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Chapter 3. Analysis of Serum Dioxin Levels of Veterans and Research on the Appropriateness of the Defoliant Exposure Index

1. Report Summary

A. Introduction

The methods for assessing veterans' exposure to defoliants consist of exposure evaluation between those who were exposed and those who were not, qualitative exposure evaluation, and quantitative evaluation through reconstructing past exposure. The report attempted to quantitatively infer the degree of exposure and examine the appropriateness of the quantitative exposure index and self-reported exposure index by using bioindices.

Since the half-life of TCDD within the body varies between individuals, establishing a defoliant exposure index using biomarkers a long time after initial exposure would not be more useful than using a qualitative exposure assessment. In this regard, the self-reported exposure index is not appropriate.

There are three types of exposure indices created by reconstructing past exposure.

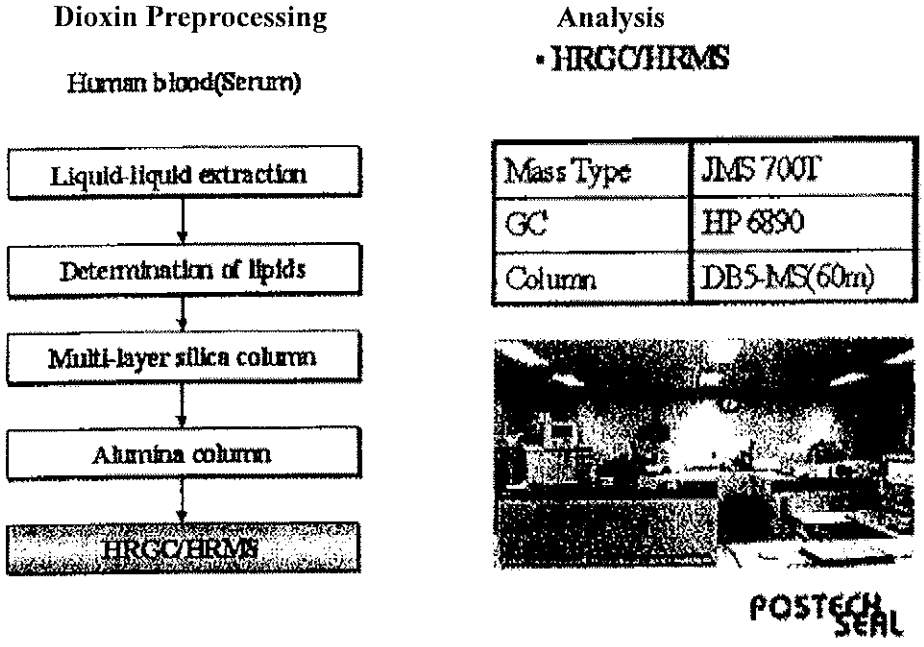
The first index was developed in the Second Epidemiological Study on Damages Caused by Defoliants in which individual exposure levels of defoliants were deduced using data on military units and period of participation during the Vietnam War, data on the period of participation and posts of Korean Vietnam War veterans, and data on the amount of defoliants sprayed in four areas of Vietnam classified by the U.S. Army (Exposure amount: 0 – non exposed group, and classified 1/3 into low, medium, and high exposure groups respectively).

The second index was developed in the Third Epidemiological Study on Damages Caused by Defoliants by using the military records of Korean Armed Forces and the Exposure Opportunity Model E4 developed by Professor [redacted] team in the United States. The Exposure Opportunity Model E4 was used to assess the amount of exposure to defoliants including dioxin for each unit from the time of deployment to Vietnam to the time of withdrawal. E4 exposure amounts of individual veterans were calculated by determining the division (battalion) and period of participation for each veteran. The common log of E4 was calculated to yield Le4 values. E4 values under 4 were classified as the low exposure group and those greater than E4 as the high exposure group.

The third index which is composed of exposure indices of participating units consisting of 156,657 veterans is also indicated by E4, the amount of exposure to defoliants of individual veterans. If the values of Le4, the log of E4, was equal to or less than 4, the subjects were categorized as the low exposure group, and if the value was equal to or greater than 4 the subjects were categorized as the high exposure group.

B. Methods

Of the veterans who submitted to medical examinations, blood was collected from 105 veterans who had consented to blood transfusions. The blood samples were submitted to Pohang University of Science and Technology for analysis using high resolution gas chromatography/mass spectrometer. The serum dioxin levels were converted and expressed as toxic equivalency (TEQs) using the international-toxic equivalency factor (I-TEFs). The values of TEQs were computed by multiplying the concentration of each homolog with TEFs and calculating the sum of these values. The concentration of dioxin in blood samples were adjusted to take into account levels of serum fat content.



The method for analyzing serum dioxin levels in blood are as shown in the figure above.

C. Results

With the exception of two blood samples which contained an insufficient amount of blood for analysis, serum dioxin levels of 103 blood samples were measured.

When reconstructing past exposure of the groups at the battalion level, the high exposure group showed a higher concentration of dioxin than the low exposure group. In

the classification up to the division level, the low exposure group's concentration of dioxin was slightly higher than that of the high exposure group.

In the self-reported exposure index I, the level of dioxin concentration was in the order of the high exposure group, the medium exposure group, the low exposure group, and the non-exposure group. In exposure index II (exposure level as compared to other people), the level of dioxin concentration was in the order of the low exposure group, the medium exposure group, and the high exposure group. The level of 2,3,7,8-TCDD was low at 0.143 pg I-TEQ/g lipid, and in the case of the index reconstructing past exposure, this level was found only in three members of the low exposure group. The concentration of dioxin in the blood of Seoul citizens was extraordinarily higher than that of the War veterans. In the analysis of the correlation between the concentration of dioxin in blood and the exposure index, a notable correlation was not observed between the index reconstructing past exposure (battalion, division level), the second year index reconstructing past exposure, and self-reported exposure index 1, 2. In the analysis of the correlation among the defoliant exposure indices, the correlation among the index reconstructing past exposure was very high.

D. Discussion and Conclusion

The TCDD concentration in the blood of War veterans was very low (0.143 pg). The TCDD concentration of 100 among the total 103 veterans was detected below the analysis critical point, and other dioxin concentrations in the blood were also negligible. Currently, it can be inferred that the dioxin concentration in the blood of Korean Vietnam War veterans has reached the point of background level.

The compilation of exposure indices using biomarkers seems to be limited in validity because most of the TCDD is seemingly eliminated from the body. Furthermore, the self-reported exposure index also seems to have limitations because it is not correlated with other indices. Currently, the index reconstructed from past exposure based on the Stellman defoliant exposure index is the most appropriate method.

2. Report Evaluation

A. Introduction

Due to the fact that many sections of Chapter 2 are duplicative, these sections require summarization.

B. Methods

1) Due to the insufficiency of the 2,3,7,8-TCDD measurement quantity, the study was undertaken without offering concrete evidence for the validity of the index reconstructed from past exposure. As a result, the problems regarding the collection, storage, and analysis of samples need to be reexamined, and it is necessary to reconsider whether 105 blood samples are representative of the entire exposed group.

2) The study classified groups into low, medium, and high risk groups and attempted to determine the validity of such classifications by measuring the quantity and correlation of dioxin amongst the groups. Moreover, the accuracy of the research is questioned because it compares the concentration of TCDD of Vietnam War veterans with that of Seoul citizens, measured under different conditions. Therefore, a comparison using an appropriate control group (i.e., soldiers who did not participate in the Vietnam War during the same time period) is necessary.

3) The study classified the subjects into low exposure group and high exposure group based on Le4, the value logged by an exposure quantity, developed by the Stellman study. However, in reality, because the Stellman study did not present the standards for selecting the Le4 value, the standard for selecting this datum value should be revealed. Moreover, if a different value (1-2) is selected as a standard, these study results should be compared with the results obtained from a study using a different standard value. Furthermore, instead of classifying the Le4 value ranging from 0 to 0.1 as the low exposure group, this group should be subdivided into two groups, a low exposure group and non-exposed group. This part is also described in Chapter 2: "Development of Indices Measuring Exposure to Defoliants."

C. Results

When comparing battalion level unit information with brigade/division unit information, the quality of information for the battalion/company is better than for the brigade because more detailed information is requested from this level. This can be supported by the fact that 1) "when risk of disease was analyzed using the exposure index obtained by using unit information of the brigade/division level, not unit information of the battalion level, diseases that were statistically significant were less frequent" (p.246) and 2)

in comparison to the index reconstructed from past exposure of each battalion level, the correlation between the exposure index of the brigade/company and the concentration of dioxin in the blood was relatively insignificant (p. 61). Therefore, applying the Le4 of each division may be problematic. Chapter 5-Investigation of Deaths Related to Exposure to Defoliants (study subjects: 153,899 persons) and Chapter 6-Investigation of Cancer Development (study subjects: 153,463 persons) appear to have used information from the battalion/company level, and the results appear to reveal that the low exposure group had a higher death and cancer development rate than the high exposure group. We believe that the Le4 value obtained from information of the division/ brigade level is problematic. Thus, it is necessary to re-analyze the results of the studies mentioned in Chapter 5 and 6 using data from the battalion/company level.

D. Discussion and Conclusion

First of all, the questions in the two self-reported surveys are unclear, and risk groups are divided based on answers to only six simple questions. Furthermore, there is no mention of what criteria was used to classify questions and thus the results of the analysis appear to lack value and connection to other data, which altogether generate an inappropriate exposure index. It is thus necessary that more detailed and appropriate questions are devised in order to categorize the various risk groups.

3. General Opinion

A. Language needs to be revised for consistency. "Dioxin" should be referred to as "dioxin congeners" whereas "2,3,7,8-TCDD" should be referred to consistently as "2,3,7,8-TCDD" or "TCDD" in order to avoid confusion. "TCDD" should not be referred to as "dioxin" as in page 60. Furthermore, "healthy laborer effect" should be corrected to "healthy soldier effect." In addition, some parts of the report state that the Le4 value was obtained by taking the log of the sum of one and the E4 exposure amount while other parts explain that it was obtained by simply taking the log of E4 (p. 48). Also, while it is stated in one part of the report that exposure groups were categorized according to their Le4 value-low exposure group if Le4 value is equal to or less than 4 and high exposure group if Le4 is equal to or greater than 4, all Le4 values less than 4 should be classified as the low exposure group. In the explanation of Table 3-5 (p. 55), the word "average" is used with the word "overall" in some parts, or the other word e "each" in other parts. Clearly, this causes confusion and should be corrected. The total number of subjects examined for presence of dioxin congeners in their body should be uniform throughout the report, i.e. 103 persons (p. 65).

B. The report's discussion on the exposure indices is illogical. While in one part of the report, it is argued that Stellman's index is appropriate whereas the self-reported index is not, this further confuses the reader by discussing dioxin as though it has no connection to dioxin concentrations. In other parts of the report, the authors state that they

had no choice but to use Stellman's index because neither the self-reported exposure index nor dioxin concentrations were appropriate. The latter argument simply appears to be justification for a weakness of the report.

C. Since multiple cycles of the half life of dioxin (9-12 years) have passed, it is important that we select an appropriate group of subjects for comparison and be able to accurately measure even minute amounts of dioxin to determine exposure to defoliants by tracing dioxin in the blood. If appropriate comparison and risk groups are selected, an analysis of study results based on subjects' diseases and the rate at which these diseases may develop, as well as information on diseases already known to be related to exposure to dioxin, would be possible. In addition, since dioxin itself can be exposed not only through defoliants but also as an ingredient in substances that pollute the environment, the group of subjects for comparison should consist of soldiers who did not participate in the Vietnam War of similar age and physical characteristics as the veterans.

D. Even if multiple cycles of the half life of dioxin (9~12 years) have passed, it is difficult to understand why the TCDD concentration of 100 subjects out of 103 was insufficient for analysis. It is advised that the report review these results and contact other institutions to reexamine the subjects' blood content or that of other veterans.

E. Rather than classifying groups with an Le4 value ranging from 0 to less than 0.1, it is necessary to subdivide this group further into non-exposed group (or a group with extremely small amounts of exposure), and low exposure group. We believe that this would eliminate bias which may result from the differences in rank, occupational specialty, and responsibility between a group with a Le4 ranging from 0 to less than 0.1 and other groups. Moreover, such a detailed classification would be more appropriate for observing the dose-response effect without a group for comparison.

Chapter 4. Survey of Veterans

1. Report Summary

A. Introduction

1) The First Epidemiological Study on Defoliant Damages was published in 1996, and the Second Epidemiological Study on Defoliant Damages was published in 2001. These studies are certainly valuable in the sense that no previous research studying the relationship between veterans and exposure to defoliants exists in Korea. However, the First Study showed weaknesses in its assessment of exposure levels and bias in selecting subjects. The Second Study is also flawed because it failed to explain the confounding variables, and because there were limitations to accurately measure individual exposure levels in developing the index reconstructed from past exposure. Therefore, the Third Epidemiological Study on Defoliants acknowledged the results of the First and Second Epidemiological Studies on Defoliant Damages while taking into account their weaknesses as well.

2) In the survey, we attempted to investigate the confounding variables which affect death, cancer development, or other diseases and included tables of information on 54 diseases to understand disease development in veterans. As regards to the diseases which appear to be possibly related to exposure to defoliants according to this survey and the Second Epidemiological Study on Defoliant Damages, we plan to confirm the causal relationship between defoliant exposure and development of diseases through additional studies. Moreover, we tried to gather detailed data on the units to which each veteran belonged, information that is crucial to developing the index reconstructed from past exposure.

B. Methods

1) Subjects and Study Methods

A) In order to secure study subjects, a list of 187,897 veterans was obtained and information on their current addresses and residency. Excluding veterans who have passed away, or those currently residing abroad, 164,208 veterans were selected as the final subjects to whom a survey was sent on two occasions.

B) The survey did not include questions only related to defoliant exposure level and disease history, but also those regarding smoking, drinking, obesity, agrichemical use, and socio-economic level, factors which may influence disease development. The survey also included questions related to mental health of veterans such as subjective health levels (SF-12), depression (GDS), social support (MOSSS), and hostility (MMPI HO Scale).

2) Exposure Evaluation

Exposure was assessed from self-reported exposure evaluations obtained from surveys and information on exposure evaluation based on the reconstruction of past exposure using military records. Self-reported exposure indices were obtained by using survey results. Through the use of these results, study subjects were classified into high exposure, medium exposure, low exposure groups, and non-exposed groups.

3) Analysis Methods

The distribution of the diseases of each exposure group was studied using the X^2 test which used logistic regression analysis to control confounding variables including age, whether or not one smoked or drank, level of exercise, income level, education level, agrichemical use, and BMI (Body Mass Index).

C. Results

1) Response rate

The total number of respondents was 114,562 persons, amounting to a response rate of 70%.

2) Disease Examination

The study first examined 54 minor classification groups of diseases which were then categorized into 7 major classification groups. Of these 7 groups, circulatory diseases (61,221 persons) constituted 53.4%, other diseases (51,401 persons) comprised 44.9%, and digestive diseases (50,784 persons) accounted for 44.3%. Of the 54 diseases that were studied, hypertension was the most common with 43,895 or (38.3%) developing hypertension.

3) General Characteristics

The average age of subjects was 60.8±3.5 years, 40,314 persons (36.4%) were smokers, and 93629 persons (87.4%) were drinkers. The average BMI was 23.7±3.3, and the range between 23 and 24.9 comprised the highest percentage at 30.8%. With regards to education level, high school graduates accounted for the greatest percentage with 32.2%. In terms of income, 1,000,000 to 1,490,000 won comprised the greatest percentage (24.9%). The average age of the high exposure group was higher than that of the low exposure group. There existed significant differences in whether or not one smoke or drank, education level, income level, and agrichemicals use among subjects in the different exposure groups. However, the difference regarding whether or not one exercised was negligible.

4) Measurement Scale

The study used methods to measure mental health conditions. GDS, or Depression indices, were higher as the exposure levels based on the self-reported exposure index increased. There were also significant differences in GDS value among the exposure groups with regards to the exposure index reconstructed from past exposure.

5) Self-reported Exposure Evaluation

A) 37,349 people (33.4%) were in the non-exposed group, 15,093 people (13.5%) in the low exposure group, 40,935 people (35.6%) in the medium exposure group, and 18,496 people (16.5%) in the high exposure group.

B) Of the diseases within the 7 major classification groups, the exposed groups were at a higher risk of developing diseases than the non-exposed group.

C) With regards to the 54 diseases classified into minor groups, the medium and high exposure groups had a higher risk of developing diseases within the minor classification of diseases than non-exposed groups such as gastric cancer, liver cancer, esophagus cancer, gall cancer, pancreas cancer, brain cancer, urinary cancer, Hodgkin lymphoma, non-Hodgkin lymphoma, cerebral hemorrhage, and multiple sclerosis. Exposed groups had a statistically significant higher risk of developing diseases than the non-exposed group with regards to the 7 minor classification groups of diseases.

6) Exposure Evaluation through Reconstruction of Past Exposure

A) The low exposure group was 1.04 times more likely to develop respiratory diseases than the medium exposure group with regards to the 7 diseases categorized into the major classification group. The medium and high exposure groups were 1.04 times and 1.06 times more likely to develop other diseases respectively. The high exposure group demonstrated a noticeably higher risk of developing circulatory diseases. The medium exposure group showed a noticeably higher risk of developing neuro-muscular diseases than the low exposure group.

B) The medium and high exposure groups were 1.05 times more likely to develop skin diseases than the low exposure group with regards to the 7 diseases classified into minor groups. The medium exposure group demonstrated a statistically significant higher risk of developing diseases than the low exposure group with regards to multiple myeloma, peripheral vascular disease, chronic bronchitis, peripheral neuropathy, and hyperlipidemia. The medium exposure group had a significantly higher risk of developing diseases such as cerebral infarction, gallstone multiple paralysis, and multiple sclerosis than the low exposure group. The medium exposure group also demonstrated a higher risk of

developing other respiratory diseases than the low exposure group. The high exposure group demonstrated a statistically significant higher risk of developing respiratory diseases, circulatory diseases, and other diseases than the low exposure group.

C) In regards to the list of diseases, the exposed groups had a significantly higher risk of developing cerebral infarction, peripheral vascular disease, other respiratory diseases, peripheral neuropathy, and multiple sclerosis than the non-exposed group. The exposed groups showed a noticeably higher risk of developing hyperlipidemia than the non-exposed group.

7) Analysis of Correlation among Exposure Indices

Since the coefficient of correlation between the index reconstructed from past exposure and the self-reported exposure index was 0.99, this indicated a low correlation between the two indices.

8) National Policies Related to Defoliants

A) In response to the question, "Are you satisfied with the national compensation policy?" 31.1% responded "Not at all" whereas 33% answered "No." The responses demonstrated that most veterans were not satisfied with national policies.

B) In response to the question, "Should we work on further increasing awareness of defoliant related policies?" more than 80% of respondents answered "Yes" (32.4% responded "absolutely" and 54.7% responded "yes").

C) In response to the question, "Should all suspected aftereffects be simply be considered aftereffects?" almost all respondents answered "Yes" (31.8% responded "absolutely" and 51.2% responded "yes").

D) In response to the question, "Should compensation for aftereffects and suspected aftereffects be standard irrespective of degree of disability?" the majority of respondents answered "Yes." In response to the question, "Should all large inpatient hospitals be required to judge the severity of suspected aftereffects?" the majority of respondents answered "Absolutely" and "Yes." In response to the question, "Should only veterans hospitals be required to judge the severity of aftereffects and suspected aftereffects?" only 24.3 % of respondents answered "Absolutely" and "Yes," which suggested that the opinion on the current efforts of the Ministry of Patriots & Veterans Affairs were generally negative.

E) In response to whether compensation for aftereffects should be increased, more than 90% of respondents answered "Yes" and "Absolutely." To whether compensation should be increased for suspected aftereffects as well, most respondents

answered in the affirmative.

D. Discussion

1) In all three indices created from reconstructing past exposure, the risk for developing cerebral infarction, peripheral neuropathy, peripheral vascular disease, multiple nerve paralysis, multiple sclerosis, and skin diseases increased with exposure to defoliants. In case of skin diseases, the exposed group had a statistically significant higher risk of developing diseases compared to the control group.

2) In two exposure indices, risk for developing multiple myeloma, chronic bronchitis, other respiratory diseases, and hyperlipidemia increased as exposure to defoliants increased.

3) In one exposure index, the diseases whose risk increased with higher exposure to defoliants were liver cancer, myocardial infarction, other cardiac disorders, artery sclerosis, gastritis, and mental illness.

4) The results demonstrated that groups with higher exposure to defoliants were statistically more likely to develop diseases. However, exposure indices and analysis of diseases using surveys might have various limitations in examining the relationship between exposure to defoliants and disease prevalence rate.

5) First, self-reported disease development and progression may differ from reality. Therefore, a more objective examination of such reported disease development should be conducted.

6) Self exposure evaluation may be limited in its validity as a tool for investigating exposure to defoliants.

7) These surveys focused more on investigating various factors such as smoking and drinking habits, obesity rates, agrichemical use, and socio-economic levels of veterans, thereby yielding confusion in assessing the relationship among exposure to defoliants and disease and death rather than determining disease condition and exposure level of veterans.

8) The survey results demonstrate that the research team believes there should be more publicity on national policies related to defoliants.

2. Report Evaluation

A. Methods

1) This study utilized a cross-sectional study design, with the entire veteran population as study subjects. The Third Study, which had a 70% participation rate and included descriptions of confounding factors and mental health, reflected attempts at improving the accuracy and depth of the study as compared to the First and Second Studies.

