GEORGE L. CLAXTON

Lansing, MI

AUG 24 1988

August 17, 1988

Admiral Elmo Zumwalt (Ret)
1500 Wilson Blvd.
Arlington, Virginia 22209

Dear Admiral Zumwalt:

In January, 1986, the Vietnam Veterans of America asked myself and two other Vietnam veterans to conduct a literature search on phenoxy acid herbicides. I have compiled reports starting in 1986, and continuing through today. These reports cover approximately 90% of the literature on phenoxy acid herbicides, and I would like to share them with you.

Enclosed are two of my reports (Nos. 9 and 31). If you find them relevant and informative, I will send you the other thirty. When you read them, remember that the first paragraph is the title, the second paragraph is the author, and the other paragraphs are quotations and my analysis. In order to eliminate any bias, please disregard my analysis and only read the quoted parts.

When you read these two reports, I hope you will see that there is a wealth of evidence showing a strong association between phenoxy acid herbicides and two cancers in humans (soft-tissue sarcoma and non-hodgkin's lymphoma).

I am hoping to hear from you as to receiving my other reports. Also, I extend my condolences for the loss of your son. We must not let him die in vain. The right to service connected disability for agent orange related cancers is a first priority with myself.

Very sincerely,

George Claxton

George Claxton

GEORGE L. CLAXTON

Lansing, MI

September 12, 1986

AGENT ORANGE REPORT IX

1. "Cancer and Clinical Epidemiology"
In the book "Herbicides in War: The Long Term Ecological and Human Consquences"; Edited by Arthur H. Westing; Taylor and Francis Publishing; 1984; Chapter 6

These are four subchapters authored by Vietnamese and American scientists. These are reports that were presented at the International Symposium on Herbicides and Defoliants in War, 1983.

The Vietnamese scientists reported that morbidity studies of the population in the South experienced the same physical problems as animals in dioxin tests. This was particularly true for the people who were located in Tay ninh Province. Chronic nervous problems and liver cancer were ascertained by case-contol studies (Dr. Trinh and Dr. Van). It is interesting to note that Vietnam veterans in Tay Ninh Province experienced the same problems.

Dr. Samuel Epstein and Dr. James Dwyer review the international literature on dioxin. These U.S. scientists confirm the fact that 2,4-D is neurotoxic and 2,4,5-T is not. 2,3,7,8-TCDD is is considered by them and found to cause a variety of illness,including cancer. No VA review.

2. "Agricultural Herbicide Use and Risk of Lymphoma and Soft Tissue Sarcoma"
Shelia K Hoar, etal., Journal of the American Medical Association, Volume 256 (number 9), page 1141-1147, 1986

Dr. Hoar of the National Cancer Institute was kind enough to forward this study to me. She also gave me some relevant studies on farmers in the midwest.

This study was released in JAMA on September 5, 1986. It found that usage of 2,4-D was specifically associated with Non-Hodgekins Lymphoma. Neither soft tissue sarcoma or Hodgekins disease was found to be associated with 2,4-D. This is quite interesting since the Swedish studies did find an association with phenoxyacetic herbicides. However, the Swedish studies concerned mainly 2,4,5-T.

The following is stated verbatim"

> "Men exposed to herbicides (2,4-D) more than 20 days per year had a six fold increased risk of non-hodgekins lymphoma"

This was a case-contol study by the National Cancer Institute and the University of Kansas. It was concerned with farmers in Kansas and the authors belive that it shows that phenoxy acetic herbicides cause Non-hodgekins lymphoma. This study carries a tremendous amount of weight and could lead to an emergency suspension of 2,4-D pursuant to FIFRA (Federal Insecticide, Fungicide, and Rodenticide

Act). In a critique (same volume of JAMA), Dr. Colton of the Boston University School of Public Health states that this study has alot of statistical precision. Also, that "the interview methodology and the climate of the Hoar study make information bias a much more unlikely explanation". Dr. Colton considers this study to be sound from an epidemiological view. Dr. Colton went on to point out other strengths of this study. Particulary the fact that exposure to other chemicals was ruled out. Dr. Colton pointed out that the Ranch Hand study of U.S. Air Force personnel in Vietnam carried little weight because of the small cohort involved. Wheras the cohort in this study was quite large.

