 1985 and not in 1992. No significant increases in internal cancer were found at any follow-up examination. Subsequent analyses based on all available data through 1997 found no significant increase in skin cancer prevalence in the Ranch Hand group and no relation with dioxin body burden. Additionally, cancer mortality among Ranch Hand veterans is now less than expected.

The diabetes results were not withheld. Diabetes results have been released in various reports since 1991, including the annual reports to Congress. The AFHS released data showing a relation between dioxin and diabetes for the first time in our 1991 report summarizing dioxin analyses of the second follow-up examination results. In 1992, the diabetes findings were presented at an international dioxin conference and published in their proceedings. The NAS summarized our diabetes results in 1994, but dismissed the results as possibly due to inadequate adjustment for body fat.

Criticism in the *San Diego Tribune* article ignored all study results since 1985 and concentrated on the baseline report period of 1982 to 1984. There was no management interference with the study. There has been no manipulation of study results. There has not been stonewalling. The Air Force has provided full data disclosure, and conclusions have not been withheld. All contractual activities have been in accordance with federal acquisition regulations. In 1988, Senator Daschle conferred with all principal investigators and solicited their opinions on the conduct of the study. Follow-up

congressional testimony provided a forum for additional study critique. The study design and conduct was affirmed. This is a premier study and an example of the government conducting good science.

Finally and foremost, the Air Force is committed to enhancing the quality of life of our military families. In support of that commitment, the Air Force Health Study has enabled us to address our concerns about any implications dioxin exposure might have on the health of our veterans and their families.

For more information, see attached questions and answers or contact the Air Force Surgeon General's Office at (202)767-4797.

**Air Force Response to Issues Raised by the San Diego Union-Tribune,  
Nov. 1, 1998, regarding the Air Force Health Study on Exposure to  
Herbicides (the Ranch Hand Study)**

**1. Question: Is the Ranch Hand Epidemiology Study flawed and tainted because the Air Force investigated itself?**

**Answer:** The Air Force always acted to maintain the integrity of the study. The study has been carried out according to its protocol and under the review of a non-governmental oversight committee. All results are published in peer-reviewed scientific journals and are available for public review. Study investigators report progress and results annually to Congress, and all results are further reviewed and summarized bi-annually by the National Academy of Sciences (NAS).

**2. Question: Did high-ranking Air Force officers interfere with the study's data analysis, thus undermining its scientific integrity?**

**Answer:** No, this study has been and is free of management interference. Air Force members of all grades are allowed to comment on the study and make suggestions regarding its direction but the final decision rests with the investigators and members of its oversight committee, the Ranch Hand Advisory Committee. It is always a concern when an agency investigates itself. The writers of the protocol thought of this and wrote safeguards into the study design to prevent inappropriate influence. Those safeguards include the oversight committee of non-governmental experts in medicine, toxicology and statistics with some members nominated by veterans advocacy organizations; peer review of our reports; and, more recently, annual reports to Congress; bi-annual review by the National Academy of Sciences; and publication of results in peer-reviewed scientific journals. Finally, seeking outside opinion from expert researchers from institutions such as the Centers for Disease Control and Prevention (CDC) and universities accomplishes another measure taken to protect the study from bias.

**3. Question: Who is on the Ranch Hand Advisory Committee and how do they provide oversight of the study (advice versus direction)?**

**Answer:** The committee currently is comprised of Dr. Robert Harrison of the University of Rochester (chairman), Dr. Turner Camp of the Veterans of Foreign Wars, Dr. Irene Check of Evanston Hospital and Northwestern University, Dr. Elissa Favata of the South Jersey Medical Center, Dr. Arleen Rifkind of Cornell University Medical College, Dr. Dolores Shockley of Meharry Medical College, and Dr. Donald Trewyn of Kansas State University. The committee meets periodically to review Air Force Health Study work and provide advice, and corresponds frequently with the Air Force Health Study (AFHS) between meetings. The committee also reviews our annual reports to Congress.

**4. Question: Was a "medical crime" committed, and has the study ever violated medical ethics?**

**Answer:** The study has always adhered to the highest standards of medical ethics. In the Air Force, all human research/studies go through a stringent and rigorous review. The group responsible for study protocol review is the Brooks AFB Institutional Review Board (IRB) as well as the Ranch Hand Advisory Committee. The Scripps Clinic IRB approved the physical examination protocol. Furthermore, study participants are fully informed regarding all procedures, tests and examinations. They sign consent forms, receive a diagnostic outbriefing, receive copies of their medical examination forms and have full access to all their results.

**5. Question: Were reports about cancer and birth defects altered? Why was the report on reproductive health not published until 1998?**

**Answer:** No. All of our reports are complete and correct. There were differences of opinion between the principal investigators regarding the interpretation of findings. It was suspected in 1984 that dioxin might cause or promote certain cancers and inhibit or prevent others. So to some scientists, combining skin and systemic cancers into a single analysis did not make biological sense, a view shared by the oversight committee. Skin cancer was not an expected outcome of dioxin exposure. This, together with the lack of adjustment for sun exposure and skin reaction to the sun motivated a guarded interpretation. The numbers in the baseline report can be added to produce a combined analysis. However, such an analysis, while statistically more powerful, is, to some reviewers, more difficult to interpret because it includes etiologically dissimilar malignancies, as pointed out by the oversight committee.