2) Although it may be an inherent flaw in such research, the appropriateness of the exposure index created from self-reported information leaves much doubt. Unlike in the First and Second Studies, more progressive methods were adopted in creating an exposure index reconstructed from past exposure in the Third Study, therefore a more advanced evaluation of exposure levels was able to be conducted.

3) It was a significant methodical improvement to investigate the relationship between defoliants and diseases while controlling confounding indices.

B. Results

1) A statistical correlation was found between many diseases and levels of self-reported exposure. It is problematic to accept these results as establishing a connection or causational relationship between diseases and levels of self-reported exposure due to limitations in reliability and appropriateness. This was evident also in the exposure indices which showed no correlation. Furthermore, an academically objective discussion about the correlation can only be conducted if more results are accumulated through diverse research methodologies and study designs,

2) Surveys on national policies evince the desire of veterans for substantial compensation for their participation in the War. Specifically, the survey showed little awareness among veterans regarding policies on defoliants and calls for more consideration on the establishment, formation and execution of political measures, and public campaigns.

3. General Opinion

This study had a larger population of study subjects compared to the First and Second Studies, and improved the response rate, thereby increasing the reliability of the study. Furthermore, as the researchers mention, the study was significant because the factors affecting health were examined. The critics evaluate and submit the following opinion on the viewpoint of the proposal for future mid-term and long term studies with the evaluation results of the Third Study.

A. Matters to be Considered and Supplemented

1) It is necessary to analyze data more specifically related to participation in the War such as rank, occupational specialty and period of service.

2) Regarding the study, general limitations in surveys, such as the possibility of selective bias and recollection bias should not be excluded. The subjects are likely to have a biased opinion about the correlation between disease and defoliants. There is also a conflict of interest because of potential interest of receiving compensation. Thus, such deficiencies should be addressed using other research methods. There is also a conflict of interest due to the possibility of receiving compensation.

3) A comparison of characteristics of non-respondents would improve the study. While the survey's response rate was approximately 70%, a significant increase from the Second Study, 50,000 subjects or 30% were omitted calling for a comparison of basic characteristics of respondents and non-respondents. Specifically, in studies such as this, participants of the surveys mainly consisted of those who are interested in the substance of the study, those who complain about their illness, and those who are existing patients, and thus may lead to over-exaggeration. This is evident in that the Central Cancer Registration has only 40 people registered as having multiple myeloma whereas in the current survey 668 people responded as having the disease. Therefore, supplemental analysis on non-respondents and those who did not qualify for the survey would improve the reliability of the study. If possible, a long-term design involving face-to-face interviews by trained researchers should be adopted rather than mail studies or self-registered information.

B. Recommendations for Future Studies

1) Of the confounding factors which may affect disease progression, there should be an investigation into employment history after participation in the War. Apart from smoking and drinking habits, which were considered and eliminated in the study, other factors such as occupational causes, which were disclosed after Vietnam War participation may greatly affect the diseases studied in this research. Therefore, there should be additional investigation on these factors.

2) Among the confounding variables, smoking and drinking habits during participation in the War should be examined in addition to current habits. Such accurate information at the time of participation in the War is necessary because some veterans might have quit smoking or drinking after the War due to diseases or other reasons.

3) In examining disease development and prevalence, an analysis of objective information such as health insurance documents or medical records from health medical providers, i.e. Provider Check, should be conducted after obtaining consent from study subjects. In case of deceased veterans, medical records containing causes of death, cancer

registration data, and health insurance data should be examined in connection with survey data.

4) Supplemental studies with a narrower focus should be conducted on illnesses including skin diseases which showed a correlation to all exposure indices. Since the results of the self-reported exposure index differ greatly from the results of the index created from reconstructing past exposure, there may be doubts about the reality of the self-reported exposure index. However, this study suggested a correlation between the risk of developing diseases and the exposure index reconstructed from past exposure, and examined health insurance data in researching disease prevalence. Therefore, there should be more detailed and precise supplemental studies on several illnesses including skin diseases which showed a correlation in all three analyses.

5) In terms of surveys conducted on national policies related to defoliants, the study calls for more comprehensive and qualitative research in addition to quantitative examinations conducted in this study. In determining whether veterans should be compensated, the decision on whether or not to compensate veterans takes into consideration the general opinion that the entire Vietnam War veteran population should be compensated regardless of exposure to defoliants and other non-scientific bases such as the viewpoint of interested parties during the policy making process. Therefore, approaching the issues of compensation and administration from only a scientific viewpoint has its limitations, and thus may be beyond what epidemiological researchers can consider. Hence, there should be political research and consideration regarding the policies.

Chapter 5. Participation in Vietnam War, Exposure to Defoliants and Death

1. Report Summary

A. Introduction

Many Vietnam War veterans believe that they have been exposed to considerable amounts of defoliants and that defoliant exposure has caused development of rashes, nervous system malfunctions, and malignant tumors. They have also expressed concern that defoliant exposure can influence the development of congenital diseases and other diseases. Because of such concerns, a variety of studies evaluating the health conditions of Vietnam veterans have been conducted in the United States.

In Korea, the only study examining the deaths of Vietnam veterans was the Second Epidemiological Study on Damages Caused by Defoliants which was conducted from 1998 to 2001, and most other previous studies were conducted abroad. The causes of death which were reported to be associated with defoliant exposure levels or participation of veterans in Vietnam by foreign studies may not be revealed in Korean veterans, while new causes of death not reported by foreign studies may occur in Korean veterans.

This study was conducted to evaluate how participation in the Vietnam War influenced death rate and causes of death by comparing the death rates of Korean veterans with that of non-veteran Korean male population of the same age. It was also conducted with the purpose of determining how death rates and causes of death among veterans differed depending on defoliant exposure levels.

B. Methods

1) Study Subjects

In the Second Epidemiological Study, the personal information of 187,897 veterans out of a total of 297,349 veterans was obtained (Air Force: 889 persons, Navy and Marine: 8,962 persons, and Army: 287,498 persons). In the Third Epidemiological Study, the current residences of the 187,897 veterans as of the end of June 2004 were confirmed. Among these veterans, study cohorts consisting of 184,681 were selected, while some veterans were excluded therefrom, such as deceased veterans, emigrants, persons who resided in foreign countries, and persons whose domestic resident registrations were erased as of December 31, 1992. Further, with respect to 153,899 veterans whose level of exposure to defoliants could be reconstructed from past exposure among the study cohorts, we compared each veteran's risk of death as a result of exposure to defoliants.

2) Follow-up Studies on Veterans' Death

We first examined mortality and causes of death using statistical data of causes of death with the cooperation of the National Statistical Office, and considered study subjects whose thirteen digits of their registration numbers matched those in the statistical data as deceased. In cases where their registration numbers were recorded under records of the deceased but not included in the statistical data, those individuals were considered dead if twelve digits of their registration number matched that in the statistical data, and the latest confirmation date of their residency status according to the Resident Registry matched that of the date of death in the statistical data. As for the causes of death, we used those listed in the statistical data on causes of death. The follow-up study covered January 1, 1993, to December 31, 2004.

3) Classification of Causes of Death

We classified the causes of death according to the 19 categories in the statistical data on causes of death and the 103 classification items of general deaths. Causes of death, which accounted for more than ten deaths in the veteran population over the last twelve years, were included in the study.

4) Exposure Index Created from Reconstructing Past Exposure

The exposure opportunity model created from the continuous exposure model developed by Professor Stellman's team at Columbia University was used to calculate E4 and Le4 values and divided the veterans into low exposure group and high exposure groups (medium exposure group, high exposure group) based on these values.

5) Analysis Methods

A) Classification of Defoliant Exposure Levels

Those veterans who were monitored for 12 years from 1993 to 2004 range in age from 37 to 82 years old, and were compared to the general Korean male population of the same age range during those 12 years. Stellman's exposure opportunity model was used to calculate E4 and Le4 values based on veterans' period of participation and division to which they belonged. Based on such values, veterans were divided into two groups (low exposure group, high exposure group), and three groups (low exposure group, medium exposure group, high exposure group), and the mortality rate of each group was compared. In dividing 153,899 subjects into two groups, 75,170 belonged to the low exposure group while 78,729 belonged to the high exposure group. In the classification into three groups, the low exposure group had 75,170 subjects, the medium exposure group had 47,535 subjects, and the high exposure group had 31,194 subjects.

B) Analysis of Mortality Rates

The mortality rates of veterans were computed by using the number of deaths and person-year, of follow-up, and the average mortality rate of the general Korean population was calculated by using the number of people registered as residents and mortality rates.

① Calculation of "Person-Years"[1]

The "person-year" for each age group was computed by using the ages at the beginning of the organization of cohorts and at the end of the follow-up. For those deaths which occurred before December 31, 2004, the day when the follow-up on mortality began, the date on which the follow-up ended was taken to be their date of death. Those not reported in mortality statistics were assumed to be living. As such, the person-years for each age group differing by one year was determined.

② General Korean Population

The number of people in age groups with an interval difference of five years between groups was determined using the resident registration data from the National Statistical Office, and the number of people per age was computed by determining the percentage of each age within every five year age group using resident registration data and census data.

③ Age Standardization

Selecting the entire male population from 1993 to 2004 as the standard population, age-adjusted mortality rate and standardized mortality ratio were directly computed from the population structure and mortality rates with intervals of by five years. Age-adjusted mortality rates and standardized mortality ratios were indirectly computed by applying the population structure and mortality rate of each age for the general male population from 1993 to 2004 to the person-years for each year and age from 1993 to 2004. In comparing the low exposure group and high exposure group within cohorts, the age-adjusted mortality rate was directly computed by setting the general male population from 1993 to 2004 as the standard population whereas the direct standardized death ratios of age-adjusted mortality rates were computed with the low exposure group as the standard population. Furthermore, the standardized mortality ratios of each exposure group, which were computed indirectly, were compared to yield group standardized mortality ratios of the exposed group.

Using the Poisson model, the confidence interval and significance level of direct and indirect standardized mortality ratios were computed to be 95%, and the significance level of standardized mortality ratios were indirectly determined by comparing standardized mortality ratios or were assessed using the Exact method.

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[1] The sum of the number of years that each member of a population has been afflicted by a certain condition or disease.

6) Proportional Hazards Regression Matrix

The death risk ratios, which monitor the strength of correlation between exposure to defoliants and death, were computed by using Cox's Proportional Hazard Regression Matrix to control the age and rank.

7) Analysis Programs

We used SAS system for Windows version 9.1, and all significance levels were calculated using a two-tailed test.

C. Results

In this study, 16,531 veterans were found to be deceased as of December 31, 2004. The investigation failed to locate 4,647 veterans while 163,524 were living. As of December 31, 2004, the current follow-up rate is 97.2%, and the total person-years was 2,102,235 years for all subjects.

1) Participation in the Vietnam War and Mortality

In most causes of death, mortality of Vietnam veterans whose ages were adjusted by direct methods was lower than the mortality of the general Korean men population, except chronic ischemic heart diseases. Similar to age interval from 37 to 82 years old, the mortality of the veterans was low in most cases of the age interval from 45 to 64 years old. However, the death due to multiple myeloma, acute myelogenous leukemia, chronic myelogenous leukemia, and murder was significantly higher than the mortality rate of the general population (Table 5-1).

The standardized mortality ratio about all causes which were age-adjusted by indirect methods was 0.83, by which the mortality of the veterans was lower than that of the general population. In the section from 45 to 64 years old, the standardized mortality ratio about all causes was 0.84, by which the mortality of the veterans was also lower than that of the general population. Statistically there are no significantly higher causes of mortality of the veterans than that of others (Table 5-2).

2) Defoliant Exposure Levels of Veterans and Mortality

The total observating term for 153,899 people whose historic exposure reconstruction was possible were 1,740,242 years. The mortality of the high exposure group by using direct standardization method about all causes of death in classification of two groups was significantly higher than that of the low exposure group. And each individual cause was tuberculosis, chronic myelogenous leukemia, chronic ischemic heart

diseases, digestive diseases, and skin diseases. But in cases of viral hepatitis, lips/oral/ pharynx cancer, small intestine cancer, and multiple myeloma, the mortality of the high exposure group was significantly lower than that of the low exposure group (Table 5-3).

The indirectly standardized mortality rate ratio (SMR) which used the indirect standardization method for all causes of death in two-group classification was 1.09, by which the mortality of the high exposure group was significantly higher than that of the low exposure group. Each individual cause was neoplasm, lung cancer, thyroid cancer, chronic myelogenous leukemia, respiratory diseases, digestive diseases, liver diseases, alcoholic liver diseases, external causes of death, transportation accidents, and falling accidents (Table 5-4).

When we controlled ages and ranks in Cox's Proportional Hazard Regression Matrix which has defoliant exposure levels as continuance variables, all causes of death was irrelevant with the defoliant exposure. But thyroid cancer, chronic myelogenous leukemia, angina pectoris, and alcoholic liver diseases were risks whose death hazards got higher as defoliant exposure levels increased. All causes of death was irrelevant with the defoliant exposure in Cox's Proportional Hazard Regression Matrix which used two-group classification, but the death caused by a neoplasm, chronic myelogenous leukemia, or angina pectoris was significantly higher in the high exposure group than in the low exposure group (Table 5-5).

When we controlled ages and ranks in Cox's Proportional Hazard Regression Matrix which used three-group classification, mortality risk of the medium exposure group was higher than that of the low exposure group in all causes of death, but there was no significant difference between the high exposure group and the low exposure group. The cause of death whose death hazard was higher in the high exposure group than in the low exposure group was thyroid cancer. The causes of death whose death hazard was higher in the medium exposure group than in the low exposure group were neoplasm, lung cancer, chronic myelogenous leukemia, angina pectoris, respiratory diseases, and chronic lower respiratory diseases (Table 5-6).

D. Discussion

1) Methods

If the people in the high exposure group which was seriously damaged by participation in the Vietnam War or defoliant exposure died before they composed a cohort on January 1, 1993, there is a possibility for a selective survival bias while composing a study cohort. In such case, this study result will underestimate the risk of death by participation in the Vietnam War and high exposure to defoliants. Defoliant exposure levels used the exposure opportunities model of the professor Stellman team in the United States. In the analysis of mortality rate, it analyzed the study results on the basis of analysis results

of the indirect standardized mortality ratios more than the standardized mortality ratios by the direct standardized mortality rate. The variable which we could control in Cox's Proportional Hazard Regression Matrix other than ages and whether there was an exposure to defoliants was the rank. In this study, when the result analyzed by standardization of the mortality rate and the result of Cox's Proportional Hazard Regression Matrix were different, it tried to analyze the results on the basis of the results of the Proportional Hazard Regression Matrix which could control the ranks additionally. In case of the analysis of cancer, it considered in collaboration with the cancer occurrence analysis. And even if the cause of death is not cancer, it would be appropriate to analyze with consideration of prevalence information analysis results which used the health insurance data.

2) Results

Among the diseases which showed significance or similar significance in high death risk in the high exposure group in the analysis of the indirect standardized mortality ratio, the diseases that showed the significantly high death risk even when we observed the defoliant exposure as a continuous variable were throid cancer, chronic myelogenous leukemia, angina pectoris, and alcoholic liver diseases.

The death caused by thyroid cancer was higher in the high exposure group than in the low exposure group, but thyroid cancer showed no significant relationship with neither the two-group classification nor the three-group classification, after the analysis of cancer occurrence. The diseases related to thyroid cancer in disease prevalence analysis showed statistically significant relationship with defoliant exposure. These results do not show that occurrence rate will particularly increase when defoliant exposure is high, but it is possible to influence the severity. In other words, it can be interpreted that the veterans who were exposed to defoliants show more serious symptoms and get thyroid cancer which has faster process of disease.

Chronic myelogenous leukemia in classification of three groups showed significantly higher causes of death in the medium exposure group than in the low exposure group. In the result of cancer occurrence analysis, the high exposure group in the two-group classification showed similar significance when it compared with the low exposure group, and in the three-group classification the death causes in the medium exposure group were significantly higher than the other groups.

Angina pectoris in the three-group classification showed higher causes of death in the medium exposure group than in the low exposure group. But we can say it is controversial for the correlation between defoliant exposure and angina pectoris because there is no consistency in the results of the classification 1 of disease prevalence analysis of the veterans of survey, disease prevalence analysis, an analysis of death, and so on.

High risk of death of alcoholic liver diseases in an analysis of death can highly

possibly be contributed to not controlling drinking, because alcoholic liver diseases have no consistency in before and after controlling drinking.

E. Conclusion

In this study, it tried to confirm whether there is any difference between Vietnam War veterans and the general men population in the same age group from year 1993 to 2004 in the mortality rate, and the mortality rate and the risk of death between exposure groups by defoliants exposure levels in the veterans by cross-analyzing follow-up study of death for 12 years from 1993 to 2004. In result of the death analysis of general male population and Vietnam War veterans, the mortality rate of the veterans was lower than the mortality rate of the general male population, and it was statistically significant. We can assume that it is the 'healthy solider effect' that the veterans are more healthy group than the general male population.

When it observed only the analysis of death based upon defoliant exposure levels in the veterans, the result that the correlation between the death caused by thyroid cancer, chronic myelogenous leukemia, angina pectoris, and alcoholic liver diseases and defoliant exposure are suspectable came out. Especially, when it considered the analysis results of the disease prevalence and cancer occurrence, we can suspect the correlation of thyroid cancer and chronic myelogenous leukemia with defoliant exposure, although there are some limitations. It is controversial in the correlation between angina pectoris and defoliant exposure after the result of the analysis of the death risk or disease prevalence of all ischemic heart diseases or myocardial infarction. The death of alcoholic liver diseases has limitations because of failure to control drinking when we consider the analysis results of disease prevalence where we could control drinking.

If the people in a high risk group which was seriously damaged by participation in the Vietnam War or defoliant exposure died before they composed a cohort on January 1, 1993, this study result will underestimate the risk of death by participation in the Vietnam War and high exposure to defoliants. Also because researchers failed to control several confounding variables which are highly related to death in the analysis between veterans and overall general population, and the cross-analysis between exposure groups in the veterans, it has limitations in observing the relationship between participation in the Vietnam War, defoliant exposure and death. Therefore, we should be careful in interpreting results.

2. Evaluation of Study Report

A. Methods

1) Standards for Exclusion

A) The Study Report excluded those who died before 1992 (969 people who were reported to have died and 1503 people whose deaths have been confirmed by date of death) without providing any reasons for such exclusion.

B) Because it excluded about 2500 deceased persons who died before 1992, no early effects were realized, which may cause some fatal information errors. Although there may be some significant results from the Study Report, there are many limitations in interpreting results because selective bias may apply. Therefore, those who died after year 1983 should have been used -- at the minimum, it would be essential to study effects on death by excluding those who died before 1983.

2) A follow-up study of death

With regard to the statement that "we have confirm a person's death if the first twelve digits of his/her resident registration numbers, the identification date of residence and the date of death are all identical", it is noted that the thirteenth digit of the resident registration number could be identified since such digit can be calculated by a specific formula based on the first twelve digit numbers. Therefore, rather than using the method above, we are of the view that identification of the thirteen digit number and then obtaining and analyzing information using such number could have reduced a chance of misclassifiction.. As an alternative method, it is noted that the information regarding the full thirteen digit resident registration numbers are available from the National Statistical Office. It appears that one could have received cooperation from the National Statistical Office if the Ministry of Patriots and Veterans Affairs felt that obtaining the full-digit numbers is a matter of national significance.

3) Index of Exposure Quantity

Because study subjects are 153,899 people, it seems that Le4 was constructed based on information relating to division/brigade levels, rather than battalion/squadron levels. The study result at page 134, on the other hand, shows that death/cancer risks were higher in the medium exposure group than in the high exposure group, which could be interpreted to suggest that Le4, which was constructed based on the information relating to division/brigade levels, may be problematic. It is necessary to construct Le4 based on the information relating to battalion/squadron levels and conduct further analyses.

B. Results

1) Participation in the Vietnam War and Death (Table 5-1, Table 5-2)

A) Table 5-1 is titled as the direct standardized mortality ratio, but it is not clear whether this direct standardized mortality ratio refers to the calculation by age-adjusted mortality rate divided by the general population group or the calculation of direct standardized mortality ratio calculated under the direct standardized method. If it is the latter, the Study Report should be supplemented accordingly since it makes no reference as to such method.

B) Tables 5-1 and 5-2 contain identical contents and the results are similar, while the only difference appears to be whether the standardization methods are direct or indirect. There is a room for confusion and some confusion may arise with respect to some results. Therefore, we recommend that a table using the format described below (See Table 1) should be constructed instead.

2) Defoliant Exposure Levels and Death in Veterans (Table 5-3, 5-4, 5-5)

A) In case of Table 5-3, results are obtained by direct standardization methods and in case of Table 5-4, results are obtained by indirect standardization methods. Similarly, these tables show different results depending on the standardization methods notwithstanding the fact that they contain identical contents. Because most results from these two tables are similar, it is necessary to make a report as a single result without confusing readers. Therefore, we recommend researchers to modify the tables in accordance with the format used in the table below (See Table 2).

B) Also it is necessary to use a direct standardized mortality rate based on the general population group rather than using the indirect standardization method (it is necessary to use the direct standardized method because, under the indirect standardized method, it is not possible to compare the standard population with other groups).

C) To compare with the general population group, it is necessary to have the ratio of mortality rate between the general population group and the low exposure group, the ratio of mortality rate between the general population group and the high exposure group, and the ratio of each mortality ratio.

D) It is necessary to supplement p-trend results showing whether or not the mortality increases or decreases when one moves from the low exposure groups to the medium and the high exposure group.