The implication of this study to Vietnam veterans should be obvious. Although soft tissue sarcoma and hodgekins disease were not implicated, alot of Vietnam veterans have died from non-hodgekins lymphoma. The implication for farmers is clear and should send a clear signal that the use of 2,4-D should be banned. The midwest studies following will show that the mortality of farmers from phenoxyacetic herbicides has been known for some time. No VA review of this study.

3. "Soft Tissue Sarcoma and Non-Hodgkins Lymphoma in Relation to Phenoxy Herbicide and Chlorinated Phenol Exposure in Western Washington" James S. Woods, et al., To be published in the Journal of the National Cancer Institute. This was presented at the 1986 Annual Meeting of the Society for Epidemiologic Research, Pittsburgh, PA, June, 1986.

Since phenoxyacetic herbicides have been used extensively in the Pacific Northwest over the past 40 years, this study was commenced. This was a "population-based case-control study conducted to evaluate the relationship between occupational exposure of men aged 20 to 79 to phenoxy herbicides and chlorophenols and the risks of developing STS and NHL in western Washingtom".

"No increasing risk of either cancer was associated with duration or intensity of chemical exposure. However, estimated risks of STS were elevated among lumber graders, and log lumber inspectors with chlorinated phenol exposure. Estimated risks for NHL were elevated among those who had been farmers, forestry applicators, and for those potentially exposed to phenoxy herbicides for 15 years or more during the period between birth and 15 years prior to cancer diagnosis".

This study does not really confirm the Swedish studies, however due to inconsitancies it does not refute them either. It is quite interesting to note that farmers, once again, have a significantly higher rate of non-hodgkins lymphoma. More interesting is the fact that some lumber persons have a significantly higher rate of soft tissue sarcoma. This may be because lumber persons used mostly 2,4,5-T and farmers used mostly 2,4-D. The following studies will confirm the 2,4-D association. This poses the serious question does 2,4,5-T cause STS, and does 2,4-D cause NHL? The Swedish studies, which showed STS, were associated with alot of 2,4,5-T. Vietnam veterans wre exposed to both 2,4-D and 2,4,5-T with its dioxin contaminant. The Denmark study showed STS with 2,4-D exposure but there was some 2,4,5-T. It can be stated, almost emphatically that farmers are acquiring NHL from 2,4-D, and I believe that any large cohort of Vietnam veterans would show a higher rate of NHL and STS. No VA review.

4. "Cancer Among Farmers"
Aaron Blair, et al., Scandanavian Journal of Workers Environmental Health, Volume 11, page 397-407, 1985

This is an extensive report of findings from epidemiologic studies of farmers; it includes statistics on mortality and morbidity from industrialized countries around the world.

The report states that "risks among farmers are not exceptionally high for most cancers". However, some cancers are high and the rate of leukemia has received the most attention. The following is specifically stated:

X "The risk of leukemia was the greatest among farmers born after 1900 and/or dying before 65 years of age, a phenomenon suggesting that more recent agricultural practices may be associated with an increase in risk"

X "Risk of leukemia was associated with herbicide use in Iowa" (Burmeister et al., Am J Epid., 115, 1982)

X "Results from case-referent studies in Sweden are consistant with the association between herbicide use and non-hodgkins lymphoma in Iowa and Wisconsin"

One of the most consistant variable that is associated with the increased risk of leukemia in farmers is herbicide use. The herbicide referred to is mainly 2,4-D and this concerns non-hodgekins lymphoma in Wisconsin. The authors make it clear that pesticides are not confirmed as the cause but indicate the result is likely. Further studies should involve patch tests for skin exposure and biological monitoring of levels of suspect agents or their metabolits in body fluids or tissues. This has not been done by the VA on Vietnam veterans. No VA review.

