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JOHN H. GIBBONS
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JOHN H. GIBBONS

Congress of the United States
OFFICE OF TECHNOLOGY ASSESSMENT
WASHINGTON, DC 20510-8025

September 25, 1990

The Honorable Douglas Applegate
Chairman
Subcommittee on Compensation, Pension and
Insurance
Committee on Veterans' Affairs
U.S. House of Representatives
Washington, D.C. 20515

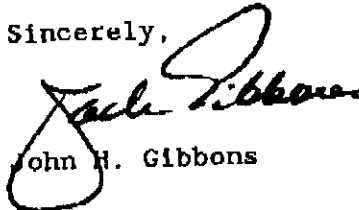
Dear Mr. Chairman:

I am writing in response to your letter of September 14, concerning the deliberations of the Department of Veterans Affairs Advisory Committee on Environmental Hazards. Senator Cranston recently asked us to review the same findings of that Committee, on non-Hodgkin's lymphoma and soft-tissue sarcoma. I enclose the memorandum that we sent Senator Cranston, which I believe is responsive to the questions you asked, as well. Our findings are summarized below.

As you know, at a meeting in November 1989, the Advisory Committee found no "statistical association," as defined by regulation, of NHL with exposure to dioxin-containing herbicides. At a meeting in May 1990, the Committee did find a "statistical association" of STS with exposure. In contrast, OTA's review of the detailed minutes of the meetings, supported by our prior review of many of the relevant studies, does not reveal a substantial difference in the quality of the evidence for an association with NHL and with STS, or any specific pieces of information that would explain the Committee's differing decisions on NHL and STS. Of course, all of these judgments are, to some extent, subjective, since there is no specific procedure, particularly not a quantitative one, that can be used to weigh the evidence.

I hope you find this analysis helpful. Please contact me if I may be of further assistance, or have your staff contact Hellen Gelband or Clyde Behney in the OTA Health Program (at 8-6590).

Sincerely,



John H. Gibbons

enclosure

OTA HEALTH PROGRAM**Staff Memorandum**

September 18, 1990

To: Jack Gibbons
From: Hellen Gelband, Health Program
Re: Review of VA Advisory Committee recommendations

As you requested, I have reviewed the recommendations made by the VA Advisory Committee on Environmental Hazards to the Secretary of Veterans Affairs concerning possible associations of non-Hodgkins lymphoma (NHL) and soft tissue sarcoma (STS) with exposure to Agent Orange. My review is based on reading the detailed minutes of the meetings at which the VA Advisory Committee formulated these recommendations, and my previous knowledge of the epidemiologic studies on which the recommendations are based.

The NHL Meeting

NHL was discussed at the November 2-3, 1989 meeting. At the beginning of the meeting, the Committee was instructed on the regulation that was to govern their assessment of the scientific literature. Mr. White from the Veterans Benefits Administration's Compensation and Pension Service explained that the Committee was to determine whether a "significant statistical association" existed between exposure to a herbicide containing dioxin and a given medical condition. According to the regulation, a significant statistical association exists when the relative weight of valid positive and valid negative studies permits the conclusion that it is "at

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least as likely as not" that the purported relationship between a particular type of exposure and a specific adverse health effect exists. The regulation also discusses criteria for judging whether a study is "valid."

The issue of validity, having to do with basic study design, the ways in which data are collected, potential biases, etc., is familiar to all experts in evaluating medical evidence. The Committee handled this professionally and competently, discussing each study put before them. They also had no problems in determining which studies were relevant to the question at hand. However, there is no specific procedure for considering the results of many different studies together and arriving at a conclusion as to where the weight of the evidence lies. The task becomes even more difficult when the endpoint is whether the association is "at least as likely as not" to exist, a term that does not lend itself to an objective definition. Any determination is bound to be somewhat subjective. The Committee discussed the issue of methods for arriving at a decision several times during both meetings, and considered various alternatives to assist in coming up with a final judgment, but did not adopt any formal procedure.

At the NHL meeting, the Committee reviewed 30 individual papers of relevance to the NHL question, characterizing 4 as valid and positive for an association of NHL; 12 as valid and negative; 10 as valid and inconclusive (mainly due to small sample sizes and consequent low power); and 4 as not valid because of severe defects in methodology or execution. Several others were dismissed as not germane to the subject. After the review of individual papers and the tally, the Committee further discussed the types of exposure in the studies, and how they might be differentiated, e.g., giving less weight to studies in which there was only the opportunity for exposure, and more to studies in which exposure was documented. They also discussed the "inconclusive" studies further to see if, as a group, they were more informative than they were separately.

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In the end, the Committee members stated their own conclusions about the existence of a "statistical association," as they understood it to be defined by the regulation. They concluded that, while they could not rule out such an association, the evidence they reviewed did not support a conclusion that such an association existed.

The STS Meeting

The meeting to review studies relating to STS, held on May 16 and 17, was conducted similarly to the NHL meeting. Before the review of individual studies began, however, Admiral Zumwalt, attending his first meeting as a Committee member, made a statement criticizing the previous work of the Committee and praising the work of the "Agent Orange Scientific Task Force," a group supported by the American Legion, the Vietnam Veterans of American, and the National Veterans Legal Services Project. Once again, after discussion of the individual papers, the idea of formalizing the process for coming to a conclusion was discussed. Some strong sentiments were expressed in favor of exploring such a process, but in the end, that was not done.

The tally of studies was: 8 considered valid and positive; 10 considered valid and negative; 27 considered valid and inconclusive; and 5 considered not valid. There was considerable discussion concerning the fact that most of the positive evidence came from studies in Scandinavia, and that similar studies elsewhere showed no such association. Eventually, the members of the Committee were polled, and the consensus was that a "statistical association" existed.

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Throughout the meeting, Admiral Zumwalt injected skepticism about studies done by researchers in industry and in the Federal Government. He cited testimony in court cases challenging some of the industrial studies, and claimed that the Federal Government exerted influence over the results of Government studies. This was contested by several members of the Committee. It is not clear to what extent Admiral Zumwalt's accusations influenced the deliberations of the Committee.

Consistency of the Recommendations

From reading the meeting minutes and from my knowledge of the studies discussed, I do not find a substantial difference in the quality of the evidence for an association with NHL and with STS. I cannot identify any specific pieces of information that would explain the Committee's differing decisions on NHL and STS, though the Scandinavian studies, which provide most of the positive findings, seemed to be influential. In my own subjective judgment, the evidence is quite similar, taking into account the levels of risk detected in the positive studies, the potential biases in the studies, the sources of exposure information, the types of exposure involved, and other factors.

The Committee has been given very difficult questions to answer. There may be no single right answer, because the standard of evidence required to decide that a "statistical association" exists, as defined by the regulation, cannot be defined precisely.