3) Interpretation and Description of Results

Regardless of the direct standardized method or indirect standardized method, if

the number of the deceased is lower than 5, one cannot exclude the possibility of coincidence even though the result may bear some significance. In such cases, therefore, it is unnecessary to describe indirect standardized mortality ratios (SMR) or ratios of direct standardized mortality rate (DMR) and their confidence intervals. In fact, when results of foreign cohort analyses are reported, researchers have reserve their opinion by not indicating any result in case there is less than 5 occurrences in a given cell. In this regard, rendering analysis on certain results are warranted only when there is a sufficient number of occurrences identified by sufficient tracing (regarding death causation classification at page 116, it is described that such classification includes only the occurrences of 10 or more). Since there is a need to continue with further studies on the mortality rate (Chapter 5), the cancer occurrence rate (Chapter 6) and the prevalence rate (Chapter 7) about defoliant exposure and such studies should be further conducted, we are of the view that one should reserve rendering his/her interpretation on certain results if such results were observed in occurrence frequency of less than 5 people in one cell. Instead, it is necessary to interpret the results when the death, occurrence or prevalence cases occur in higher frequency.

4) In case of Table 5-2, there is a classification called [37-82 years of age exposure groups]. The accuracy of the 37 year old must be verified, however. In case of the 37 year old, assuming that he participated in the war in 1970 and died in 1992, he should have been 42 years old. Assuming that the age 37 is correct, on the other hand, it means that he participated in the war at the age of 14. Therefore, it is necessary to verify the exact ages of the study subjects.

3. Overall Opinion

The Study Report failed to realize any early effects by excluding from the study subjects those who died before 1992, which may result in fatal information bias as well as many limitations in interpreting the results because selective survival bias may apply. As for the exposure marker, it is necessary to construct Le4 using the information relating to battalion/squadron levels and conduct further analyses thereon.

Since there is a room for confusion with respect to standardization methods in the participation in the Vietnam War and death, it is desirable to present a single, consolidated table, and same also applies to the defoliant exposure levels and death of the veterans. When the death occurrence is observed in less than 5 people, it is desirable not to insert any indirect standardized mortality ratios (SMR) or ratios of direct standardized mortality rate and their confidence intervals in the "interpretation and description of results" section because one cannot exclude a possibility of coincidence. If the death occurrence of less than 5 is observed in a given cell, it is necessary to interpret the results when the death, occurrence or prevalence cases occur with respect to a larger subject pool.

Table 1. Participation in Vietnam War and death

Causes of death	ICD-10	General population group		All exposure groups			SMR of all exposure groups as against general population group (95% CI)	37-82 years old exposure group		SMR of 37-82 years old exposure group as against general population group (95% CI)	45-64 years old exposure group		SMR of 45-64 years old exposure group as against general population group (95% CI)
		Number of death	Normal mortality rate	Number of death	Normal mortality rate	Age-adjusted mortality rate		Number of death	Age-adjusted mortality rate		Number of death	Age-adjusted mortality rate	

** When numbers of cases are less than 5, the results need to be reserved (It is recommended that RR[95% CI]) is not provided.

Table 2. Defoliant exposure levels and death

Causes of death	ICD-10	General population group		High exposure group		Low exposure group		MRR1 between high exposure group and general population group (95% CI)	MRR2 between low exposure group and general population group (95% CI)	Ratios between MMR1 and MMR2 (95%)	High exposure group		Medium exposu group	
		Number of death	Normal mortality rate	Number of death	Direct standardized Age-adjusted mortality rate	Number of death	Direct standardized Age-adjusted mortality rate				Number of death	Age-adjusted mortality rate	Number of death	Ag adju mor y r

** When the number of cases is smaller than 5, reserve the results (better not to provide RR[95% CI]).

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Chapter 6 Participation in the Vietnam War ▪ Exposure to Defoliants, and Occurrence of Cancer

1. Report Summary

A. Introduction

The purposes of this study include as follows:

First, to examine how participation in the Vietnam War affected occurrence of cancer by comparing the Korean veterans of the Vietnam War with general Korean male population belonging to the same age groups. Second, to examine if there is any difference among the Korean veterans of the Vietnam War depending on the level of exposure to defoliant.

B. Study Methods

1) The subject of study

A) The subjects of this study are the veterans of the Vietnam War, specifically 184,681 males who were believed to be alive as of December 31, 1992, and whose cancer occurrences are estimated to be traceable out of 187,897 veterans identified by the second epidemiological study on defoliant damages.

B) After 504 veterans, who contracted cancer before 1992, were excluded, 184,177 veterans out of 184,681 veterans were selected as study cohorts for tracing cancer occurrence.

C) Among the above individuals, 153,463 veterans, whose defoliant exposure markers could be constructed by the historic exposure reconstruction, were selected for comparing risk comparisons between cancer occurrence and exposure to defoliants.

2) Follow-up study on cancer

A) For confirmation of occurrence of cancer (existence thereof and relevant part of the body), the cancer occurrence data in Korea from the Central Cancer Registration office in National Cancer Center were used.

B) The period for person-years was from January 1, 1993 through December 31, 2003.

3) Types of Cancer

A) The types of cancers were classified according to ICD-10 diagnoses which were provided by the National Cancer Center.

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B) ICD-10 standard which was used in the book titled "Cancer Incidence in Five Continents" Vol VIII (WHO, IRAC) was primarily used.

C) In case of cancers of great interest such as Hodgkin's disease and Lymphoma, detailed classification was used using ICD-10 4-digit classification.

4) The Defoliant Exposure Marker by Historic Exposure Reconstruction

A) Using E4 value of the exposure opportunity model, the exposure groups were divided into the low exposure group, of which Le4 value is less than 4 and the high exposure group, of which Le4 value is 4 or higher. (2 Group Division)

B) Then, the high exposure group of the 2 Group Division was further divided into the medium exposure group, of which Le4 value is below 5, and the high exposure group, of which Le4 value is 5 or higher.

5) Method of Analysis

A) Classification by the defoliant exposure level

① Only 153,463 persons could be classified into the 3 groups (low exposure group: 74,978 persons, medium exposure group: 47,535 persons, high exposure group: 31,194 persons).

② Le4 value was used as a continuous variable.

B) Analysis of the cancer occurrence rate

The cancer occurrence rates of the veterans were calculated per 100 thousand persons, and standardized for comparison by observing term for follow-up and number of cancer patients.

C) Proportionate Risk Regression Model

The cancer occurrence ratios were calculated after controlling ages and military ranks as confounding variables.

D) Program for Analysis

SAS Windows V9.1 was used.

C. Results

As a result of comparison between the high exposure group and low exposure group in Ratio of the Indirect Standardization of Incidence Rate (RSIR), the types of cancers, of which the death rates were significantly higher or borderline higher in the high exposure group than the low exposure group, were lip cancer/oral cancer and chronic myeloid leukemia (Table 6-4). In the comparison of the 2 groups of the Cox Proportional Regression Model in which ages and military

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ranks were controlled, the types of cancers, of which the occurrence rates were significantly higher or borderline higher in the high exposure group than the low exposure group, were lip cancer/oral cancer, stomach cancer, small intestine cancer, rectal cancer and chronic myeloid leukemia (Table 6-5). When observing the exposure to defoliants as a continuous variable, the types of cancers, of which the occurrence risks increased with an increase in the exposure, were lip cancer/oral cancer, salivary gland cancer and T-cell lymphoma (Table 6-5). In the comparison of the 3 groups of the Cox Proportional Regression Model, the type of cancer, of which the occurrence rate was significantly high or borderline high in the high exposure group, was small intestine cancer, while the types of cancers, of which the occurrence rates were significantly high or borderline high in the medium exposure group were lip cancer/oral cancer, stomach cancer, lung cancer and chronic myeloid leukemia (Table 6-6).

D. Discussion

1) Discussion on study methods

In this Study Report, the data from the Korea Cancer Registry were used to follow up the occurrence of cancer. Although there are some limitations as to the substantiality of the pre-dated information in Cancer Registry, such limitations did not present any significant limitations since the purpose of this study was not to precisely calculate any cancer occurrence rate and the purpose was instead to compare the cancer occurrence rates and risks of the veterans and the general male population and among the veterans themselves depending on the exposure to defoliants among the general male population. But, there is a possibility of underestimating the actual cancer occurrence risks caused by participation in the Vietnam War or exposure to defoliants if there were many veterans who died of cancer before January 1, 1993, i.e., when the cohort on a severely damaged group was constructed and such veterans were excluded from the purview of this Study Report. The defoliant exposure level was constructed by the exposure opportunity model developed by Professor [redacted] of the United States. In the analysis of occurrence rate of cancer, researchers focused on the output by the indirect standardization of incident rate rather than the output by the direct standardization of incident rate. In the Cox's proportional risk regression model, the only controllable variable except ages and exposure/non-exposure to defoliants was the military ranks. In this research, researchers tried to focus on the output of proportional risk regression model in which the military ranks were additionally controlled in the event that there were discrepancies between the output from standardization of incidence rate and the output of Cox's proportional risk regression model.

2) Discussion on study results

As a result of comparison between the veterans of the Vietnam War and the general male population regarding the occurrence rates of cancer, such rates of the veterans were lower than the general male population, and this result was statistically significant. This result can be attributable to the "healthy soldier effect," i.e., the veterans generally belongs to a group which is healthier than the general male population. Accordingly, it is more desirable to compare among the veteran groups rather than to compare the veterans with the general male population for exposure to defoliants and cancer.

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In the analysis of the incidence of cancer according to the defoliant exposure level, the two most suspicious types of cancers were small intestine cancer and salivary gland cancer, while chronic myeloid leukemia was also suspected of having a correlation with the exposure to defoliants when the cancer occurrence and death analyses were taken into consideration. Regarding stomach cancer, lip cancer and oral cancer that showed significant results in some analyses notwithstanding the fact that the veterans' occurrence rates were lower than those of the general male population, there is a need to further study the relation between such rates and the exposure to defoliants the general male population.

In the comparison between the veterans and the general male population, only ages and the year of observation were controlled whereas, in the comparison among the exposure groups within the veterans, only ages, the year of observation and the military ranks as of the completion of the war participation were controlled as the confounding variables. Thus, there were still some limitations in examining the relations among the exposure to defoliants, the incidence of cancer and the participation in the Vietnam War, necessitating care in interpretation of the results.

In case of lip cancer/oral cancer, the incident rate of cancer was significantly high when the exposure level was examined as a continuous variable in the Cox's proportional risk regression model, and such rate was higher in the high exposure group than the low exposure group in the 2 group comparison. It is more desirable to make an individual evaluation because this result was based on the sum of 10 different cancers. When the evaluation was made by excluding gland cancer, the result was not statistically significant.

Oral cancer and stomach cancer did not accord with the increase of incidence of cancer according to the exposure to defoliants. In case of salivary gland cancer, the occurrence rate was significantly high when the exposure level was constructed as a continuous variable in the Cox proportional risk regression model. However, an analysis was not possible because no one from the low exposure group in the 2-group comparison contracted this type of cancer. In case of small intestine cancer, the risk of cancer occurrence was significantly high when the exposure to defoliants was constructed as a continuous variable in the Cox proportional risk regression model, and such risk was statistically higher in the high exposure group than the low exposure group in the 2-group comparison. In the 3-group comparison, there was no significant difference in the medium exposure group, but the risk of cancer occurrence was significantly high in the high exposure group. In case of rectal cancer, the risk of cancer occurrence was statistically significant in the 2-group comparison in the Cox proportional hazard regression model. In case of lung cancer, the risk of incidence was higher in the medium exposure group than in the low exposure group in the 3-group comparison of the Cox proportional hazard regression model. In case of chronic myeloid leukemia, the risk of cancer occurrence showed similar significance in the 2-group comparison of the Cox proportional hazard regression model. Prostate cancer was the cancer of which the death rate of veterans was significantly higher than death rate of the general male population.

D. Conclusion

As a result of the comparison of incidence rates between the veterans and the general male population, those of the veterans were lower than those of the general male population, and

this result was statistically significant. This result is attributable to the "healthy soldier effect," i.e., that the veterans generally belonged to a group which is healthier than the general male population. Accordingly, it is more desirable to make the comparison among the veterans themselves than to compare with the general male population regarding the exposure to defoliants and cancer.

In the analysis of the incidence of cancer according to the defoliant exposure level, the two most suspicious cancers were small intestine cancer and salivary gland cancer, while chronic myeloid leukemia was also suspicious of having a correlation with the exposure to defoliants when analyses on the cancer incidence and death were taken into consideration. Regarding stomach cancer, lip cancer and oral cancer that showed significant results in some analyses notwithstanding the fact that the veteran's incident rates were lower than the general male population, the correlation with the exposure to defoliant should be further examined.

There is a possibility of underestimating the actual cancer occurrence risks caused by participation in the Vietnam War or exposure to defoliants, if there were many veterans who died of cancer before January 1, 1993, i.e., when the cohort on a severely damaged group was constructed and such veterans were excluded from the purview of this Study Report. In the comparison between the veterans and the general male population, and in the comparison among the exposure groups among the veterans, certain confounding variables having high correlations with the cancer occurrence could not be controlled. So, there are some limitations in examining the relation among the participation in the Vietnam War, the exposure to defoliants and the incidence of cancer, necessitating careful interpretation of the results.

2. Report Evaluation

A. Study Methods

1) Study Subjects

A) Limitations which are inherent with the subject of epidemiological study cannot be solved.

B) If personal information of 187,897 veterans were available, identification of death caused by cancer and cancer incidence could be verified.

C) If the exposure to defoliants increased the cancer incident risk, such risk and death caused by cancer should be observed immediately after the exposure to defoliants, which is not possible.

2) Follow up Study for incidence of cancer

A) Because of incompleteness of Korean cancer registry database, it is possible to underestimate the actual risk ratio if the subjects' cancers were not registered. Especially, the data before 1998 were the ones newly registered by treating hospitals and it is impossible to calculate the national incidence rate based thereon, and thus, it is estimated that about 20% of cancer occurrences were not registered (After 1999, it is estimated that more than 90% of national cancer occurrences were registered).

B) It is most desirable to implement a survey to soldiers who were exposed to defoliants to examine if a cancer actually occurred by both active and passive surveillance. In some cases, however, cancer patients may not know their diseases even though they were diagnosed with cancers, and it is too difficult to identify the existence of cancers if patients were reluctant to report their cancers. If self-reported data were available, one may try to identify unregistered cancer by active surveillance to the medical institutions, which would be impossible, however.

3) Classification of Cancers

A) There is no problem because they were classified in accordance with the international standard.

B) The errors stemming from converting diagnosis made in the ICD-O-3 classification system used in cancer registration into ICD-10 and especially the accuracy of Non-Hodgkin's lymphoma, Hodgkin's disease and Chronic lymphatic leukemia, which were identified as having a correlation with the exposure to defoliants in U.S. were the very limitations which the researchers could not overcome.

4) Defoliant Exposure Indices by Historic Exposure Reconstruction

It is impossible to know the defoliant exposure level by means of the amount of defoliants sprayed in the Korean participating units' base and tactical areas. Other than the foregoing, however, there are no other data, which is a limitation in itself.

5) Method of Study

A) In this Report Study, those who contracted cancer before 1992 were excluded from the population group, but the reason for that exclusion was omitted. Since the cases in which cancer occurred immediately after exposure to defoliants were also excluded, we are of the view that the initial effect was not realized. Since non-realization could result in a significant difference if there had been some strong initial effect, detailed reasoning is further needed.

B) The period of person-years was from 1993 to 2003, and one may know the differences in influences from mid- and long term effects by dividing such period into 2 sub-periods, i.e., 1993-1997 and 1998-2003 in the comparison of directly standardized incidence ratio between the target groups and the general male population. Although one may not overcome the inherent limitations as to the fact that substantiality of the cancer registry data varied depending on a period, we believe that some meaning can be attached to a result which is based on the assumption that substantiality of the subjects was the same as that of the general male population.

B. Results

Due to the limitations as to the study method, it is difficult to render interpretation of the results.

C. Discussion

Due to the limitations as to the study method, it is difficult to render interpretation of the study results and some suggestions were made as to such method.

D. Conclusion

A) Possibility of developing a new defoliant exposure index which was described in Purpose of Research has its own limitations.

B) Although researchers did their best to utilize data and information available to the applicable data, such data and information have their own limitations, resulting in distortion of study results.

C) We suggest person-years be divided into 5-year periods. This is to compare impacts on each of such periods from the exposure to defoliants through incidence of cancer.

3. Overall Opinion

A. Researchers identified how the veterans of the Vietnam War were exposed to defoliants, and examined whether the exposure to defoliants acted as a risk factor by comparing

with Korean national incidence rate of cancer.

B. They utilized all of the data available in Korea, which, however, had some inherent limitations which could not be overcome.

C. Because of many limitations, no other researchers could produce a better study than this Study Report.

D. It is possible that the cancer risks of the Korean veterans of the Vietnam War could be different from those of other countries who were exposed to a different level of defoliants and cancer risks. However, if the identical study method and exposure level were used, one may be forced to interpret that the respective veterans were subsequently exposed to different environments after their exposure to the defoliants, as opposed to certain peculiar cancer-causing factors unique to Koreans.

E. If the veterans were entitled to compensations by the mere fact that they were exposed to defoliants, any epidemiological study of which the sole purpose is to collect evidence seeking to establish the standard for such compensation would be meaningless. However, the follow up study on the exposure to defoliants and its influence on diseases should continue.

F. Regarding the incidence of cancer, as was the case with the mortality number, it is desirable to reserve one's analysis and explanation if it is less than 5 people.

Chapter. 7 Exposure to Defoliants and Prevalence of Diseases

1. Report Summary

A. Introduction

Health hazard from the exposure to defoliants varies greatly, depending on various factors such as race, heredity and environments. Accordingly, one may not rely on foreign studies in their entirety and there is a need to conduct studies on Korean veterans of the Vietnam War. This Study Report sought to see if there is a difference in the prevalence rates of the Korean veterans of the Vietnam War depending on different defoliant exposure levels.

B. Study Methods

1) Subject of Study

Among 291,220 veterans, 187,897 veterans' resident registrations were identified in the second epidemiological study on the defoliant damages. Of these veterans, and of 164,208 veterans whose resident information were verified as of June 2004, 136,603 veterans whose health insurances were identified as the general veterans. Of these veterans, 96,126 veterans were identified as surveyed veterans [low exposure group: 56,876, high exposure group: 39,250 (medium exposure group: 20,638, high exposure group: 18,566)] whose confounding variables could be controlled.

2) Disease Prevalence Survey

A) For the veterans, we examined periodic prevalence rate with health insurance inspection data and veterans' hospital medical treatment data for 5 years and 9 months during 2000.1 ~ 2005.9. For the general male population, we examined periodic prevalence rate with health insurance inspection data for 4 years and 9 months during 2001.1 ~ 2005.9.

B) For the definition of disease prevalence, two classification methods were used. For type 1, the main disease and the first sub disease names were used while, as for type 2, only the main disease names were used. In case of hospitalization of one time or more or ambulatory care was identified as disease prevalence.

C) Defoliant exposure level: in case of the surveyed veterans, the groups based on military bases of the operation forces at the level of battalion/squadron were used.

3) Classification of Prevalent Diseases

For classification of prevalent diseases, ICD-10 was used, and the diseases were classified into those relating to aftereffects and suspected aftereffects of defoliants excluding cancer.

4) Statistical Analysis

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A) For prevalence rate, a periodic prevalence rate was used.

B) Age-adjustment was conducted by taking year 2003 as the basis and using one generation structure. For p-value, Poisson distribution was used.

C) Using logistic regression analysis, factors relating to military ranks, ages, smoking, drinking, education, income, BMI (Body Mass Index) were supplemented.

C. Results

1) Comparison between general veterans and general population group - indirect standardization

In Type 1 prevalence analysis, veterans' prevalence rates were statistically lower than the general male population in most diseases, but as for post traumatic stress disorder, multiple sclerosis and other polyneuropathy, the veterans' prevalence rates were significantly high (See Table 7-1).

In Type 2 prevalence analysis, veterans' prevalence rates were significantly lower than the general male population in most diseases, but as for hyperlipidemia, Post-traumatic stress disorder, multiple sclerosis, other polyneuropathy, Buerger's disease, atopic dermatitis, seborrheic dermatitis, other epithelial hypertrophy and xeroderma, veterans' prevalence rates were significantly higher than the general male population (See Table 7-2).

2) Comparison of veterans' prevalence rate according to the exposure level

In Type 1 prevalence analysis, the diseases, of which the prevalence rates of the high exposure groups is 1.2 times higher than those of the low exposure group, were benign neoplasm of adrenal gland, benign neoplasm of pituitary gland, neoplasm of uncertain behavior of thyroid gland, neoplasm of uncertain behavior of adrenal gland, neoplasm of uncertain behavior of pituitary gland, immune related diseases, hyperfunction of pituitary gland, hyperprolactinemia, hypofunction of pituitary gland, hyperaldosteronism, primordial hyperalsostreonism, amyloid degeneration, post traumatic stress disorder, secondary Parkinson's disease, other degeneration of nervous system, Alzheimer's disease, demyelinating disease of the central nervous system, multiple sclerosis, cerebral infraction, Buerger's disease, pulmonary emphysema, celiac sprue, leukoplakia, necrotizing respiratory granuloma and osteonecrosis.

In Type 2 prevalence analysis, general atrophy due to central nervous system, spinal muscular atrophy, polyneuropathy, antherosclerosis, other peripheral vascular disease, Behcet's disease were added, and cerebral infarction and pulmonary emphysema were excluded (See Table 7-3).