5. "Farming and Mortality from Non-Hodgkins Lymphoma: A Case Control Study"
Kenneth P. Cantor; International Journal of Cancer, Volume 29, page 239-247, 1982

This is a case-control study of non-hodgkins lymphoma from the State of Wisconsin. "Major findings were of elevated risk among younger farmers for reticulum-cell sarcoma in counties high in summary measures of general agricultural activity, of small grain acreage and acres treated with insecticides, and of wheat acreage"

"Statistically significant odds ratio for reticulum cell sarcoma in the younger farmers are observed in counties high in per capita acres treated with insecticides".

X "Significant elevations of odds ratio for reticulum-cell sarcoma were observed among farmers aged less than 65 years in counties high, respectively, in insecticide use, herbicide use, acreage of small grains".

X "Chlorinated phenoxy acids are widely used in the United States as herbicides in corn and wheat production (U.S. Department of Ag-

riculture, 1968). A Swedish study has reported more frequent exposure to phenoxy acids among males with histiocytic lymphoma (RCS) than among matched controls (Hardell et al, 1981). Our results are generally consistant with these findings."

This is not conclusive evidence that RCS is caused by 2,4-D but the evidence is becoming stronger. No VA review.

6. "Leukemia Among Nebraska Farmers: A Death Certificate Study" Aaron Blair et al., American Journal of Epidemiology, Volume 110, (3), page 264-273, 1979

This is a death rate study of farmers from Nebraska. The risk of leukemia for farmers was greatest for the ones born after 1900 and dying before age 66. This factor is crucial because it suggests that agricultural practices may be involved (modern agricultural chemicals came into use).

"An excess risk for acute unspecified leukemia occurred among farmers from counties with a high corn acreage (OR=2.27), with greater herbicide usage (OR=1.75)." The herbicide that is normally used by farmers is 2,4-D. This is particularly true with corn acreage. I want to point out that the National Cancer Institute sent me these studies because they were relevant to 2,4-D.

"Although several agricultural factors were associated with the risk of leukemia, corn production was the most consistant". I have taken alot of quotes from these studies so that there will be no possibility of misquotation.

"The high risk among farmers from heavy corn, hog, and chicken producing and herbicide using counties applied primarily to the acute unspecified type." These factors were all broken down individually. The herbicide is 2,4-D almost all of the time and the animals would account for a cancer virus. But the chemical factor would be herbicide. NO VA review

7. "Lung Cancer and Other Causes of Death Among Licensed Pesticide Applicators"
Aaron Blair et al.; Journal of the National Cancer Institute, Volume 71 (Number 1), page 31-37, 1983

This is a mortality study of pesticide applicators in Florida. All applicators have to be licensed in Florida. The risk of lung cancer increased with the number of years licensed. The workers were broken down into catagories. Most catagories were too small to be mutually exclusive, however, the catagory of "Lawn and Ornamental Pests" was mutually exclusive. Obviously, Florida would have alot of licensed applicators for lawn and ornamental pests. The catagory of "Lawn and Ornamental Pests" had the types of chemicals listed. These were "2,4-D, 2,4,5-T, paraquat, Silvex, Captan, Folpet, Pentachlorophenol, and phenylmercuric acetate". I would like to point out that 2,4-D, 2,4,5-T, Silvex, and pentachlorophenol are all phenoxy acetic compounds, and all contain one or more isomers of dioxin. Unquestionably, 2,4-D, 2,4,5-T,

and Silvex(2,4,5-TP) were used the most. They are all herbicides that were the basis of "Agent Orange".

"A slight deficit of lung cancer occurred among persons employed by firms licensed only to treat lawn and ornamental pests. This group showed a slight excess mortality from colon cancer". However, even in the lawn and ornamental catagory, the number of deaths due to lung cancer was 26 compared to 19.0 expected.