The emphasis on skin cancer was a misinterpretation, as pointed out in an Aug. 25, 1987, letter to Senator Thomas Daschle. It was not true that most cancers were of the skin since a nonsignificant increase in internal cancers was also seen at baseline. The same analyses were repeated in subsequent reports and the significant increase in skin cancer was found in 1987, but not in 1985 and not in 1992. No significant increases in internal cancer were found at any follow-up examination. Subsequent analyses based on all available data through 1997 found no significant increase in skin cancer prevalence in the Ranch Hand group and no relation with dioxin body burden. Additionally, cancer mortality among Ranch Hand veterans is now less than expected.

In response to the issue about birth defects, because the birth defect data in the baseline report was not verified, the majority of the principal investigators determined that presenting a guarded interpretation was a more accurate assessment than using a stronger interpretation. Subsequently, a preliminary follow-up birth defect report reanalyzed the data after children with reported defects were verified by medical records but prior to the verification of all children. The oversight committee was critical of the preliminary follow-up report and recommended that it not be released and that the AFHS should verify all of its data before writing another report. The principal investigators agreed with the committee and began verifying the birth defect status of ALL children in 1984. This five-year effort represents the verification of over 10,000 reproductive

outcomes. The AFHS collaborated with CDC to write a reproductive outcome report based on verified data. Articles were published in a peer-reviewed journal; two were co-authored with CDC. The research found little or no relation between paternal dioxin body burden and birth defects or any of the other outcomes studied. However, small numbers of children with spina bifida fathered by veterans with high dioxin levels were found. The numbers were too small for statistical analysis (a total of 3 for Ranch Hand vs. 0 for Comparison veterans). The NAS interpreted this data as suggestive, and Congress responded by enacting compensation legislation for these children.

**6. Question: Why were hundreds of subjects omitted from the birth defects analysis?**

**Answer:** We analyzed the birth defect data in many different ways. Some analyses did not include all children, such as those including only those children born after the fathers' exposure. However, for each analysis conducted with children removed, corresponding analysis including all children were included in the same report.

**7. Question: Why does the Air Force regret saying that "results are reassuring," and why did Dr Michalek state that this is a "forbidden interpretation"?**

**Answer:** In 1984, the term "reassuring" was intended to convey the lack of obvious or statistically extreme adverse findings in the Ranch Hand group as has been predicted in the popular media. The AFHS has discouraged use of the term because, statistically, it can be interpreted to mean that dioxin is "safe". No epidemiological study can demonstrate safety, so the investigators have repeatedly expressed the view that "reassuring" is a forbidden interpretation and regret use of it in earlier interpretations.

**8. Question: Why was information on diabetes not released to the public for five years?**

**Answer:** The diabetes results were released to the public. Diabetes results have been released in various reports since 1991 including the annual reports to Congress. The AFHS released data showing a relation between dioxin and diabetes for the first time in our 1991 report summarizing dioxin analyses of the second follow-up examination results. In 1992, the diabetes findings were presented at an international dioxin conference and published in their proceedings. The NAS summarized our diabetes results in 1994, but dismissed the results as possibly due to inadequate adjustment for body fat. The AFHS continues to study the relation between dioxin and diabetes and anticipates a follow-up report in 2002.

**9. Question: Why was Dr. Albanese removed from the study?**

**Answer:** In late 1984, two of the original principal investigators had retired from active duty, and the study was progressing smoothly toward the first follow-up examination phase. Dr. Albanese's skills were required in the studies of microwave and laser

radiation. Dr. Joel Michalek had worked on the AFHS since 1979 and was fully prepared to assume Dr. Albanese's role in the program.

**10. Question: Weren't Dr. Albanese's allegations addressed in a 1988 congressional hearing?**

**Answer:** Yes. Dr. Albanese's personal allegations regarding management interference, birth defects, and cancer were raised and discussed during a 1988 hearing before the Committee on Veteran's Affairs, United States Senate. The committee of non-governmental experts in medicine, toxicology and statistics with some members nominated by veterans advocacy organizations concluded that the study was being properly conducted. Subsequently, legislation was passed to ensure there was no interference from any federal employee with communication between the scientists and the Ranch Hand Advisory Committee. This legislation also implemented Air Force desires to include veteran advocates on the advisory committee.

**11. Question: Why didn't the San Diego Union-Tribune article discuss the last 14/15 years of AFHS research?**

**Answer:** We do not know why the reporter did not include this information, although the Air Force did make it available to him. Criticism in the article ignored all study results since 1985 except the diabetes finding and concentrated on the baseline report period of 1982 to 1984.