In Type1 prevalence analysis, the diseases, of which the prevalence rates increased with an increase of defoliant exposure level constructed in the continuous variable model, were benign neoplasm of pituitary gland, neoplasm of uncertain behavior of thyroid gland, diabetes mellitus,

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insulin independent diabetes mellitus, primordial hyperalsostreonism, metabolic disease, hyperlipidemia, amyloid degeneration, post traumatic stress disorder, intermittent holding disease, sheep liver fluke, nerve/nerve root and structural disorder, polyneuropathy, hypertension, primary hypertension, ischemic heart disease, agina pectoris, cerebral infarction, other peripheral vascular disease, pulmonary emphysema, gastric duodenal ulcer, gastroduodenitis, alcoholic hepatism, unclassified chronic hepatitis, liver cirrhosis, seborrheic dermatitis, allergic contact dermatitis, pruritus, erythema nodosum, other epithelial hypertrophy, xeroderma and osteonecrosis (Table 7-4).

On the other hand, the diseases, of which the prevalence rates of the high exposure group were significantly higher than the low exposure group were neoplasm of uncertain behavior of thyroid gland, diabetes mellitus, insulin dependent diabetes mellitus, insulin independent diabetes mellitus, other endocrine disease, hyperfunction of pituitary gland, hypofunction of pituitary gland, metabolic disease, hyperlipidemia, amyloid degeneration, intermittent holding disease, nerve/nerve root and structural disorder, polyneuropathy, hypertension, primary hypertension, ischemic heart disease, agina pectoris, acute cardiac infarction, cerebral infarction, other peripheral vascular disease, gastric duodenal ulcer, gastroduodenitis, alcoholic hepatism, unclassified chronic hepatitis, liver cirrhosis, Seborrheic Dermatitis, pruritus, other epithelial hypertrophy and xeroderma (See Table 7-4).

In the 3-group comparison in Type 1 prevalence analysis, the diseases, of which the prevalence risks were high in the high exposure group were benign neoplasm of thyroid gland, benign neoplasm of adrenal gland, benign neoplasm of pituitary gland, neoplasm of uncertain behavior of thyroid gland, neoplasm of uncertain behavior of adrenal gland, neoplasm of uncertain behavior of pituitary gland, thyroid gland disease, diabetes mellitus, insulin independent diabetes mellitus, other endocrine gland disease, hyperfunction of pituitary gland, hyperprolactinemia, hypofunction of pituitary gland, metabolic disease, hyperlipedemia, amyloid degeneration, post traumatic stress disorder, intermittent holding disease, epilepsy, nerve/nerve root and, polyneuropathy, ischemic heart disease, agina pectoris, acute cardiac infarction, cerebral infarction, gastric duodenal ulcer, gastroduodenitis, unclassified chronic hepatitis, liver cirrhosis, pruritus, leukoplakia and xeroderma (table 7-5).

On the other hand, the diseases, of which the prevalence risks were high in the medium exposure group were diabetes mellitus, insulin dependent diabetes mellitus, insulin independent diabetes mellitus, intermittent holding disease, nerve/nerve root and structural disorder, polyneuropathy, hypertension, primary hypertension, cerebral infarction, other peripheral vascular disease, Bueger's disease, pulmonary emphysema, gastric duodenal ulcer, gastroduodenitis, alcoholic hepatism, liver cirrhosis, seborrheic dermatitis, pruritus, other epithelial hypertrophy and xeroderma (Table 7-5).

In Type 2 prevalence analysis model in which the defoliant exposure levels were constructed as continuous variables, the diseases of which the prevalence risks increased with an increase in the exposure level were benign neoplasm of pituitary gland, neoplasm of uncertain behavior of thyroid gland, diabetes mellitus, insulin independent diabetes mellitus, post traumatic stress disorder, general atropy due to central nervous system, intermittent holding disease, epilepsy, nerve/nerve root and structural disorder, polyneuropathy, hypertension, primary

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hypertension, ischemic heart disease, agina pectoris, cerebral infarction, antherosclerosis, gastric duodenal ulcer, gastroduodenitis, alcoholic hepatism, unclassified chronic hepatitis, liver cirrhosis, seborrheic dermatitis, allergic contact dermatitis, pruritus, leukoplakia, other epithelial hypertrophy and xeroderma (Table 7-6).

The diseases, of which the prevalence rates of the high exposure group were higher than the low exposure group were diabetes mellitus, insulin dependent diabetes mellitus, insulin independent diabetes mellitus, hyperprolactinemia, intermittent holding disease, nerve/nerve root and structural disorder, polyneuropathy, hypertension, primary hypertension, ischemic heart disease, agina pectoris, cerebral infarction, antherosclerosis, gastric duodenal ulcer, gastroduodenitis, alcoholic hepatism, unclassified chronic hepatitis, seborrheic dermatitis, pruritus, leukoplakia, other epithelial hypertrophy, and xeroderma (Table 7-6).

In the 3-group comparison of Type 2 prevalence analysis, the diseases of which the prevalence risks were high in the high exposure group were neoplasm of uncertain behavior of thyroid gland, neoplasm of uncertain behavior of adrenal gland, hyperprolactinemia, metabolic disease, hyperlipedemia, post traumatic stress disorder, intermittent holding disease, epilepsy, polyneuropathy, primary hypertension, ischemic heart disease, agina pectoris, acute cardiac infarction, cerebral infarction, chronic bronchitis, gastric duodenal ulcer, gastroduodenitis, unclassified chronic hepatitis, seborrheic dermatitis, pruritus, leukoplakia, other epithelial hypertrophy and xeroderma (Table 7-7).

The diseases, of which the prevalence risk of the medium exposure group were high, were diabetes mellitus, insulin dependent diabetes mellitus, insulin independent diabetes mellitus, nerve/nerve root and structural disorder, polyneuropathy, ischemic heart disease, agina pectoris, antherosclerosis, other peripheral vascular disease, Buerger's disease, gastric duodenal ulcer, gastroduodenitis, ulcerative colitis, alcoholic hepatism, seborrheic dermatitis, other epithelial hypertrophy and xeroderma (Table 7-7).

When confounding variables by logistic regression analysis were controlled, the diseases, of which the prevalence risks increased with an increase of the exposure level in the same manner as Type 1 prevalence analysis, in which the defoliant exposure levels were constructed a continuous variable, were benign neoplasm of pituitary gland, neoplasm of uncertain behavior of thyroid gland, neoplasm of uncertain behavior of pituitary gland, Idiopathic thrombocytopenic purpura, thyroid gland disease, hypothyroidism, autoimmune thyroiditis, diabetes mellitus, insulin independent diabetes mellitus, other endocrine gland disease, hyperfunction of pituitary gland, hyperprolactinemia, hypofunction of pituitary gland, metabolic disease, hyperlipedemia, amyloid degeneration, paranoid schizophrenia, post traumatic stress disorder, general atropy due to central nervous system, Alzheimer's disease, intermittent holding disease, epilepsy, nerve/nerve root and structural disorder, polyneuropathy, cerebral palsy, cerebral infarction, chronic bronchitis, gastric duodenal ulcer, gastroduodenitis, liver cirrhosis, seborrheic dermatitis, allergic contact dermatitis, unspecified contact dermatitis, chronic simplex nuchae/ prurigo, erythema nodosum, other epithelial hypertrophy and xeroderma (Table 7-8).

The diseases, of which the prevalence risks were significantly higher in the high exposure group than in the low exposure group were benign neoplasm of thyroid gland, benign

neoplasm of pituitary gland, neoplasm of uncertain behavior of thyroid gland, neoplasm of uncertain behavior of adrenal gland, neoplasm of uncertain behavior of pituitary gland, thyroid gland disease, other hypothyroidism, other nontoxic goiter, autoimmune thyroiditis, diabetes mellitus, insulin dependent diabetes mellitus, insulin independent diabetes mellitus, other endocrine gland disease, hyperfunction of pituitary gland, hypofunction of pituitary gland, other hormonal disorder, metabolic disease, lipoprotein metabolic disorder, Alzheimer's disease, epilepsy, nerve/nerve root and structural disorder, polyneuropathy, cerebral palsy, agina pectoris, cerebral hemorrhage, intracerebral hemorrhage, cerebral infarction, chronic bronchitis, asthma, gastric duodenal ulcer, gastroduodenitis, liver cirrhosis, seborrheic dermatitis, allergic contact dermatitis, unspecified contact dermatitis, chronic simplex nuchae/prurigo, psoriasis, erythema nodosum, other epithelial hypertrophy, xeroderma and Behcet's disease (See Table 7-8).

When confounding variables were controlled by logistic regression analysis, the diseases, of which the prevalence risks were high in the high exposure group of the 3-group classification in Type 1 prevalence analysis were neoplasm of uncertain behavior of thyroid gland, neoplasm of uncertain behavior of adrenal gland, neoplasm of uncertain behavior of pituitary gland, thyroid gland disease, other nontoxic goiter, autoimmune thyroiditis, other endocrine gland disease, hyperfunction of pituitary gland, hyperprolactinemia, metabolic disease, hyperlipedemia, amyloid degeneration, paranoid schizophrenia, post traumatic stress disorder, Alzheimer's disease, epilepsy, polyneuropathy, cerebral hemorrhage, intracerebral hemorrhage, cerebral infarction, chronic bronchitis, gastric duodenal ulcer, seborrheic dermatitis, unspecified contact dermatitis, chronic simplex nuchae/ prurigo, hidradenitis, suppurativa, other epithelial hypertrophy and xeroderma (Table 7-9).

The diseases, of which the prevalence risks were high in the medium exposure group were benign neoplasm of pituitary gland, neoplasm of uncertain behavior of thyroid gland, hypothyroidism, diabetes mellitus, insulin dependent diabetes mellitus, insulin independent diabetes mellitus, hypofunction of pituitary gland, other hormonal disorder, Alzheimer's disease-dementia, extrapyramidal movement disorder, Parkinson's disease, secondary Parkinson's disease, nerve/nerve root and structural disorder, polyneuropathy, cerebral palsy, cerebral infarction, chronic bronchitis, asthma, gastric duodenal ulcer, gastroduodenitis, liver cirrhosis, seborrheic dermatitis, allergic contact dermatitis, unspecified contact dermatitis, chronic simplex nuchae/prurigo, erythema nodosum, other epithelial hypertrophy and xeroderma (Table 7-9).

When confounding variables were controlled by logistics regression analysis, the diseases, of which the prevalence risks increased as was the case with the exposure level in Type2 prevalence analysis, in which the defoliant exposure levels were constructed as continuous variables, were benign neoplasm of pituitary gland, neoplasm of uncertain behavior of thyroid gland, neoplasm of uncertain behavior of pituitary gland, diabetes mellitus, other endocrine gland disease, metabolic disease, hyperlipedemia, schizophrenia, general atropy due to central nervous system, spinal muscular atrophy, Alzheimer's disease, intermittent holding disease, epilepsy, nerve/nerve root and structural disorder, polyneuropathy, ischemic heart disease, agina pectoris, cerebral infarction, antherosclerosis, chronic bronchitis, gastric duodenal ulcer, gastroduodenitis, liver cirrhosis, seborrheic dermatitis, allergic contact dermatitis, unspecified contact dermatitis, chronic simplex nuchae/prurigo, pruritus, erythema nodosum, suppurativa, other epithelial hypertrophy, xeroderma and Behcet's disease (Table 7-10).

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Comparing to the low exposure group, the high exposure group's prevalence risks were significantly high in benign neoplasm of thyroid gland, benign neoplasm of pituitary gland, neoplasm of uncertain behavior of thyroid gland, neoplasm of uncertain behavior of adrenal gland, neoplasm of uncertain behavior of pituitary gland, thyroid gland disease, other hypothyroidism, other nontoxic goiter, diabetes mellitus, insulin dependent diabetes mellitus, insulin independent diabetes mellitus, other endocrine gland disease, hypofunction of pituitary gland, other hormonal disorder, metabolic disease, hyperlipedemia, Alzheimer's disease-dementia, paranoid schizophrenia, general atropy due to central nervous system, Alzheimer's disease, epilepsy, nerve/nerve root and structural disorder, polyneuropathy, ischemic heart disease, agina pectoris, cerebral infarction, chronic bronchitis, gastroduodenitis, seborrheic dermatitis, allergic contact dermatitis, unspecified contact dermatitis, chronic simplex nuchae/prurigo, pruritus, erythema nodosum, suppurativa, other epithelial hypertrophy, xeroderma and Behcet's disease (Table 7-10).

When confounding variables by logistics regression analysis were controlled, the diseases, of which the prevalence risks were the highest in the high exposure group in the 3-group comparison in Type 2 prevalence analysis were benign neoplasm of thyroid gland, neoplasm of uncertain behavior of adrenal gland, neoplasm of uncertain behavior of pituitary gland, other endocrine gland disease, hypofunction of pituitary gland, metabolic disease, hyperlipedemia, paranoid schizophrenia, post traumatic stress disorder, Alzheimer's disease, epilepsy, ischemic heart disease, agina pectoris, cerebral infarction, chronic bronchitis, gastroduodenitis, atopic dermatitis, seborrheic dermatitis, unspecified contact dermatitis, suppurativa, other epithelial hypertrophy, xeroderma and Behcet's disease (Table 7-11).

The diseases of which the prevalence risks were high in the medium exposure group were benign neoplasm of pituitary gland, neoplasm of uncertain behavior of thyroid gland, neoplasm of uncertain behavior of pituitary gland, hypothyroidism, diabetes mellitus, insulin dependent diabetes mellitus, insulin independent diabetes mellitus, hypofunction of pituitary gland, other hormonal disorder, Alzheimer's disease-dementia, general atropy due to central nervous system, nerve/nerve root and structural disorder, polyneuropathy, cerebral infarction, chronic bronchitis, asthma, seborrheic dermatitis, allergic contact dermatitis, chronic simplex nuchae/prurigo, erythema nodosum, other epithelial hypertrophy, xeroderma and Behcet's disease (Table 7-11).

D. Discussion

1) Discussion about the Study Methods

The names of main disease and sub-disease of government-sponsored treatment and health insurance examination data were used as the prevalence marker. Even though the validity of the main disease names as set forth in the national health insurance data has increased in comparison with the past, the fact that such disease names were recorded in the health insurance data does not necessary mean that veterans actually suffered from such diseases. Accordingly, it is of critical importance to examine how precisely the prevalence data from the main disease and sub disease names used in the health insurance data reflect the actual prevalence by conducting

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validity tests of significant diseases in the result of analysis.

Because those who died before June 2004 were excluded from this analysis, this prevalence study can underestimate the actual prevalence rates of specific disease, which is why the result of mortality analysis needs to be examined additionally. In this study, susceptibility of discovery of disease can be decreased when prevalence is considered only by main disease names, and thus a focus was made with respect to the results from Type 1 composed of the main disease names and the first sub-disease names.

In case of 136,603 people whose marker was constructed using the historic exposure reconstruction, the information relating to division/brigade level data for defoliant exposure level were used, and in case of 96,126 who participated in the survey, those relating to the battalion/squadron level data were used. Accordingly, the defoliant exposure marker the surveyed veterans was constructed more precisely.

To control many confounding variables, the logistics regression analysis was used. To the extent that there were any discrepancies in the analytic results from 136,603 veterans whose ages and military ranks were controlled only and those from the 96,126 surveyed veterans, a focus has been made on the analytic result from the surveyed veterans in which other factors such as smoking, drinking, obesity were controlled and thus a more detailed defoliant exposure marker could be constructed.

Since it is possible to have certain minute differences in prevalence due to the defoliant exposure in view of the number of study subjects and prevalence rates, certain diseases, which were suspected of having a correlation with defoliant exposure levels from all of various analyses, were mainly considered, rather than diseases showing statistical significance from each of such analyses.

2) Discussion about the Results

In the prevalence analysis of veterans, prevalence rates of many diseases were significantly lower than those of the general male population. This can be attributable to the "healthy soldier effect." Generally, indirect standardization prevalence ratio of Type 2 was higher than Type1, and this shows that a less number of veterans tends to visit hospitals with multiple diseases than the general male population. Also, the diseases of which the prevalence rates were significantly higher than those of the general male population were related to aftereffects or suspected aftereffects of defoliants. Like death analysis or analysis of incidence of cancer, to show the relation between exposure to defoliants and prevalence, we intend to mainly use veterans' internal comparison results according to the defoliant exposure level.

The result of prevalence analysis regarding relation between defoliant exposure and prevalence implies various significances. First, the result of prevalence analysis shows that defoliant exposure evaluation in this study is significant. Also this study will serve as a stepping-stone for studying the relation between defoliant exposure and prevalence going forward.

Second, this study raises the possibility that defoliants and diseases may be related to

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each other, and that that the relation between defoliant exposure and diseases can be identified by further studies. These diseases are not discovered at random, but their statistical significance was found in certain disease groups relating to certain specified systems in human body. Thus, we are of the view that this study demonstrates a possibility that the exposure to defoliants in one's youth may have impact on the diseases in 30~40 years. Accordingly, one may be able to better observe a correlation between defoliants and certain diseases of which such correlation is not currently clear by way of additional follow up studies.

E. Conclusion

As a result of prevalence analysis, the diseases of which the relation with defoliants was deemed as the most relevant were autoimmune thyroiditis, Alzheimer's disease and hypofunction of pituitary. There were many other diseases which had statistical significance.

The prevalence investigation was conducted retrospectively on the subjects who were alive as of June 2004. This study was not a study about occurrence of diseases, but a study about prevalence of diseases, so bias regarding occurrence-prevalence may be formed. Particularly, in case certain subjects died of certain diseases before June 2004, this study can underestimate the applicable disease prevalence risks.

Although main disease names and sub-diseases names recorded in health insurance inspection data were used as the prevalence marker, there are still some limitations as to the validity of such names in the health insurance inspection data, and it is reported that there are significant differences depending on specific disease types. In the future, an examination to see how precisely the prevalence data from the main disease names and sub-disease names used in the health insurance inspection data reflect patients' actual prevalence will be the key factor in evaluating the relation between defoliants and diseases.

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2. Evaluation

A. Introduction

1) Although the purpose is to try to establish causation between exposure and prevalence, it would be advisable to state that it is very difficult to establish such causation in any one-dimensional studies such as this Study Report.

2) Also it is better to mention that this study conducted not only the comparison within veterans of the Vietnam War, but also comparison with the general male population as well.

B. Study Methods

1) In this study, the explanation about the method of selection is necessary because not only among veterans, but also comparison with the general male population was conducted additionally.

2) In this study, researches used the health insurance inspection data and the treatment data of veteran's hospital for the period of 5 years and 9 months from January 2000 to September 2005 for veterans, while the health insurance inspection data for the period of 4 years and 9 months from 2001.1 to 2005.9 for the general male population was used. So the explanation about the different prevalence investigation period is necessary and certain adjustments are also needed because there were errors in calculating some periodic prevalence rates.

3) In this study, researchers used two grouping methods (type 1 using main disease and the first-sub disease names, type 2 using only main disease names) and classified hospitalization of one time or more or ambulatory care as a type of prevalence. Even though the accuracy of diagnosis is uncertain, it appears to pose no significant problem in comparing prevalence ratios as long as the accuracy level is same in every group. However, an explanation in this regard is still necessary. Going forward, however, further studies seeking to verify the disease names of the veterans and the general population by way of sampling, are necessary to increase accuracy of future analyses.

4) As it is explained in the examination section of this report, the more serious the disease is, the more accurate the diagnosis in the insurance record becomes. Accordingly, the validity of this study was seriously damaged because the method in which one time ambulatory care is also counted as prevalence may include one-time visit for diagnostic purposes. Thus, it is necessary to narrow down qualifications for prevalence such as at least two-time ambulatory cares of the same disease or hospitalization.

5) Researchers used a periodic prevalence rate to calculate the prevalence rate, notwithstanding the fact that the periods for comparison as applied to the veterans and the general population were different. We also note that no explanation was given as to why the period for prevalence rate determination started from 2000, while, in case researchers wished to rely on the insurance inspection data, those from as early as year 1997 or so were available. An additional

explanation in this regard is necessary.

6) Among the confounding factors which were controlled in logistic regression analysis, no reference was made as to any interaction among the military rank, age, education and income. An explanation about selection of the model is necessary.

7) As was the case with the number of death, it is desirable to defer any explanation on the number of prevalence if it is less than 5 people.

C. Results

1) Comparison of Veterans with General Population

The healthiest Korean people are presumed to have participated in the war among the same age group at the time of their entry into the war. Also, if the veterans survived for 30 years or more following the end of the Vietnam War, it is highly likely that the surviving veterans were healthier than other veterans. Moreover, the exposure level is different among the veterans. Therefore, we hereby suggest the following for the accurate comparison.

A) Comparison between Veterans and General Population

① Low exposure group among veterans vs. general population (a) → The prevalence rate of the low exposure group is expected to be lower than that of general population due to the healthy soldier effect.

② High exposure group among veterans vs. general population (b) → Despite the healthy soldier effect, the prevalence rate of the high concentration exposure group is expected to be higher than that of the low exposure group.

③ Evaluation of the prevalence rate by dividing (b) with (a), that is, the comparison value of the above two values → For example, assuming that (a) is 0.6, and (b) is 0.9, while these are lower than the prevalence rate of general population, the ratio of (b/a) is 1.5. We believe this method would supplement the prevalence rate due to the healthy soldier effect, and that, going forward, it would be desirable to see if there are any dose-response effects through further analyses on the trends among the low, medium and high exposure groups (Table 3).

B) Comparison between Veterans and Non-veterans

While this study compared among the veterans according to their exposure level, the exposure marker may be inaccurate, and the harmful effects from the fact of participation in the Vietnam War could not be identified. Hence, we believe that the most credible method would be to make a retrospective cohort comparison with a group of military personnel who were the members of non-participating forces as of the war participation (in the same manner as used in the study on the veterans) (regular-duty military personnel, career military personnel). The introduction of the study provides that such study method is not possible, but does not explain any reason. We hereby suggest reviewing the feasibility of the above method for implementation

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for future studies.