The authors were carefull to rule out bias in this study. Since the risk of lung cancer might be higher in the coastal regions of Florida due to World War II asbestos exposure, this was taken into account and the following was stated:

> "The lung cancer risks of pesticide applicators in our study, however, remained high when Florida mortality rates were used for comparison. Furthermore, the lung cancer cases among pesticide workers did not cluster along the coast, but were distributed across the state with concentrations in metropolitan areas".

Smoking was also considered and ruled out as a factor. Although age was considered a factor, intensity of exposure appeared to be a much more important factor. No VA review.

8. "Leukemia and Farm Practices in Iowa"
Leon F. Burmeister, et al.; American Journal of Epidemiology, Volume 115 (5), page 720-728, 1982

This study is a "death certificate analysis of 1675 Iowans over age 30 years who died of leukemia in 1964-1978". All cases were matched with two controls. "For those born after 1900, odds ratios for farmers were increased in counties with the greatest numbers of egg-laying chickens and the largest number of acres treated with herbicides. The types of leukemia causing mortality in Iowa farmers were chronic lymphatic and unspecified lymphatic".

"Of particular concern are the upper midwestern states because of the importance of farming in these states and because of the identification of high-rate leukemia mortality counties in this area" (Mason, et al. DHEW publication (NIH) 75-780).

"Chronic lymphatic leukemia is elevated in both the high and low production counties for the five county characteristics investigated. The strongest association, both in magnitude of the odds ratios and differences in the high and low producing counties, are with soybeans per acre and acres treated with herbicides".

The association should be immeadiately clear. The herbicide would be 2,4-D, and this is consistant with the Nebraska study. It is basically consistant with the Florida, Kansas, and the overall study by Blair. No VA review.

GEORGE L. CLAXTON

Lansing, MI

July 23, 1988

AGENT ORANGE REPORT XXXI

1. "A Case-Control Study of Non-Hodgkin's Lymphoma and Agricultural Factors in Eastern Nebraska"

   S. Hoar Zahm (National cancer Institute) et al., The abstract presented at the meeting of the Society For Epidemiologic Research; held at Vancouver, British Columbia on June 15-17, 1988.

   This is a follow-up study to the studies that were included in Agent Orange Report IX. These studies were all studies relating certain cancers to farming. With the inclusion of Dr. Hoar's study from Kansas showing an association between 2,4-D and non-hodgkin's lymphoma. The authors for this study are the same as in report IX; Drs Hoar, Cantor and Blair.

   I do not intend to interpret this abstract because I do not want any bias. Therefore, politicians can read it and come to their own conclusions.

   This abstract is on page 2; and on page three is a letter from Dr. Hoar indicating the heavy public relations campaign that the chemical industr has waged against her studies and Dr. hardell's. Why does the chemical industry want to play down the results of studies that show a relationship between phenoxy herbicides and cancer? The answer is easy--MONEY.

2. "The Association Between Soft-Tissue Sarcomas and Exposure to Phenoxyacetic Acids: A New Case-Referent Study"

   Lennart Hardell MD, PhD and Mikael Eriksson, MD.; to be published in the Journal "Cancer". 1988

   I originally reported on this in Agent Orange Report 28 but am now printing the entire abstract so that the politicians can read it. I will not give any interpretation for fear of bias. This study is a follow-up to the earlier ones. The chemical industry has influenced the Associated Press to not give Dr. Hardell's study credability. But on page 3 you can see that Dr. Hoar does not feel that the chemical industry is correct. The time has come when reputable scientists should stand up and disagree with the chemical industry instead of letting the industry discredit their results.