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3. Overall Opinion

1) The number of veterans should be corrected from 133,603 to 136,603.

2) Given that there are no explanations on the results of comparison between veterans and the general population, such explanations should be added. For example, "post traumatic stress disorder" was found to be significant only in this comparison.

3) Further explanations are necessary as to whether any diseases, which were previously unknown or found to have a low correlation, are found to have a high correlation through this study (or vice versa).

4) It is necessary to provide comparison tables and explanations according to the level of correlation. That is, it is necessary to identify types of diseases continuously did or did not show a correlation, regardless of exposure level, disease classification method and variation of analysis method, and provide the reasons therefor.

5) No explanation was given with respect to a disparity between the contents of document review set forth in Chapter 8 and the study results set forth in Chapter 7.

6) It is necessary to carefully analyze any diseases of which the accuracy of diagnosis is low and it would be desirable to set forth such details and to add the interpretation of the study results taking into account the accuracy of diagnosis.

Table 3. Comparison between the prevalence of disease developed among veterans and that among general population

Disease entity	ICD-10	General Population		General Veterans				High Exposure Group		Medium Exposure Group		Low Exposure Group		MRR1 between High Exposure Group and General Population (95% CI)	MRR2 between Medium Exposure Group and General Population (95% CI)	MRR3 between Low Exposure Group and General Population (95% CI)	Ratio of MRR2 (95% CI)	Ratio of MRR1 (95% CI)	p-trend (analysis of trend of age-adjusted prevalence rate among low, medium and high exposure groups)
		Number of Prevalence	Prevalence Rate	Number of Prevalence	Prevalence Rate	Expected Prevalence	Indirect Standardization Prevalence Ratio(95% CI)	Number of Prevalence	Prevalence Rate	Number of Prevalence	Prevalence Rate	Prevalence	Prevalence Rate						

** when the number of cases is less than 5, the results need to be reserved (It is recommended that RR 995% CI) is not provided).

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Chapter 8. Review of Literature on Defoliants

1. Report Summary

A. Introduction

This report reviewed and organized the domestic and overseas study results after reviewing the correlation between defoliants and resulting diseases. The review mainly focused on documents reported after the second epidemiological study on damages caused by defoliants, and briefly summarized and inserted data available prior to 2001 if deemed necessary. As for the exposure effects, the 2004 report by the Institute of Medicine of the U.S. (IOM) was mainly referred to, and Pubmed was used to research most recent studies. This report first explained the background surrounding respective diseases, summarized the results of reviewing documents up until 2001 when the second epidemiological study on damages caused by defoliants was about to commence, and lastly, analyzed recent documents and their review methods. The document analysis was conducted according to the type of exposure (e.g., occupation, environment and participation in the Vietnam War) and concluded with the level of basis for epidemiological study by disease, biological relevance, and the foundation for the Vietnam War veterans and epidemiology.

B. Basic Direction to Document Review

As the basic direction to the document review, researchers considered the following points: (i) whether or not statistical correlation exists between the exposure to herbicide and the diseases, in consideration of the portion of scientific evidence and appropriateness of statistical and epidemiological methods; (ii) whether or not the risk to diseases is higher for soldiers who were exposed to herbicides during their participation in the Vietnam War; and (iii) whether or not biological relevance or other evidence existed with respect to the causation between the exposure to herbicides and diseases.

C. Approach to Document Review

This study focused on reviewing the epidemiological study of humans as well as experimental studies. In order to evaluate the correlation between the exposure to herbicides and diseases, researchers reviewed the studies conducted on the Vietnam War veterans and the results of studies conducted on various participants. Also, inspections were conducted to see whether or not numerous factors including confounding factors, coincidence or selection bias or error in measurement factors that may affect the correlation existed, for the purpose of assessing credibility of evidence.

D. Scope of Review

The review mainly covered the toxicity of applicable ingredients and the assessment of exposure to toxic elements. Further, in order to examine the correlation between the exposure and specific diseases, this review classified the diseases largely into caner, genitalia and development effects, nerve disorder and other diseases in keeping with the method used by the Institute of Medicine of the U.S.

E. Conclusion

1) Disease

Table 8-1 summarizes the correlation between diseases and exposure identified through the document review, but the results of this pending study were not reflected.

2) Risk of Occurrence of Disease to Vietnam War Veterans

Numerous studies on Vietnam War veterans have been conducted, but most of the studies contained insufficient exposure evaluation on herbicides and TCDD, or had some problems in methods. Although sufficient evidence existed to draw a general conclusion on the correlation between diseases and the exposure to herbicides, there were limitations in quantifying and evaluating the disease occurrence risks of individual Vietnam War veterans or veteran groups, in view of the circumstances where the information on exposure level of the Vietnam War veterans was inaccurate.

2. Report Evaluation

Through the table 8-1, this report systematically categorized domestic and overseas documents by summarizing the results of primary studies on the correlation between the exposure to herbicides and diseases. Especially, it maintained homogeneity and validity when drawing a conclusion after evaluating the results of other studies by maintaining same standard for exposure type (occupation, environment, participation in the Vietnam War), level of foundation for epidemiological study by disease, biological relevance, foundations for the Vietnam War veterans and epidemiology.

V. Conclusion and Recommendations

Chapter 1. Introduction

The introduction systematically describes the past procedures and various facts related to Vietnam War veterans and defoliants, in order to help readers understand the overall development of this research study.

However, whereas the Vietnam War and defoliants section specifically described the ingredient of dioxin in great detail, researches on the correlation between veterans and defoliants and the measurement of diseases due to the exposure to defoliants which should be considered in the epidemiological study on damages caused by defoliants in Korea, were not sufficiently described. In addition, it is desirable to concisely state the exposure evaluation method as it can be sufficiently discussed in the detailed study method section. Description of the current compensation system (Aftereffect/Suspected aftereffect) pertaining to the basis for compensation for the Vietnam War veterans as well as the causation between the exposure to defoliants and diseases should be described in the main text, not the introduction section. It described that there will be a review on the difference between participants and non-participants in the medical examination and survey of the second epidemiological study. However, since such comparison was excluded in the main text, further explanations should be given in this regard.

Chapter 2. Development of Defoliant Exposure Index

In order to ascertain the relationship between the exposure to defoliants and related disease, accurate classification of exposure group and non-exposure group is essential, and to this end, the exposure to defoliants should be evaluated first. The general evaluation method of defoliant exposure are (i) exposure evaluation depending on the exposure or non-exposure, (ii) qualitative exposure evaluation; and (iii) quantitative evaluation, but all of which are vulnerable; it is thus necessary to develop a new exposure marker. For this reason, it would be desirable to specifically classify exposure groups by using defoliant exposure markers through self-reported exposure markers and historic exposure reconstruction, and use the outcome in reviewing the relevance among the markers.

Accurately evaluating exposure is exceedingly difficult where a fairly long period has lapsed since the occurrence of the exposure to defoliants. In this respect, there is no choice but to utilize the Stellman method, i.e., exposure index through the historic exposure reconstruction which was developed and used abroad; and thus, it can be evaluated as a desirable method. However, this report does not specifically explain the calculation of exposure amount by the aforementioned method nor does it sufficiently provide examples of the outcome and utilization of existing studies. Furthermore, it seems that this report does not sufficiently explain the consideration and supplementary measures with respect to the limitation of application such as shortage in specific information or assessment of low exposure. Given that the historic exposure reconstruction marker in the Stellman method plays a significant role, this should be supplemented in the preparation of the report.

Chapter 3. Analysis of Dioxin Concentration in the Blood among Veterans and Study on Validity of Index of Defoliant Exposure

Consistent terms should be used throughout this report. Dioxin is a kind of dioxin congeners and thus, 2,3,7,8-TCDD should be replaced with 2,3,7,8-TCDD or TCDD to avoid confusion. It is also desirable to use the phrase "healthy soldier effect," rather than "healthy worker effect". Where Le4 is 4 and Le4 is no more than 4, these cases should be all classified as the low exposure group. When explaining a concept of average in Table 3.5 (p.55), the terms "generally" or "respectively" were used, which may cause confusion. As such, an accurate choice of wording should be made. The number of dioxin congeners analyzed should be consistently used as 103 participants (p. 65).

In some respects, the flow of this report on the exposure index is illogical. Although the self-reported exposure marker is unreasonable whereas the Stellman index is reasonable, the report emphasized on the technology of dioxin as if such markers are not related to dioxin concentration, which gives rise to confusion to the readers. Logically, a better flow would be to say that one has no choice but to use the Stellman markers since the self-reported exposure marker and dioxin concentration are unreasonable, which would in turn better deliver the authors' assertion or position to the readers.

Dioxin's half life period was proven to have lapsed on several occasions so as to determine the exposure or non-exposure through the measurement of dioxin. Thus, the exact measurement on a fairly small amount of dioxin and selection of a comparison group based on which appropriate comparison is to be made would be most crucial. As such, if the appropriate comparison group and hazardous group are selected, it is possible to analyze the results of the study based on the occurrence rates of specific diseases and relevant diseases which are already known. In addition, because dioxin itself may be exposed to externally contaminated environments, it would be appropriate that the comparison group should be selected mainly among non-war participating military personnel whose physical conditions, ages or other factors are similar to those of the Vietnam War veterans.

Even considering the dioxin half life period (9~12 years), it is difficult to understand that the TCDD concentration which is below the minimum analysis level was detected in 100 among 103 persons. Drawing blood samples from the same study subjects or other Vietnam War veterans and having other institutions re-examine such samples should be considered.

Rather than classifying those having Le4 of 0 to less than 0.1 as falling under the low exposure group, it is desirable to subdivide such persons as the non-exposure group (or exceedingly low-exposure group), low exposure group, etc. Such subdivision would be more appropriate to observe the dose-response effect where no comparison group exists.

Chapter 4. Survey of Veterans

This study was significant in that it performed surveys on a much larger number of people relative to the first and second prior studies, improved the response rate and strengthened credibility towards the study results, and investigated factors that affect health levels, as mentioned by the researchers. Matters that could be supplemented or further considered include data related to war participation such as military rank, military branch, and duration of service, and more detailed analysis of such data. The general limitations in surveys such as the possibility of selective bias or retrospective bias may also exist and should be supplemented by other methods. Comparing the characteristics of persons that did not respond could also increase the validity of this study.

Provider checks on confounding factors, for example, jobs after the war of veterans, drinking and smoking during the war, and objective data of disease incidence and prevalence, such as health insurance data or medical records by health care providers are necessary. Moreover, further and more concentrated researches are necessary with regard to certain diseases such as skin diseases that commonly show a relation to exposure markers. Surveys on national policies regarding defoliants should be more comprehensive and quality-based, in addition to the quantitative research conducted in this study. There are limitations in using an approach based solely on scientific grounds when studying the problems of compensation and management, which is beyond the capabilities of epidemiological study researchers. Therefore, political and policy oriented studies and consideration are necessary.

Chapter 5. Participation in the Vietnam War, Exposure to Defoliants and Mortality

By excluding persons who died before 1992 from the subjects of this study, this study could not show any early effects. If many members of a high risk group that suffered serious harms from serving in Vietnam or being exposed to defoliants died before January 1, 1993, when a cohort was formed, it is possible to underestimate the risk of death from Vietnam War participation or defoliant exposure. It is possible to make critical errors in information and there are many restrictions in interpreting the results if selection survival bias comes into play. Thus, in constructing exposure level marker, it is necessary to perform further analysis applying Le4, which uses data on the squadrons or troops level.

Due to possible confusion on the standardization methods in Vietnam War participation and deaths, it is proper to display all in one table, and this applies to defoliant exposure levels and deaths regarding veterans. Even in cases where the number of deaths is low and less than five, notwithstanding any statistical significance attached thereto, the possibility of coincidence cannot be ruled out, and it is necessary to refrain from writing anything on Standardized Mortality Ratio (SMR), Direct Mortality Ratio (DMR), and the ranges of credibility concerning them. When less than five cases are observed in a single cell, it is proper to interpret the results when cases of death, incidence, or prevalence of disease are based on a larger number of study subjects.

Chapter 6. Participation in the Vietnam War, Exposure to Defoliants and Development of Cancer

This study dealt with defoliant exposure to Vietnam War Veterans and conducted an analysis of whether such exposure acted as factors that increased the risk of cancer based on Korea's cancer rate. It is important to note that the possibility for development of new defoliant exposure marker stated in the purpose of the study is limited. Moreover, even if all currently available data in Korea is applied, it is difficult to overcome the data restraints in Korea. Due to the inherent limitations in conducting such studies, it would be difficult for other researchers to conduct studies better than the one conducted here.

Cases of cancer that arose before 1992 were not dealt with in this study and the reason for this was not detailed. By excluding cases where cancer diagnosis occurred immediately after defoliant exposure, the early effects were excluded from this analysis of the risk of cancer as a result of exposure. If the early effects are significant, it would increase the chance of producing error. Therefore, indicating the reason for this omission is necessary. While the investigation and follow-up period was from 1993 to 2003, it is desirable to observe whether there are differences in the mid to long term effects shown by subdividing this 11-year period into two periods, (e.g. 1993 to 1997; and 1998 to 2003) in a comparative analysis of cancer rates among the study subjects and direct standardized cancer rate applying the cancer rate of the general Korean male population to standardized rates. It is appropriate to defer rendering analysis and explanation on data of less than five people with regard to cancer incidence, as well as deaths.

Although it is possible that defoliant exposure and risk of cancer for Korean veterans are different from those of other countries, if the study methods and levels of exposure are the same, interpretation of such differences is unfeasible, not because there is anything distinctive about Koreans in cancer diagnosis, but since it is impossible to rule out the different environments that veterans have been exposed to defoliants. Granting compensation for the sole reason that one is a veteran exposed to defoliants would render epidemiological studies seeking to obtain evidence for the purpose of setting standards for compensation meaningless. However, observing and following up on high risk factors like defoliant Exposure, including tracking diseases that arise from the effects, should continue.

Chapter 7. Exposure to Defoliants and Prevalence of Disease

This study retrospectively investigated the prevalence of diseases among the subjects currently living. It is possible that this study will be biased towards studying the incidence of diseases instead of the prevalence of diseases. If subjects with diseases have died before the study began, this prevalence study could underestimate dangers regarding the prevalence of the diseases. Moreover, by comparing Vietnam War veterans and the general public, the healthy soldier effect may heavily influence the study results. The reasonableness of the diagnosis recorded on health insurance data, used in this study, still has limitations and large differences are reported depending on the disease. Observing the accuracy of whether a patient actually has the disease stated in health insurance records, by way of an investigation into the validity of the diagnosis stated, will be very important in evaluating the relation between defoliants and diseases.

It is necessary to identify certain diseases, among the diseases that were perceived to have a weak correlation to the defoliants or were not well known, which is found to have a strong correlation to the defoliants according to this study, and vice versa. Tables and explanations comparing the different levels of connections are necessary. In other words, it is important to explain which diseases show and which do not show continuous correlation regardless of variations in exposure level, disease classification method, or analysis method. In addition, it is important to exercise caution when interpreting diseases that have low accuracy rates in diagnosis, make a note of such fact, and add interpretations of research results in accordance with the level of accuracy in the diagnosis.

Chapter 8. Review of Literature on Defoliants

Through Table 8-1, this report systematically categorized domestic and overseas documents by summarizing the results of primary studies on the correlation between the exposure to herbicides and diseases. Especially, it maintained homogeneity and validity when drawing a conclusion after evaluating the results of other studies by maintaining same standard for exposure type (occupation, environment, participation in the Vietnam War), level of foundation for epidemiological study by disease, biological relevance, foundations for the Vietnam War veterans and epidemiology.

Chapter 9. Policy Proposals

The results should be used to present the type of compensation to be granted, as well as how and under what conditions such should be granted, so that policy proposals can be made. Separate research on this policy issue is necessary in this regard. Since this study was conducted with a key focus on scientific evaluation, the policy aspect should be considered separately from such scientific evaluation in the future.

The Act Related to Support for Patients Suffering from Quasi-Aftereffects of Defoliants (the "Act") considers defoliant victims to include, not only Vietnam War veterans, but also persons that worked in the North-South border area, civilians attached to the military, and members of the press. However, the Act limits Vietnam War Veterans as the subjects of defoliant epidemiological studies, and it is necessary to expand the scope of study subjects. Dividing and presenting various diseases of this study into such that have "aftereffects" and "suspected aftereffects" would help in the understanding of laws and disease incidence phases. Moreover, if this study should provide grounds for compensation in the future, it is necessary to consider the validity of dividing diseases into such that have "aftereffects" and "suspected aftereffects" presented under the Act, as well as new diseases that may need to be considered additionally in the future. The Act specifies support measures related to different types of compensation and medical treatment, and deeper research and analysis is necessary in learning the actual effectiveness of the Act, including the amount of actual compensation and problems in the procedures for compensation and medical treatment. The second generation victims of defoliants, who suffered from Spinal bifidia, peripheral neuropathy, and paraplegia due to spinal cord lesion, are recognized as aftereffects patients. It is necessary to review defoliants and its genetic effects through broad research on second generation victims.

The Second Epidemiological Study on Damages Caused by Defoliants and the scientific evaluation report on the study presented proposals for researching policies relating to defoliants and evaluations on such, but the proposals and evaluations were hardly reflected in this study. There is a need for further research on the effectiveness of policies for defoliant victims in the future.

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Levy

Human TCDD 2,4,5-T

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Potential Exposure of Humans to 2,4,5-T and TCDD in the Oregon Coast Ranges

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ABSTRACT

Potential Exposure of Humans to 2,4,5-T and TCDD in the Oregon Coast Ranges.[1] Newton, M. and Norris, L.A. (1981). *Fundam. Appl. Toxicol.* 1:339-346. Research on the use of 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) contaminated with 2.5×10^{-6} parts 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in forests of the Oregon Coast Ranges permits estimates of human exposures for both compounds. Estimated total exposure of nearby (~1/8 mile distant) residents during the first week after application is 0.0039 mg/kg of 2,4,5-T for a 70-kg adult. Exposure to TCDD in the same episode would be 1.9×10^{-10} mg/kg. Nearly half the total exposure, *i.e.* 0.0019 mg/kg 2,4,5-T and 5.0×10^{-11} mg/kg TCDD would occur the first day. Based on published and unpublished acute no-effect estimates of 40 mg/kg for 2,4,5-T and 0.0001 mg/kg for TCDD, the smallest safety factors for the two chemicals are 20 000:1 for 2,4,5-T for 1 day and 1 000 000:1 for TCDD for 1 week. Applicators are far more heavily exposed, with daily maximum actual intake for helicopter loaders (the highest exposure group if they do not wear gloves) of 0.063 mg/kg per day 2,4,5-T and 1.6×10^{-9} mg/kg per day TCDD. Minimum safety factors for the most heavily exposed workers based on these data are estimated at 635:1 for one-time exposure to 2,4,5-T; 83 333:1 for one-time exposure to TCDD; 318:1 for daily exposure to 2,4,5-T; and 625:1 for daily exposure to TCDD. Nearly all exposure to 2,4,5-T in forestry operations is through dermal contact. Inhalation appears minor. Urine is a reliable indicator of exposure to 2,4,5-T if collected within 1 to 4 days of exposure (depending on the degree of exposure). Human skin exposed to a concentrated spray mixture containing 38.4 g 2,4,5-T per liter, as the ester, transmitted 0.0013 mg/cm^2 per hr during the period of saturated contact.

INTRODUCTION

Use of phenoxy herbicides in forested areas of Oregon and elsewhere has prompted fears that applicators and residents might be exposed to harmful amounts of the chemicals. This paper is a synthesis of data obtained through 16 years of research and provides insight into the extent of exposure of humans from forest applications of 2,4,5-trichlorophenoxyacetic acid (2,4,5-T), with its contaminant 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD).

Humans may be exposed to herbicides through drift; ingestion of wild and domestic meat, vegetables, and fruit; consumption of water; and dermal contact while handling the chemicals, equipment, and treated vegetation. The range of potential exposure extends from zero, if there is no encounter with the herbicide, to the worst situation where the person has encountered the highest levels of water contamination, drift exposure, meat contamination, and dermal exposure simultaneously. We have brought estimates of all sources together to determine the possible range of total exposure from all sources.

The human health risk from short-term exposure to a chemical is a function of the level, duration, and frequency of contact dose with the chemical, compared with the maximum level, duration, and frequency of exposure producing no symptoms. The frequency of exposure producing no symptoms is estimated from animal tests in the absence of controlled human experiments. We are operating under the general assumption that exposure has no health implications unless the chemical enters the body where physiological processes must deal with it. The degree of risk is estimated by the ratio between the maximum no-observed-effect level (NOEL) and that level of intake encountered in various relevant human activities. This ratio may be used to express a "safety factor." Thus, a safety factor of 100 means the maximum no-effect level is 100 times larger than the maximum exposure. Safety factors calculated from "worst case" exposures provide the most conservative estimates of actual safety. Safety margins increase as frequency of exposure decreases and the risk of chronic intoxication subsides. We have assembled data from various sources to estimate several worst-case types of exposures.

METHODS

The findings reported here are based on a study of human exposure through dermal contact, research and monitoring of field applications and water quality since 1963, and studies of wildlife contamination occurring with field use of herbicides. We relied on literature to provide estimates of drift and threshold or maximum "no-observed-effect" parameters of toxicity.

Exposure through dermal contact — applicators

A commercial herbicide applicator may come in direct contact several days per week during a 3- to 6-month spray season. Applicator exposure is reported as largely dermal (USEPA 1978, USDA 1979). It is therefore necessary to estimate the rate of transport through skin when a mixture containing a specific concentration maintains contact with a given area of skin.

[1]A preliminary report of this publication was presented at the 1980 Weed Science Society of America meeting, Toronto, Canada, February 6, 1980. This publication reports research involving pesticides. It does not contain recommendations for their use nor does it imply that the uses discussed have been registered. All uses of pesticides must be registered by appropriate State and/or Federal agencies before they can be recommended.

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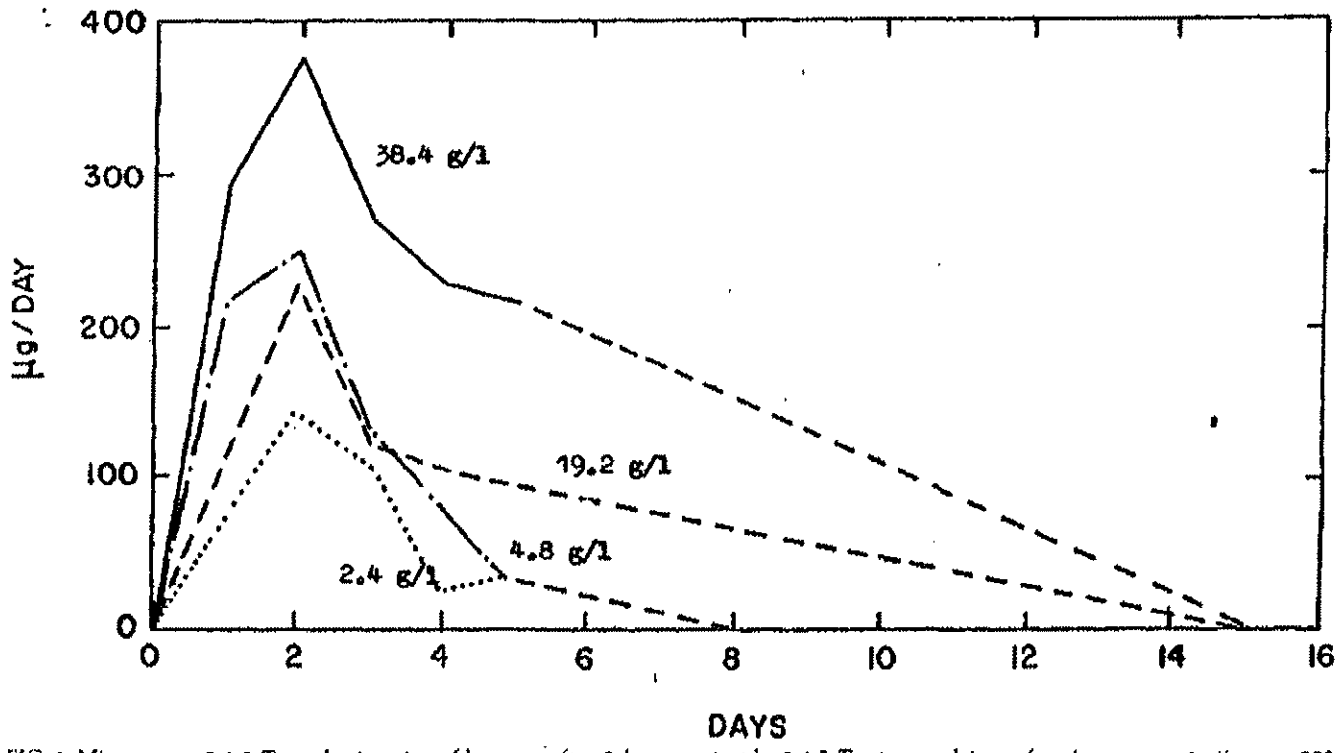

FIG. 1. Micrograms 2,4,5-T per day in urine of humans after 2-hour contact by 2,4,5-T ester emulsions of various concentrations on 900 cm^2 of skin.

Specific absorption rate by human skin — experimental

Data on the absolute penetration of 2,4,5-T through skin was lacking in the literature. It was therefore necessary to conduct an exploratory controlled experiment to determine the rates at which operationally used mixtures of 2,4,5-T would lead to physiological exposure of humans. An exposure test was run on four volunteers, including one woman. Contact was provided by placement of 900-cm^2 bleached denim patches on the thigh, at which time 40 mL of 2,4,5-T propylene glycol butyl ether ester emulsion was applied by syringe, saturating the patch to the drip point. Concentrations applied to patches included the range of those in registered use, varying from 2.4 to 38.4 g/liter acid equivalent in the spray mixture (2 to 32 lbs/100 gal).

After application of herbicide to the patch, the patch was covered with plastic film to prevent drying, and pressed against the skin firmly with an elastic bandage, bringing a continuous liquid phase into contact with skin. After 2 hours, the bandage and patch were removed and skin cleaned with isopropyl alcohol swabs. All patches and swabs were saved for analyses.

Physiological exposure was measured in terms of recoverable 2,4,5-T in urine. Absorption of 2,4,5-T was measured by analysis of the total amount of herbicide eliminated in the urine, as described by Gehring *et al.* (1973). Urine collection began 24 hours before application of the treated patch, with 24-hour samples being composited for a period of 5 days. Aliquots of the composites were analyzed using a procedure similar to the method of Smith and Hayden (1979) using the macroreticular resin XAD-7.[2] According to Gehring *et al.* (1973), 2,4,5-T taken by mouth is almost entirely eliminated in urine within 6 days. According to their calculations, half the 2,4,5-T in plasma disappeared in about 23 hours, suggesting that the total physiological body burden would at no time exceed twice the amount recovered in any 23-hour period.

The denim patches offered some opportunity for adsorption of the chemical, hence there is a degree of uncertainty as to how much chemical was free to move into the skin. Adsorption to denim is weak, however, as evidenced by the apparent ease with which nearly all unhydrolyzed ester may be washed from such fabric. In contrast, skin with its lipid content, has substantial affinity for the ester. A precise calculation of partitioning between skin and denim was beyond the scope of this experime approximation of that
originating from liquid contact. Furthermore, the reservoir represented by the large volume of emulsion held in contact by the cloth is substantially greater than would be present in typical exmay be washed from
such fabric. In contrast, skin with its lipid content, has substantial affinity for the ester. A precise calculation of partitioning between skin and denim was beyond the scope of this experimeposures through splattering or incidental contact.

Excretion of 2,4,5-T in urine after the highest levels of dermal exposure was not as rapid as Gehring *et al.* (1973) observed after oral ingestion. Lower concentrations approximated the rate of elution they observed, but higher concentrations showed evidence in skin of a rate-limiting phenomenon of unknown cause. It was therefore necessary to extend the recovery curves by extrapolation according to proportional degradation curves from exposed applicators (USDA 1979), so that they could be integrated for estimation of total output (fig. 1). Analyses of patches and swabs demonstrated that such a small proportion of total applied herbicide was taken up by skin (≈0.2 percent) that we could not estimate unmeasured retention by difference because of its remaining within the analytical error for the large residue on the patches. Each curve on figure 1 represents the recovery from a single dosing.

[2]E.R. Johnson and M.L. Montgomery, Department of Agricultural Chemistry, Oregon State University, Corvallis, analyzed the urine for 2,4,5-T.

TABLE 1
Total Absorption, Rate of Absorption, and Maximum Exposure Level in Humans Subjected to 2-Hour Dermal Contact with 2,4,5-T Ester Emulsion on a 900-cm² Area

Concentration of 2,4,5-T on patch	2,4,5-T Absorbed			Maximum[A] body burden per hour of contact	Absorption rate
	Measured[B]	Estimated[C]	Total		
g/L	mg	mg	mg[D]	mg	mg cm $^{-2}$hr $^{-1}$
2.4	0.381	0.060	0.441	0.284	0.000245
4.8	0.718	0.120	0.838	0.500	0.000466
19.2	0.664	0.480	1.140	0.444	0.000633
38.4	1.380	0.960	2.340	0.752	0.0013

[A]These data (derived from fig. 2) are expressed in total exposure. To estimate toxic burden, milligrams must be divided by kilograms body weight.

[B]Measured 2,4,5-T recovered in urine in first 5 days.

[C]From extended curves as in figure 2. Integrals plotted and values obtained from function: mg eluted = 30X (concentration, ach g) which is a linear approximation of the integrals.

[D]Sum of measured and estimated postmeasurement amounts.

TABLE 2
Maximum Field Exposure to 2,4,5-T in 70-kg Applicators[A] Estimated from Dermal Experiments with Humans and Compared to Measured Exposure in the Field

Job description	Skin exposed	2,4,5-T concentration	Dermal uptake		From Ramsey *et al.* (1979)
			Total	Net	
	cm²	g/liter	mg	mg/kg[A]	mg/kg
Backpack applicator, 3 hr/day nozzle time (long-sleeved shirt, but no hat or gloves)	1800	19.2	3.42	0.049	0.015-0.108
Mixer-loader[B] (gloves, hat, coveralls)	225 (900)	48	1.10 (4.39)	0.016 (0.063)	0.015-0.121
Flagger (hat and long-sleeved shirt)	900	24	0.367	0.005	0.0015-0.004

[A]70-kg body weight.

[B]Difference between our data and those of Ramsey *et al.* (1979) may be attributable to assumption that gloves were worn constantly. Figures in parentheses reflect expected exposure without gloves.

We regard the total measured and estimated recovery of 2,4,5-T in urine as a reasonable approximation of dermal absorption during a continuous, saturation-level exposure lasting 2 hours. Based on this assumption, it is possible to estimate total physiological exposure from dermal contact with 2,4,5-T on the basis of spray concentration, duration of exposure, and area of skin exposed. Table 1 illustrates total measured and estimated absorption, rate of absorption per unit of skin area by concentration, and maximum momentary physiological exposure resulting from exposures encountered in this experiment.

Clearly, this experiment is only a preliminary estimate of absorption, with too few persons to provide useful statistical treatment. There is uncertainty in the extrapolation curves in that their kinetic properties were determined by another series of observations with dermal exposures of 2,4,5-T on the senior author, on whom the highest concentration had been applied. In view of the majority of elution having taken place during the first 5 days, we believe the error from this origin to be small. Another potential uncertainty arises from using denim patches with an unknown partition coefficient for 2,4,5-T. We feel that this uncertainty is also small, because 2,4,5-T ester appears to

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be weakly bound by bleached cloth, the ratio of herbicide to cloth was high, and the occurrence of fatty substances in skin would favor partition of herbicide toward skin instead of cloth. Thus, despite acknowledged uncertainties and small sample size, we feel that these data are internally consistent and are a reasonable first approximation of absorption of 2,4,5-T by human skin in the absence of other data.

Estimated absorption from discontinous contact

Exposure of applicators who soak clothing, or who otherwise come in continuous contact with a spray mixture, may be estimated from the above calculations. The flaggers, who guide aircraft from below, encounter a different type of exposure. Droplets do not cover the skin completely, and the vertical orientation of skin does not expose a frontal target. Absorption must then be estimated from vertical projection of exposed skin, coverage estimates, number of times hit per day, and percent of chemical absorbed. For the latter quantity, we rely on the measurement of 5-percent absorption for 2,4-D by Serat *et al.* (1973), and assume that the flagger was directly sprayed eight times per day at a rate of 2.2 kg/ha. Table 2 provides such estimates for several tasks associated with application of 2,4,5-T, based on expectation of exposing known areas of skin.

Table 2 compares estimates derived from our experiment with data observed under field conditions by Ramsey *et al.* (1979). It is noteworthy that there is reasonable agreement where chemical of known concentration is encountered by reasonably well-defined areas of skin for a finite interval.

Exposure of forest residents through water, food, and air

Exposure through drinking water

Our research on levels of herbicide contamination resulting from forest usage near streams extended from 1963 to 1968 continuously, and intermittently to the present. Much of the research was conducted before untreated buffer strips were required along streams to reduce direct stream contamination in Oregon. This program has determined the range of contamination levels likely to be encountered in streams flowing from or through forest areas treated operationally with herbicides for vegetation control with or without streamside buffers. In addition to research, monitoring by public agencies has provided extensive data regarding field-use levels of contamination when buffer strips are used. These monitoring data indicate that contamination levels under practical conditions of herbicide use are substantially below the maximum observed in our research intended to measure "worst-case" situations.

In the research and monitoring program for herbicide contamination of forest watersheds, streams were sampled at various intervals, extending from before treatment to 13 months later. Phenoxy herbicides were emphasized in these studies because of their wide use. Similar but less detailed studies of atrazine, amitrole, dicamba, glyphosate, picloram, and triclopyr have yielded similar findings. Results of specific experiments with streams have been summarized (Norris, 1967, 1978; Norris and Moore, 1976).

Our findings to date have demonstrated that, with few exceptions, herbicide found in stream water is the result of direct application to the water, including deposit of fine droplets at the edge of swaths. At most, marginally detectable quantities have reached water through runoff subsequent to application unless heavy rains followed application immediately. Virtually all stream contamination represented by our data is the result of aerial application. In all instances, contamination has been at very low levels and of very brief duration.

For our calculations, we used data from the most heavily phenoxy-contaminated stream under study in western Oregon to estimate the upper limit of exposure through drinking water (Norris, 1967). Our watershed of maximum contamination was treated with 2,4-dichlorophenoxyacetic acid (2,4-D), a compound closely related to 2,4,5-T. The pattern of concentration in this stream showed an abrupt peak of 0.071 mg/liter shortly after treatment, followed by a decline to 0.044 mg/liter 4.5 hours after treatment. This concentration decreased gradually in the pattern of slow-moving water, reaching nondetec-

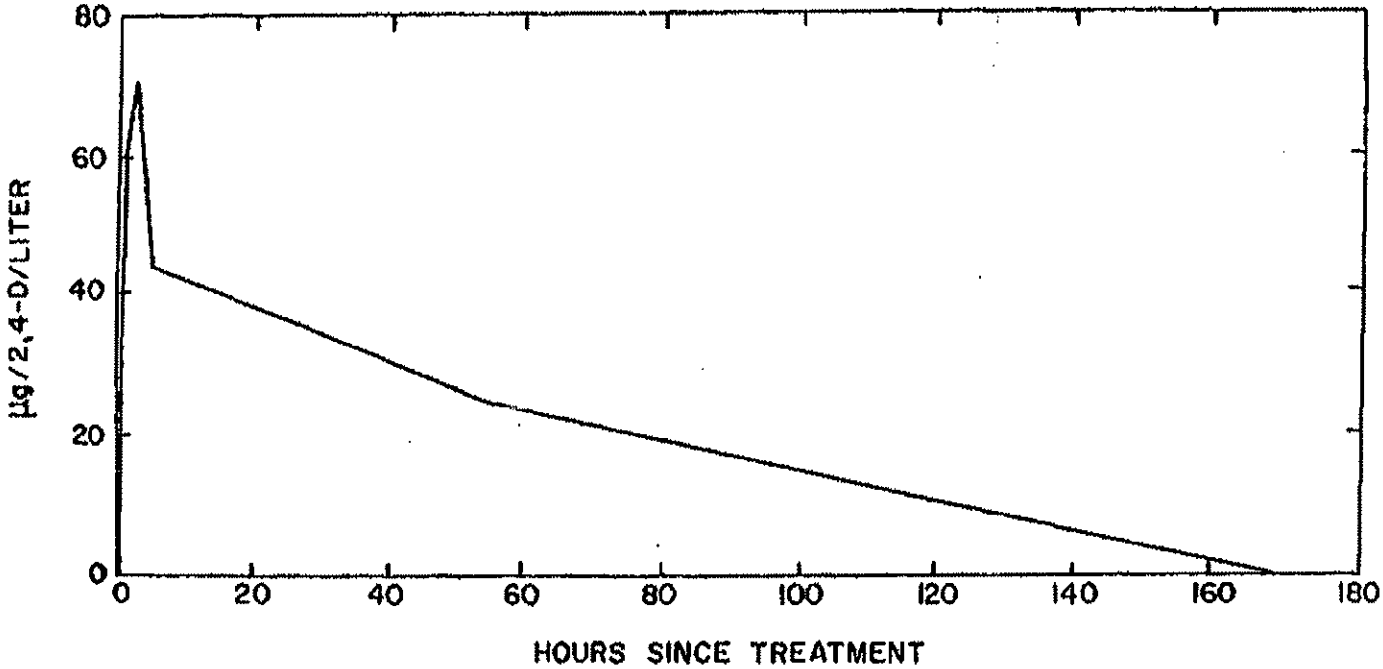

FIG. 2. Herbicide concentration in the most heavily contaminated forest watershed (Hunt Cr., 1965) treated with 2½ pounds 2,4-D per acre without buffer zones.

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TABLE 3
Maximum Total Exposures of Nearby Residents to 2,4,5-T and TCDD from Water, Wildlife, and Drift After Application[A]

Source	Total		Dose (70-kg person)		Safety factors	
	24 hrs	168 hrs	24 hrs	168 hrs	24 hrs	168 hrs
	.....mg.....		.....mg/kg.....			
2,4,5-T						
Water (creek)	0.136	0.267	0.0019	0.0038		
Venison	0.0021	0.0095	0.00003	0.00014		
Atmosphere	0.00075	0.00075	0.00001	0.00001		
Total	0.139	0.277	0.0019	0.0039	21 053	35 897
TCDD						
Water (creek)	3.4×10^{-9}	6.67×10^{-9}	4.9×10^{-11}	9.5×10^{-11}		
Venison	5.2×10^{-11}	2.37×10^{-10}		7.43×10^{-13}		3.4×10^{-12}
Atmosphere	1.9×10^{-11}	1.9×10^{-11}	2.7×10^{-13}	2.7×10^{-13}		
Total	3.5×10^{-9}	6.9×10^{-9}	5.0×10^{-11}	9.8×10^{-11}	2 000 000 [C]	1 010 101 [C]

[A]Residents not involved in handling materials. Assumes 100 g deer liver per day; 454 g per week. Safety factors based on acute and chronic no-effect levels of 2,4,5-T, and acute levels of TCDD taken in one or seven increments. No-effect levels are:

2,4,5-T: 24 hrs - 40 mg/kg; chronic dose - 20 mg/kg per day; 168 hrs - 140 mg/kg (*i.e.*, seven daily doses of 20 mg/kg per day)

TCDD: 24 hrs - 0.0001 mg/kg; 168 hrs - 0.0001 mg/kg (*i.e.*, the single no-effect dose delivered in seven increments)

table levels (≤0.001 mg/liter) 168 hours after treatment (fig. 2).

The maximum amount of herbicide that could be taken internally by a human using this water for total water supply was estimated by assuming ingestion of water at the rate of 2 liters per day, integrated for the 168-hour period. Integrating the total for the week of contamination, a total ingestion of 0.267 mg of herbicide would result, of which 0.136 mg would be ingested the first day.

The 2,4-D-treated watershed represents an example of highest potential contamination with 2,4,5-T. We use herbicide levels to calculate the maximum contamination with TCDD, making the assumption that the ratio of 2,4,5-T to TCDD remains constant in water after initial contamination. Recent data indicates that TCDD concentration in 2,4,5-T acid ranges downward from 2.5×10^{-8} (USEPA, 1979a). Based on 0.071 mg/liter of 2,4,5-T (containing 2.5×10^{-8} parts TCDD) our worst-case example provides a peak stream loading of 1.77×10^{-9} mg/liter TCDD (1.77 parts per quadrillion), with a week-long integral of 6.67×10^{-6} microgram if 2 liters of water are consumed per day. Such concentrations of TCDD are substantially below the present detection limit for TCDD in water, and, in fact, TCDD has not been detected in any stream.

The low solubility of TCDD (Anonymous, 1978) suggests that there will be greater differential adsorption of TCDD on sediments in preference to 2,4,5-T, and that the actual exposure to TCDD will be lower than the calculated level (Isensee and Jones, 1975). Although adsorption is reversible, release of the TCDD into water would be minor because of the extremely low original input and the strong partition in favor of the sediment. Degradation takes place during the period of adsorption, hence total exposure would be reduced both by the adsorption phenomenon and by degradation *in situ*. Thus, our estimate of exposure is not likely to be exceeded, or even used.

Contamination of wildlife

Ingestion of contaminated wild foods from sprayed areas represents another potential source of human exposure. Forests with serious brush problems abound with deer and occasionally support edible blackberries and mushrooms. Our data are limited to wildlife because of the low expectation of finding edible, accessible fruit or mushrooms in sprayed areas. The obvious odor during the period immediately after application, and visible signs of damaged vegetation later, indicate that such foods have been treated with chemical. These signs, therefore, render them unlikely to be collected for consumption.

Venison is often a part of the diets of rural residents, and deer are exposed when their habitat has been treated. Other forest wildlife species also may be consumed in smaller amounts by humans. We will summarize some of our findings from analysis of wildlife in herbicide-treated areas.

Forest wildlife have been examined for residues of 2,4,5-T, TCDD, and atrazine in forested areas aerially treated with 2,4,5-T or atrazine (Newton and Norris, 1968; Newton and Snyder, 1978; USDA, 1979). We have found residues of 2,4,5-T in deer to be nondetectable (<0.006-0.010 mg/kg detection limit) in all edible parts of animals except the liver when the animals were killed 10 to 43 days after application (Newton

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and Norris, 1968). A residue of 0.021 mg/kg was observed in the liver of one animal. Deer were observed to have concentrations in the rumen of roughly one part per million or less of either herbicide per acre-pound of 2,4,5-T used on the habitat. The lack of retention of 2,4,5-T, we noted, was consistent with the findings of Clark *et al.* (1975) and St. John *et al.* (1964) for other ruminants. These workers observed that 2,4,5-T is excreted unchanged, largely in the urine, with a low degree of retention by tissues other than the liver.