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SER, Vancouver, 6/15-17/8

A Case-Control Study of Non-Hodgkin's Lymphoma and Agricultural Factors in Eastern Nebraska. S. Hoar Zahm*(National Cancer Institute, Bethesda, MD 20892), D. D. Weisenburger, P. A. Babbitt, R. C. Saal, K. P. Cantor, A. Blair

A recent study conducted in Kansas reported a six-fold excess risk of non-Hodgkin's lymphoma (NHL) among farmers exposed to agricultural herbicides 20 or more days per year. To further investigate the association between NHL and agricultural factors, a population-based case-control study was conducted in Eastern Nebraska. Telephone interviews were conducted with 385 (201 men, 184 women) histologically confirmed NHL cases and 1432 (725 men, 707 women) controls. Among men, use of the herbicide 2,4-D was associated with a non-significant 50% increased risk of NHL (OR=1.5; 95% CI= 0.9,2.4). Exposure to 2,4-D more than 20 days/year increased risk 3-fold (OR=3.3; 95% CI=0.5,22.1). Use of the herbicide 2,4,5-T had an OR of 1.5 (95% CI=0.7,3.2). Risk among atrazine users (OR=1.4; 95% CI=0.8, 2.2) increased with duration with ORS of 0.9, 0.8, 2.0, and 2.0 for use of 1-5,6-15,16-20,and 21+ years, respectively. Several classes of insecticides were associated with increased risk: chlorinated hydrocarbons (OR=1.4; 95% CI= 0.8,2.3), carbamates (OR=1.8; 95% CI= 1.0,3.2), and organophosphates (OR=1.9; 95% CI=1.1,3.1). Specific insecticides associated with significant excess NHL included chlordane (OR=2.1), diazinon (OR=2.0), dyfonate (OR=2.4), and malathion (OR=2.2). Risk rose with increasing duration of use of lindane and sevin. Multiple exposures will be evaluated.

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DEPARTMENT OF HEALTH & HUMAN SERVICES

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July 7, 1988

George L. Claxton

Lansing MI

Dear Mr. Claxton:

Thank you for your letter and the copy of Lennart Hardell's latest study on soft-tissue sarcoma. I appreciate it. I share your frustration with the inaccurate criticisms of Dr. Hardell's work and our Kansas study. The industry has waged a heavy public relations campaign citing possible limitations of the studies. They fail to mention that most of the limitations mean the studies probably underestimate risk, not create spurious risks.

We recently presented some preliminary results from the Nebraska study at a scientific conference. I have enclosed the abstract (although it is not very informative, it was prepared months ago). I will keep you on our mailing list for the final manuscript. However, there will be some delay in its preparation since I will out a few months on maternity leave. The results appear to be consistent with the Kansas study, although the risks are not quite as large.

Thank you for your interest.

Sincerely,

Shelia Hoar Zahm

Shelia Hoar Zahm, Sc.D.
Occupational Studies Section

4

Cancer, accepted

The association between soft-tissue sarcomas and exposure to phenoxyacetic acids: A new case-referent study.

Lennart Hardell MD, PhD

Mikael Eriksson MD

From the Department of Oncology, University Hospital, S-901 85 Umea, Sweden.

Supported by grants from the Swedish Work Environment Fund.

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The authors thank Mrs Gunnel Sehlstedt for performing the interviews and Mats Fredriksson, B.Sc., Department of Occupational Medicine, University Hospital, Linkoping for assistance with the statistical analysis.

Abstract

A case-referent study on soft-tissue sarcomas (STS) was conducted, to see if previous findings regarding an association between exposure to phenoxyacetic acids or chlorophenols and this tumour type could be reproduced. Fifty-five male STS patients were thereby compared with 220 living and 110 deceased population-based referents. Furthermore, another referent group consisting of 190 patients with another type of malignant disease was used, in order to evaluate any influence of recall bias on the results. To obtain information about exposure to the studie chemicals, as well as about any other exposures that might be of interest, questionnaires were used, and if necessary these were completed over the phone by an interviewer who had no information regarding case/referent status. All analysis and interpretation of expsoure data were done in a blinded manner. Exposure to phenoxyacetic acids gave a roughly 3-fold increased risk for STS, thereby confirming previous fidnings, whereas exposure to chlorophenols was not associated with STS in this study.