If a forest resident consumes 454 g (1 pound) of deer liver with the maximum level of contamination (0.021 mg/kg 2,4,5-T) during 1 week, total exposure from that source will be 0.0095 mg of 2,4,5-T. TCDD from the same source cannot be estimated precisely, because detectable residues of TCDD in livers of deer, cattle, or rodents have not been reported in the scientific literature[3] at detection limits down to 3 ng/kg (3 parts per trillion) (Newton and Snyder, 1978). If TCDD were present at 2.5×10^{-8} times the amount of 2,4,5-T, the total amount of TCDD would be 2.375×10^{-10} mg per 454 g liver. In view of the compensatory tendencies of TCDD to be retained in liver more than 2,4,5-T, but to degrade more quickly on forage, we believe the ratio of TCDD to 2,4,5-T given is reasonable in the short term and generous in the long term.

[3]Two recent reports have been presented at the U.S. Environmental Protection Agency cancellation hearings on 2,4,5-T indicating detectable residues of TCDD in fat of deer and elk. One data set, presented by USDA, observed that penned deer exposed to food supplies treated directly with 3.3 kg-ha 2,4,5-T showed TCDD residues in fat of 0-0.0046 μg/kg. The presence of TCDD residues in one of two control deer opens questions as to the source of dioxin. Assuming the levels reported originated from 2,4,5-T, and applying a five percent factor to allow for the proportion of the total range of unpenned deer likely to be treated, the USDA levels are nearly identical with those we have used. The other unpublished data set was presented by the Environmental Protection Agency. They described TCDD in fat of deer and elk collected in unspecified proximity to sites with some history of 2,4,5-T treatment. These data have been discounted in our analysis because of their finding (in addition to the 2,3,7,8-TCDD) two isomers not found in 2,4,5-T. This finding casts considerable doubt as to whether 2,4,5-T could have been the source.

Atmospheric exposure

Drift from forest applications tends to be a transitory phenomenon. Aerial applications of herbicides to forests use large droplet sizes and high volumes. When applied from a low-flying airplane, droplets have a volume adjusted mean diameter (VMD) on the order of 450 microns. According to Yates *et al.* (1974), an average of approximately 1 percent of total spray volume may move more than 100 m away from the point of application at wind velocities of 8.3 to 16 miles per hour. Forest spray operations are typically conducted early in the morning, when air movement is nearly still. Applications are terminated when winds begin to move in gusts of more than 5 miles per hour. Such gusts, when they do occur in the morning, are the result of thermal currents, usually up-valley. Typically, residences are down-valley from large tracts of commercial timberland, or downslope. Thus fine spray particles, if present, tend to move away from residences or do not travel.

Phenoxy herbicide esters have low but measurable vapor pressures. Air vapor content varies with temperature and area treated. Vapors move downhill as air cools during the evenings of hot days. Only low-level exposure upwind will occur. The vapor load carried by air has been summarized for various esters of 2,4-D by the National Research Council of Canada (Anonymous, 1978). The maximum concentration in air reported for a low-volatile ester of 2,4-D was 0.0031 mg/m^3 at unspecified distances downwind from large-scale applications of 2,4-D in wheat. Forest spray units are usually widely scattered and seldom more than 40 ha (100 acres). Given that 2,4,5-T is less volatile than 2,4-D (USDA, 1979), that conditions are unfavorable for evaporation, and that mass effect of treating range areas is absent when applications are made to scattered patches in the cool forested areas of the Coast Ranges, a reasonable upper limit for the level of 2,4,5-T in air might be about 0.001 mg/m^3. This figure compares with a range of 0.000012 to 0.000895 mg/m^3 in a 2,4,5-T treated forest area reported by Cheney *et al.* (n.d.) and 0.00004 to

TABLE 4
Estimated Dermal Exposure for 70-kg Applicators Per Day, and Safety Factors Calculated for Daily and One-Time Contact[A]

	Daily exposure max.		Safety factors	
	One exp.	Daily exp.		
	mg	mg/kg		
2,4,5-T				
Backpack sprayer (bare hands, short sleeves)	3.420	0.049	816:1	408:1
Helicopter mixer-loader (without gloves)	4.390	0.063	635:1	318:1
Flagger	0.367	0.005	8000:1	4000:1
TCDD				
Backpack sprayer	8.6×10^{-8}	1.2×10^{-9}	83 333:1	833:1
Helicopter loader	1.1×10^{-7}	1.6×10^{-9}	62 500:1	625:1
Flagger	0.9×10^{-8}	1.3×10^{-10}	769 200:1	7692:1

[A]No-effect levels: 2,4,5-T - one exposure 40 mg/kg, daily exposure 20 mg/kg per day
TCDD - one exposure 0.0001 mg/kg, daily exposure 0.000001 mg/kg per day

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0.0036 mg/m^3 observed by Young *et al.* (1978) from a volatile point source of concentrated 2,4-D and 2,4,5-T.

The volume of air inhaled has been variously reported as 0.9 to 1.8 m^3/hr (USDA, 1979; USEPA, 1978). If the average human breathes 1.5 m^3 of air during a 1-hour drift exposure, and absorbs all the 2,4,5-T, respiratory exposure may be estimated from the integral of the total breathed air in which the concentration increases from zero to 0.001 mg/m^3 then decreases from 0.001 mg/m^3 to zero, to be a total of 0.00075 mg of 2,4,5-T. Acknowledging that there are major uncertainties in the above assumptions of drift, it is evident that the total exposure via this route is exceedingly small, even in a worst-case situation. Because of the very low volatility of TCDD, respiratory exposure via vapor is regarded as negligible. If TCDD were vaporized proportional to its concentration in the 2,4,5-T formulation (2.5×10^{-8}), exposure would be 1.87×10^{-11} mg TCDD. Although the possibility of occurrence in fine droplets cannot be excluded, degradation would be extremely rapid in the presence of oil, 2,4,5-T, or other solvents in the presence of light (Crosby and Wong, 1977).

No-toxic-effect exposure levels for 2,4,5-T and TCDD and estimation of safety factors

In determining the maximum exposures that can be tolerated with no effect, we have identified levels reported in the literature as follows for single acute exposures and for chronic exposure for 2,4,5-T and TCDD:

2,4,5-T

Single dose	40 mg/kg[4]
Chronic dose/day (lifetime basis)	20 mg/kg per day (USEPA, 1978)

TCDD

Single dose	0.0001 mg/kg[5] (monkeys, rats)[6]
Chronic dose/day (lifetime basis)	0.000001 mg/kg per day (USEPA, 1979b; Murray *et al.*, 1979)

The calculations for exposure of forest residents is summarized in Table 3 to estimate the total range of exposure for persons who do not handle the chemicals during application, and who reside adjacent (≥ 1/8 mile distance) to a major spray unit receiving a single treatment of 2.2 kg/ha of 2,4,5-T containing 2.5×10^{-8} parts TCDD.

For applicators, Table 4 illustrates the safety factors (number of exposures that must be encountered simultaneously to reach a "maximum" no-effect level), based on acute (1-day exposure) of 40 mg/kg for 2,4,5-T and 0.0001 mg/kg for TCDD. These levels may be debated. If further assessment of toxicological data suggests that no-effect levels be adjusted upwards or downwards, a proportional shift will be appropriate for the related safety factors. These safety factors are reduced if the subject comes in daily contact; chronic exposure maxima are reduced only slightly (to 20 mg/kg per day) for the acutely toxic 2,4,5-T, but are severely reduced (to 0.000001 mg/kg per day) for the highly chronic toxicant, TCDD.

The safety factors shown for applicators are applicable for the highest risk cohort of exposed persons. These may be contrasted with those for residents whose exposure occurs once or at wide intervals. Such a comparison suggests that applicators are the group most likely to offer observable symptoms for epidemiological investigation. All safety factor values are based on maximum exposures. One would expect much lower mean exposures, for both residents and applicators, than we have used here. Thus, our estimates of safety factors are probably considerably smaller than average estimates for any given population, and our findings should not be construed that such exposures are likely events.

CONCLUSIONS

Our data confirm that applicators are substantially more heavily exposed than persons who live in or near sprayed forest lands. Based on published and unpublished estimates of no-effect levels compared with observed and calculated absorption rates, applicators are unlikely to receive exposures leading to a safety factor lower than 300:1 for 2,4,5-T and 600:1 for TCDD. Applicators who handle 2,4,5-T infrequently have larger safety factors for 2,4,5-T and negligible exposure to TCDD. These estimates are in reasonable agreement with field-exposure studies. For occasional exposure, the slow penetration of 2,4,5-T into body fluids leads to lower body fluid concentrations per unit of intake than provided by oral ingestion.

Exposure of forest residents from all sources is extremely low, even when residents are in close proximity to operations.

Analysis of 2,4,5-T in urine is a useful measure of exposure to 2,4,5-T. Samples can be collected during the 4 days following suspected exposure and provide a reasonable approximation of total intake and physiological exposure when extrapolated back to the time of contact.

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[4] No-effect level for single exposure is calculated at twice the chronic level of 20 mg/kg per day, based on pharmaco-kinetics of a substance with mean retention time of roughly 24 hours.

[5] Maximum acute no-effect level of TCDD is based on 1/10 of the cumulative "effect" dose reported by W.P. McNulty (1980 *Oregon Regional Primate Laboratory*, Beaverton, Oregon. Unpublished) and J.R. Allen (University of Wisconsin, Madison, unpublished) as producing reproductive effects in monkeys. Dr. McNulty has indicated reservations about 0.0001 mg/kg as a "no-effect" dose, based on observed fetotoxicity at 0.001 mg/kg in rhesus monkeys. To our knowledge, no effects have been reported at single dosages of 0.0001 mg/kg in any species, but this must be very close to the minimum "effect" level.

[6] Available data on no-effect levels of TCDD are based on studies of laboratory rats and rhesus monkeys. These species respond rather differently to acute intoxication dosages but rather similarly to chronic dosing in terms of reproductive effects. In view of the long-term nature of the chronic tests and larger numbers of animals involved in tests, we conclude that the estimate of "no-effect" level for chronic exposure is defined with greater certainty than that of one-time dosing.

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HISTORICAL, LOGISTICAL, POLITICAL AND TECHNICAL ASPECTS OF THE HERBICIDE/DEFOLIANT PROGRAM

1967-1971

A resume of the activities of the
Subcommittee on Defoliation/Anticrop Systems for JTCG/CB
(presently known as Vegetation Control Subcommittee)

Compiled by
Dr. [redacted], USA/Fort Detrick
1971 Subcommittee Secretary

September 1971

For Official Use Only

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PREFACE

This historical summary was prepared from the minutes of the meetings of the Subcommittee on Defoliants/Anticrop Systems of the Joint Technical Coordinating Group/Chemical-Biological since its inception in June 1967. Topics and source material discussed by the Subcommittee at its quarterly meetings have been collated with emphasis on a chronology of events and presentation of prior and current status of each topic discussed.

This report contains only unclassified materials. Reference is given to the original minutes and accompanying documents available to JTCG/CB and Subcommittee members for additional classified information.

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I. ORGANIZATION AND FUNCTION OF SUBCOMMITTEE

A. INSTRUCTIONS AND GUIDANCE IN ESTABLISHMENT OF SUBCOMMITTEE

The JTCG/CB Defoliants/Anticrop Systems Subcommittee was established by the Joint Technical Coordinating Group for Chemical/Biological (JTCG/CB) in June 1967 for the purpose of providing interservice exchange of information at the technical working level in the RDTE programs in defoliants and anticrop systems. A copy of the letter of instruction from Merl Ringenberg, Executive Secretary, JTCG/CB to LT [redacted], AFATL, Eglin Air Force Base, Florida, as Chairman of the new subcommittee is given in Appendix A.

In addition to RDTE responsibilities, cognizance of logistics, production and procurement problems were included in the purview of the subcommittee.

The organizational meeting of the subcommittee was held at Fort Detrick, Frederick, Maryland on 21 September 1967.

B. CHARTER OF DEFOLIANTS/ANTICROP SYSTEMS SUBCOMMITTEE

The charter outlining the mission, composition and functioning of the subcommittee was developed during the initial meeting of the subcommittee at Fort Detrick, 21 September 1967. Copies of the charter were included with minutes of that meeting (see Appendix B).

At the September 1970 meeting recommendations were made that JCS, CINCPAC, and MACV each be invited to provide a member of the subcommittee to serve in an advisory status.

C. CHRONOLOGICAL LIST OF SUBCOMMITTEE OFFICERS

	Chairman	Secretary
1967	LT [redacted], USAF Eglin AFB b6	[redacted] b6 Fort Detrick
1968	LT [redacted], USAF Eglin AFB b6	[redacted] b6 Fort Detrick
1969	[redacted] b6 Fort Detrick	[redacted] b6 US Naval Air Systems Command
1970	[redacted] b6 USAF, SAAMA	[redacted] b6 Eglin AFB

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1971 [redacted] Eglin AFB b6 [redacted] Fort Detrick b6

D. DATES AND LOCATIONS OF SUBCOMMITTEE MEETINGS

Date	Location
21 September 1967	Fort Detrick, Frederick, Maryland
6 February 1968	Eglin AFB, Florida
12-13 June 1968	SAAMA, Kelly AFB, San Antonio, Texas
19-20 September 1968	Edgewood Arsenal, Maryland
21-22 January 1969	US Naval Air Systems Command Headquarters, Washington, D. C.
6-7 May 1969	SAAMA, Kelly AFB, San Antonio, Texas
19-20 August 1969	Fort Detrick, Frederick, Maryland
2-3 December 1969	Eglin AFB, Florida
25-26 March 1970	US Naval Air Systems Command Headquarters, Washington, D. C.
4-5 June 1970	CINCPAC Headquarters, Hawaii
2-3 September 1970	SAAMA, Kelly AFB, San Antonio, Texas
8-9 December 1970	Naval Air Systems Command, Washington, D. C.
2-3 March 1971	Eglin AFB, Florida
9-10 June 1971	Fort Detrick, Frederick, Maryland

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E. REFERENCE LIST OF INCLOSURES AND ATTACHMENTS DISTRIBUTED WITH MINUTES OF SUBCOMMITTEE MEETINGS

1. Meeting of 21 Sep 1967, Fort Detrick, Maryland. Minutes of Defoliants/Anticrop Systems Subcommittee of the JTCG/CB (Confidential)

Incl. 1 Agenda
Incl. 2 List of Attendees
*Incl. 3 Charter of Joint Technical Coordinating Group for Chemical-Biological Defoliants/Anticrop Systems Subcommittee

2. Meeting of 6 Feb 1968, Eglin AFB, Florida

Incl. 1 Minutes for meeting of the Defoliants/Anticrop Systems Subcommittee of the JTCG/CB, Eglin AFB, Florida

Attach. 1. Agenda
Attach. 2. Attendees
*Attach. 3. Statement dtd 31 Jan 68, State of the Art on Analysis of ORANGE, presented by Dr. J. W. Brown, Fort Detrick

3. Meeting of 12-13 June 1968, Kelly AFB, San Antonio, Texas

Incl. 1 Minutes (For Official Use Only)

4. Meeting of 19-20 Sep 1968, Edgewood Arsenal, Maryland

Minutes (For Official Use Only)

Incl. 1 Technical Information on HUSS Spray System, 19 Feb 1968 by Okanagan Copter Sprays, Richmond, B. C., Canada
Incl. 2 Dept. of Defense Instruction 5160.5. 7 Feb 1964. Subject--Responsibilities for Research, Development, Test and Evaluation on Chemical and Biological Weapons and Defense

5. Meeting of 21-22 Jan 1969, US Naval Air Systems Command Hdqtrs., Washington, D. C.

Incl. 1 Minutes (Confidential)
Incl. 2 Technical article by W. A. Gentner, "Herbicidal activity of vapors of 4-amino-3,5,6-trichloropicolinic acid" published in Weeds 12:239-240, 1964.

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* Items starred (*) are included in appendix of this report.

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6. Meeting of 6-7 May 1969, San Antonio Air Materiel Area, Kelly AFB, Texas

Incl. 1 Minutes (Unclassified)

7. Meeting of 19-20 August 1969, Fort Detrick, Maryland

Incl. 1 Minutes (Unclassified)
Incl. 2 Additions to Minutes of Meeting of 6-7 May 1969 prepared by CPT R. Richter, USAF, AFATL and Mr. S. Childers, USAF, AFML
Incl. 3 Subcommittee Roster of August 1969

8. Meeting of 2-3 Dec 1969, Eglin AFB, Florida

Incl. 1 Minutes (Confidential)

9. Meeting of 25-26 Mar 1970, US Naval Air Systems Command Hdqtrs., Washington, D. C.

Incl. 1 Minutes (Unclassified)

Attach. 1. Technical Report ADTC-TR-70-74, Subj: High-Speed Defoliation Tests with a Modified TMU-28/B (PAU-7/B) Tank, dated Apr 70 (U)
Attach. 2. Technical Report ADTC-TR-70-36, Subj: Calibration Test of the UC-123K/A/A45Y-1 Spray System, dated Feb 70 (U)
Attach. 3. Annual Report JTCG for Chemical & Biological Subcommittee Activities for Calendar Year 1969, dated 2 Feb 70 (Confidential)

10. Meeting of 4-5 June 1970 at CINCPAC Headquarters, Hawaii

Attach. 1. Minutes (Confidential)
Attach. 2. Agenda

11. Meeting of 2-3 Sep 1970, Kelly AFB, Texas

Attach. 1. Minutes (Unclassified)
Attach. 2. Agenda (Unclassified)
*Attach. 3. Rpt of C. E. Minarik to JTCG Defoliant Anticrop Subcommittee dtd 2 Sep 70 (U)
Attach. 4. CINCPAC Study "Assessment of Psychological Effects of the Crop Destruction Program" (Confidential) pp 42-50, prepared by CINCPAC Social Sciences Research Team of the Scientific Advisory Group

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Attach. 5. Newspaper Articles on Defoliation (Nelson and Goodell)

*Attach. 6. Letter from [redacted] Dep. Asst. Secy of Defense to Hon. Charles E. Goodell, US Senate dated 14 Aug 1970 in reponse to letter of 13 Jul 1970 to Sec. Def. Laird requesting termination of crop and defoliation program in RVN. (U)

Attach. 7. Subcommittee Recommendation to AFLC, Subject: Disposal of 2,4-D and 2,4,5-T held at Contractor's Facilities. (U)

12. Meeting of 6-9 Dec 1970, US Naval Air Systems Command Hdqtrs., Washington, D. C.

Attach. 1. Minutes (Secret)
Attach. 2. Agenda
*Attach. 3. Preliminary notes, 2 Dec 1970, on incineration of ORANGE (U)
Attach. 4. Ltr. [redacted] b6 to [redacted] b6 (MACV) (U)
Attach. 5. Ecological Information from Eglin Test Grid (U)
Attach. 6. USDA Trip Report by [redacted] b6 International Economist: AAAS Vietnam Herbicide Assessment Conference (Limited Official Use) Discussion of planning conference at Woods Hole, Mass. 14-21 June with synopsis of presentations.

13. Meeting of 2-3 Mar 1971, Eglin AFB, Florida

Incl. 1 Agenda
Incl. 2 Minutes (Unclassified)
Incl. 3 Trip Report of C. E. Minarik to AAAS Meetings in Chicago, 29 Dec 1970. Includes discussions of presentations by AAAS Herbicide Assessment Commission and a AAAS panel session "Implications of Continued Use of Herbicides in Southeast Asia"
Incl. 4 Transcribed papers from AAAS Panel Session "Implications of Continued Military Use of Herbicides in Southeast Asia." AAAS Annual Meeting, Chicago, Ill. 29 Dec 1970. Dr. [redacted] b6, Chairman. Participants were:
[redacted] b6 ARS, USDA
GEN William Stone, USA Retired, formerly CG, ACSFOR
[redacted] b6 Dept. of Government, Harvard Univ.
[redacted] b6 Prof. of Law, Univ. of Wisconsin
Hon. Richard D. McCarthy, US House Representative
[redacted] b6 Dept. of Biology, Harvard Univ.
Incl. 5 Trip Report--CINCPAC Meeting on Herbicides, Camp Smith, 8-10 Feb 1971 by [redacted] b6

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14. Meeting of 9-10 June 1971, Fort Detrick, Maryland

Incl. 1 Agenda
Incl. 2 Minutes (Unclassified)
Incl. 3 Herbicides and Military Operations, Prospectus for Study, Engineer Strategic Studies Group (ESSG), 10 pp with memo for record dtd 24 May 1971 by [redacted], DDR&E, subject: Status of the DDR&E-sponsored military utility of herbicides study.
Incl. 4 TWX dated 14 May 1971 from Ambassador [redacted] 66 to GSA, Wash., D.C., subject: Herbicides.
Incl. 5 Statement dtd 15 Mar 1971 on Disposal of Herbicide ORANGE by Armed Forced Pest Control Board
Incl. 6 Draft Department of Defense Instruction dtd 10 Jun 71 subject: "Responsibility for Research, Development, Test and Evaluation on Vegetation Control Agents/ Systems".

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II. DEFOLIATION/ANTICROP AGENTS

A. ORANGE: SPECIFICATIONS, CLASSIFICATION AND ANALYSIS

Prior Status

Agent ORANGE, consisting of 50:50 ratio by volume of n-butyl esters of 2,4-D and 2,4,5-T, was selected for operational use as a defoliant in RVN in 1963, replacing PURPLE, a patented mixture with lower melting point. Military specifications for the two components of ORANGE were issued by MUCOM, 19 Jul 1963 as MIL-H-51147 (MU) for 2,4-D and MIL-H-51148 (MU) for 2,4,5-T. Revisions of these specifications were made 7 Nov 1966. Type classification of agent ORANGE was accomplished by US Army Materiel Command as AMCTC Item 4055, approved 20 Jan 1966.

Defense Logistics Services Center (DLSC), which is responsible for designation of defense item Federal Stock Numbers, assigned FSN 1380-915-6351 in November 1965 to this agent as a Defoliant described under a then-classified military specification, MIL-D-51239 (MU). Subsequently Air Force, San Antonio Materiel Area, secured an assignment of ORANGE as an herbicide under FSN 6840-926-9095 on 27 Oct 1966. Procurement of ORANGE throughout the period of use in RVN was made by Air Force through Defense General Supply Center (DGSC) under FSN 6840.

On 20 Sep 1967, a revision of the "limited coordination" military specification MIL-D-51239A (MU) was issued including two additional agent formulations, ORANGE II and ORANGE III.

Attempts to secure a fully-coordinated military specification for ORANGE as a Defoliant under FSN 1380 were initiated 7 Nov 1967 by Army which would put the item under commodity management by Fort Detrick (US Army Biological Laboratories) and procurement as an Air Force item would be handled by Ogden Air Materiel Area. Procurement of ORANGE by Air Force had previously been handled by SAAMA under FSN 6840, Herbicides.

Quality control analysis of contract procurement prior to Sep 1967 revealed deficiencies in analytical procedures for determining percent composition and purity, based on the Parr bomb techniques outlined in the existing military specifications for ORANGE and its component 2,4-D and 2,4,5-T esters. Until this date quality control checks on contract shipments were made by DGSC.

Chronology

September 1967. Discussions based on manufacturers recommendations indicated that methods of analysis of ORANGE were outdated. Mr. Vandeventer, SAAMA, urged that new specifications in preparation include the infrared technique of quantitative analysis.

October 1967. SAAMA submitted a purchase description for procurement of herbicide ORANGE under FSC 6840 using infrared technique for quality control.

February 1968. Dr. Brown, Fort Detrick, reviewed procedures for quality determinations of agent ORANGE samples (Appendix C).

June 1968. Mr. Anderson, Edgewood Arsenal, stated that EA has mission responsibility for preparation of purchase descriptions of FSC 6840 items.

Fort Detrick indicated that gas-liquid chromatography methods were preferable for compositional analysis of 2,4-D and 2,4,5-T components of ORANGE.

September 1968. Air Force Purchase Description AFPID 6840-1 issued for interim use in procurement pending development of a military specification. Infrared method of analysis was specified in AFPID 6840-1.

Edgewood Arsenal was instructed by DCSA to prepare a fully coordinated specification for ORANGE.

May 1969. Responsibility for quality control analyses of ORANGE and other agents transferred from DSA to Air Force Materials Laboratory at Wright-Patterson AFB. This laboratory is also responsible for supplying standard samples of ORANGE herbicide to contract suppliers.

August 1969. Required military specification for ORANGE delayed due to conflicting FSC designations. Edgewood Arsenal prepared a specification under Project 6840-0215 and Fort Detrick under Project 1365-0193. DOD (DLSC) recently confirmed the FSC 6840 classification for ORANGE and related herbicides.

8 August 1969. Assistant Secretary of Defense (Installation and Logistics) in memorandum to Air Force and DSA directed the management transfer of agents ORANGE, WHITE, and BLUE to Air Force under FSC 6840.

March 1970. DOD program analysis for FSC 6840 dated 25 Feb 1970 recommended: (1) Reclassification of FSC 1365 numbers to FSC 6840 under item name herbicide; (2) transfer preparing activity responsibility for specification MIL-D-51239 (ORANGE) to the Air Force.

Air Force Purchase Description AFPID 6840 dated 2 Jan 1970 and Amendment 1, dated 10 Feb 1970, were reported to be in use for procurement contracts for ORANGE. Amendment No. 1 specifies gas-liquid chromatographic procedure for analysis of ORANGE.

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Current Status

With cessation of procurement of ORANGE due to suspension of use in RVN on 15 April 1970, no further action has been taken in conversion of AFPID 6840-1, ORANGE herbicide, into a military specification.

Analysis of ORANGE in reference to its dioxin content is discussed under 2,4,5-T.

B. WHITE

Prior Status

Agent WHITE (Tordon 101, a combination of 20% picloram and 80% 2,4-D) was initially used in RVN in late 1966 on the basis of recommendations by Dow Chemical Company as a substitute for ORANGE for defoliation in proximity to rubber trees and other crop plants. Limited tests of WHITE and other picloram formulations by Fort Detrick had not established its value as a recommended defoliant.

Procurement was made by Air Force on the basis of a purchase description for a proprietary compound.

Chronology

January 1969. Dow Chemical Company suggested the incorporation of picloram ester with ORANGE to make "Modified ORANGE".

May 1969. Suggested extensive procurement of WHITE was cancelled in view of the current surplus of ORANGE and the lack of field data confirming the requirement for WHITE near rubber plantations. On a trial basis, ORANGE would be used in lieu of WHITE until field data were obtained.

April 1970. Agent WHITE continued in use for defoliation following suspension in use of ORANGE due to reported teratogenic effects of component 2,4,5-T.

March 1971. No supply support given for SEA due to curtailment in use of WHITE.

Current Status

No current procurement.

C. BLUE

Prior Status

The term BLUE was first used in 1962 for the powder form of cacodylic acid to be field mixed with water for spray application in crop destruction missions. In 1964 procurement of BLUE from Ansul Company was changed to Phytar 560G, a neutral liquid formulation of sodium cacodylate and cacodylic acid containing surfactant.

Chronology

September 1965. Because of foaming problems in the use of BLUE, Defense General Supply Center added an antifoam agent to BLUE contract requirements in June 1968. Procurement of BLUE by Air Force has been conducted by purchase order from Ansul Company on a sole source basis.

January 1969. A limited coordination military specification, MIL-A-60733 (MU), dated 24 Jan 1969, was prepared by Army Munitions Command for the liquid sodium cacodylate formulation with 3 to 5% surfactant and 0.5% antifoam agent.

May 1969. Availability of BLUE from additional commercial suppliers was established by Fort Detrick permitting procurement on a competitive basis.

August 1969. Military Specification MIL-A-60733 in use by Air Force and DGSA in procurement contracts to obtain SEA requirements.

October 1969. Revised military specification MIL-V-60733A dated 27 Oct 1969 issued with reduced surfactant content (0.8 to 3%).

March 1971. No existing demands for procurement of BLUE for SEA activities.

Current Status

Valid military specification currently available. Procurement demands suspended.

D. PROCUREMENT AND SUPPLY OF DEFOLIANT/ANTICROP AGENTS

Prior Status

Procurement of defoliants and herbicides for SEA activities (agents ORANGE, BLUE, and WHITE) was assigned to Air Force (AFLC) operating through Defense General Supply Center. Contract orders from US suppliers were accumulated and handled for overseas shipment at the US Navy Construction Battalion Center, Gulfport, Mississippi.

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The increasing requirements for ORANGE over the period 1963-67 and projected future demands in excess of commercial sources led to the development of plans for a new ORANGE production capability GOCO by Army. Conversion of a surplus AEC plant at Weldon Springs, Missouri to create an annual production capability of 8 million gallons of ORANGE was initiated in late 1967 by Edgewood Arsenal with production scheduled for December 1969.

Chronology

February 1968. Contract let by Edgewood Arsenal for design and construction of the Weldon Springs facility.

June 1968. Contracts let by Edgewood Arsenal for procurement of tetrachlorobenzene, a critical requirement for production of ORANGE at the proposed Weldon Springs facility.

During the TET offensive of Jan-Feb 1968, RANCH HAND aircraft were diverted to other missions and a backlog of herbicides resulted in RVN. Stockpiling also occurred at Gulfport, Mississippi with suspension of SEA shipments during April-May 1968.

Reduction in procurement of BLUE was noted following release of a RAND report on crop destruction program in RVN; supplies of WHITE adequate to meet requirements.

September 1968. A thorough review of progress in construction of the Weldon Springs facility is given in the minutes of the meeting of this date (Item 3).

Reduction in requirements for ORANGE in FY 69 to FY 70 were announced by Asst. Secretary of Defense (Installation and Logistics) in a meeting on 30 Aug 1968 attended by JCS, Army, Air Force and Defense Supply Agency personnel. At this time it was anticipated that the Weldon Springs plant would furnish the entire FY 70 requirement for ORANGE at a reduced production level from that initially planned.

January 1969. Reduced requirements coupled with accumulation of some 75,000 drums of ORANGE at Gulfport, Mississippi led to termination of supply contracts. Manufacturer's supplies of raw materials (basic 2,4-D and 2,4,5-T esters) used in the manufacture of ORANGE became the liability of the Government.

Proposal submitted by Dow Chemical Company for conversion of ORANGE to "Modified ORANGE" by adding one part of picloram ester to three parts of ORANGE. Concern was expressed by CINCPAC that the proposed conversion might render the ORANGE unsuitable for use in RVN because of the residual nature of picloram.

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31 January 1969. Edgewood Arsenal announced the termination of the Weldon Springs project.

May 1969. Accumulation of ORANGE at Gulfport represents a potential disposal problem if SEA requirements are reduced or terminated.

August 1969. Hurricane Camille struck the Gulfport, Mississippi herbicide storage facility during shipload operations. About 1,000 drums of BLUE and ORANGE on the pier were scattered in the water and on the beach. Later investigation showed the drums to be intact with no signs of leakage; 52,000 drums in open storage 1.5 miles from the coast were not damaged. All damaged drums from the pier site were subsequently recovered.

April 1970. Suspension in use of ORANGE in RVN announced by Deputy Secretary of Defense Packard. As of 1 May 1970 the stocks of ORANGE on hand at Gulfport, Mississippi amounted to 15,161 drums.

December 1970. Contracts for BLUE and WHITE were awarded in October and July 1969, respectively. Deliveries of BLUE have been suspended and only one shipment of WHITE was made to SEA in 1970.

June 1971. No herbicides are currently being sent to SEA.

Current Status

Procurement and supply of ORANGE, BLUE and WHITE to SEA has terminated. Surplus stocks of ORANGE at Gulfport and in RVN and of basic 2,4-D and 2,4,5-T esters at Kelly AFB have created a disposal problem.

E. DISPOSAL OF SURPLUS ORANGE AND COMPONENTS

Prior Status

No herbicide disposal problems were existent prior to September 1967 because of heavy demands for SEA activities.

Chronology

January 1969. Recognition was first given to a potential disposal problem in the accumulation of surplus ORANGE at the Gulfport, Mississippi site. As of January 1969, 75,000 drums of ORANGE were on hand at Gulfport. Procurement contracts for ORANGE were being terminated with reduced future requirements.

May 1969. SAAMA and Fort Detrick considering plans for disposal of ORANGE.

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April 1970. Suspension of use of ORANGE in RVN announced by Deputy Secretary of Defense Packard because of possible teratogenic effects of 2,4,5-T.

June 1970. Three disposal problems were presented by Mr. [redacted] resulting from suspension of the use of ORANGE in RVN:

(1) Stockpile of ORANGE at Gulfport, Mississippi of 15,161 drums (most of which had been in open storage since 1968).

(2) Stockpile of ORANGE in RVN. (Cited as consisting of 668,304 gallons as of 1 May 1970 but later estimates place amount in excess of 1.4 million gallons.)

(3) Raw materials inventory of 2,4-D and 2,4,5-T n-butyl esters owned by Government and in storage at contractor facility at Government expense since Government termination of ORANGE contracts.

September 1970. Procedures developed by SAAMA and Army for disposal of CONUS stockpiles of ORANGE include the following alternatives:

(1) Use by military for vegetation control in isolated areas of military bases. (Subcommittee recommendation)

(2) Use in AID programs for vegetation control in undeveloped nations. (Subcommittee recommendation)

(3) Burial in soil pits or settling ponds.

(4) Destruction by incineration. Recommendation for incineration was based on restrictions imposed on the use of 2,4,5-T because of its reported teratogenic effects.

December 1970. Shipment of contractor raw materials inventory to Kelly AFB, Texas for stockpiling.

Summary of information on incineration of ORANGE solicited from industrial sources by Fort Detrick is given as Appendix D.

March 1971. Proposal for incineration of Gulfport stockpile of ORANGE was submitted by SAAMA to Headquarters, US Air Force 19 Feb 1971 based on utilization of equipment under development at Rocky Mountain Arsenal.

Options proposed by the Subcommittee for disposal of ORANGE in RVN include: Marketing in-country, destruction of stockpile at present locations, move stockpile offshore for temporary storage, move stockpile back to CONUS for subsequent disposal, and develop uses for herbicide.

Plans for disposal of RANCH HAND assets including the stockpile of ORANGE in RVN were prepared by MACV for submission through channels on 1 March 1971.

June 1971. Air Force staff study submitted in April 1971 recommending disposal of CONUS stockpile of ORANGE did not receive concurrence. A continued search was being made for possible uses of ORANGE which would avoid the limitation imposed by the variable dioxin content.

A plan was submitted on 23 Apr 1971 by JCS, J-4 to Deputy Secretary of Defense Packard outlining practicable options and reviewing political factors involved in disposal of CONUS and OCONUS supplies of ORANGE. The report considered: (1) Existing situations where herbicides could be used by the military, (2) providing ARVN with a capability for herbicide operation, (3) alternative uses of existing stockpiles by nonmilitary groups, and (4) destruction by incineration. No action had been taken as of 10 June 1971 on the recommendations provided in this report.

Details of a survey and review of the status of the Gulfport stockpile are given in Appendix E in a Memorandum dated 15 Mar 1971 from LTC H. W. Fowler, Jr., Armed Forces Pest Control Board.

Current Status

No action has been taken on Air Force proposals concerning the Gulfport stockpile or on the JCS plan for both CONUS and OCONUS supplies.

Contractor termination inventories of 2,4-D and 2,4,5-T remain in storage at Kelly AFB and at contractor facilities at Government expense for storage.

F. USE OF 2,4,5-T IN RELATION TO TERATOGENIC EFFECTS AND DIOXIN

Prior Status

2,4,5-T, one of the two basic components of agent ORANGE, had been extensively used for the control of woody plants and weeds since 1949 under registration by US Department of Agriculture and Food and Drug Administration. Extensive toxicological studies had shown no hazard to man, livestock or wildlife at rates of application used in vegetation control and industrial vegetation management. In a summary of toxicological data prepared by the Toxicology Department, Edgewood Arsenal, the combination of 2,4-D and 2,4,5-T butyl esters in ORANGE was stated to have an acute oral toxicity LD_{50} in rats of 550 mg/kg.

Agent ORANGE, with its 2,4,5-T component, was recommended for military uses without reservation because of its long history of use in agriculture with no incidence of animal toxicity.

Chronology

29 October 1969. Dr. Lee A. DuBridge, Science Adviser to the President, announced a partial curtailment of the use of 2,4,5-T. The decision was made shortly after the attention of the White House was called to a report by Bionetics Research Laboratories, Bethesda, Maryland on contract research conducted for the National Cancer Institute which indicated that offspring of mice and rats given relatively large oral doses of the herbicides during early stages of pregnancy showed a higher than expected number of birth deformities.

The White House announced that the Defense Department would restrict the use of the herbicide (in agent ORANGE) as a defoliant in Vietnam to areas remote from population.

Actions taken by the Department of Agriculture, Health, Education and Welfare, and Interior are outlined in the press release from the President's Office of Science and Technology (Appendix F).

December 1969. Publication of the "Mrak Report" by HEW: "Report of the Secretary's Commission on Pesticides and Their Relationship to Environmental Health" in which a summary of the Bionetics report data was included. (Bionetics report was still not released to the scientific community up to this date.)

In a briefing at Office of Science & Technology, Dow Chemical Company personnel suggested that the teratogenic effects attributed to 2,4,5-T in the Bionetics study might be due to the contaminant dioxin (2,3,7,8-tetrachlorodibenzo-p-dioxin) based on experience in the Dow manufacturing process in which this contaminant caused chloracne among plant workers. The Diamond Alkali sample of 2,4,5-T used in the Bionetics study was found to contain 27 ppm of dioxin. Dow had modified their 2,4,5-T manufacturing process in 1965-66 to give a dioxin content of less than 0.5 ppm. Dow had furnished information to other companies concerning the dioxin contaminant but had made no public release of information on dioxin.

March 1970. Registration of 2,4,5-T was extended by US Department of Agriculture until 1 Jan 1971 for use on apples, blueberries, grains, pasture, rangelands, rice and sugarcane.

In a briefing for ACSFOR and other Army personnel, Dow representatives reported that tests of 2,4,5-T containing less than 1 ppm dioxin showed no teratogenic effect on mice and rats. Dow had supplied samples of pure 2,4,5-T to National Institute of Environmental Health (NIEH) personnel for similar studies.

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15 April 1970. Based on recently completed NIEH studies which indicated that both pure 2,4,5-T and the contaminant dioxin may be teratogenic, Surgeon General, HEW, in a joint announcement by HEW, Agriculture and Interior, called for immediate suspension of the use of 2,4,5-T around homes, water supplies, and food crops. The ban did not affect its use on pastures, rangeland, rights-of-way and other nonfarm areas (Appendix G).

Simultaneously Deputy Secretary of Defense Packard announced that "pending an evaluation, the use of agent ORANGE--a defoliant consisting of 2,4,5-T and a chemically related pesticide, 2,4-D--is being suspended."

4 May 1970. Cancellation by US Department of Agriculture of Federal registration for all uses of the herbicide 2,4,5-T around the home and for all uses on food crops intended for human consumption, on the basis that "exposure to this herbicide may present an imminent health hazard to women of child-bearing age." (Appendix H)

September 1970. A summary of research in progress on 2,4,5-T, 2,4-D, and dioxin was presented by Dr. Minarik to the Subcommittee (Appendix I).

28 September 1970. US Department of Agriculture warned manufacturers and formulators of the herbicide 2,4,5-T that regulatory action would be taken if their products were found to be contaminated with toxic chlorodioxins (Appendix J).

December 1970. Publication of a survey of records from 22 RVN hospitals of the incidence of stillbirths and birth defects in the Republic of Vietnam conducted at request of DDR&E by COL R. T. Cutting, US Army Medical Research Team, with assistance of Dr. [redacted] 46 [redacted] Professor of Medicine, University of Maryland. The survey showed a decrease in stillbirths and birth defects (hydatiform moles and congenital malformations) from the 1960-65 period of pre- or light-rate spraying of herbicides to 1966-69 with heavy rates of spraying.

March 1971. Release of the "Report on 2,4,5-T" by the Panel on Herbicides of the President's Science Advisory Committee, Office of Science and Technology, which indicated that the present curtailment in use was a hasty decision and that the chemical is not as hazardous as indicated.

Environmental Protection Agency (EPA), which succeeded US Department of Agriculture as the regulatory agency concerned with the use of 2,4,5-T and all pesticide chemicals announced that no additional restrictions will be made on the use of 2,4,5-T.

Current Status

Pending actions on the status of 2,4,5-T for domestic use include:

(1) Study by a National Academy of Sciences Committee on validity of the use of 2,4,5-T based on questionnaires to farmers and users to assess the experience and safety of this herbicide.

(2) Settlement of a suit filed against EPA to provide information establishing whether or not 2,4,5-T is an "imminent hazard".

The "temporary" suspension of the use of ORANGE in RVN is still in effect "pending evaluation".

References

Bionetics Research Laboratories (1969). 1970. Evaluation of the carcinogenic, teratogenic and mutagenic activity of selected pesticides and industrial chemicals. Vol. III. Evaluation of the teratogenic activity of selected pesticides and industrial chemicals in mice and rats. Report submitted under Contracts PH43-64-57 and PH43-67-735 with the National Cancer Institute. 33 pp. plus 60 appendix tables. Bionetics Research Laboratories, Bethesda, Maryland.

Courtney, K. Diane, et al. 15 May 1970. Teratogenic evaluation of 2,4,5-T. Science 1168:864-866. (Resume of Bionetics report.)

Mrak, M. R. (Chairman). December 1969. Report of the Secretary's Commission on Pesticides and Their Relationship to Enviornmental Health. US Health, Education, and Welfare. 677 pp.

Committee on Commerce, Subcommittee on Energy, Natural Resources and the Environment. April 7 and 15, 1970. Effects of 2,4,5-T on man and the environment. 91st Congress Second Session. US Senate, Serial 91-60, 1970. 469 pp.

_____. June 17-18, 1970. The effects of 2,4,5-T and related herbicides on man and the environment. 91st Congress Second Session, US Senate Serial No. 91-83, 1970. 112 pp.

Cutting, R. T., et al. December 1970. Congenital malformations, hydatiform moles and stillbirths in the Republic of Vietnam 1960-1969. Department of Defense unnumbered report. 29 pp. Govt. Printing Ofc., Washington, D. C.

Office of Science and Technology. March 1971. Report on 2,4.5-T. A Report of the Panel on Herbicides of the President's Science Advisory Committee. 68 pp. Executive Office of President, Office of Science and Technology, White House.

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Whiteside, Thomas. 1970. Defoliation. 168 pp. Ballantine Books Inc., N.Y. (paperback). A portion of text originally appeared in New Yorker for 7 Feb and 14 Mar 1970.

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III. DISSEMINATION SYSTEMS

A. AIR FORCE

1. A/A45Y-1 Internal Defoliant Dispenser, C-123B; C-123K

Concept: The A/A45Y-1 defoliant dispenser is a modular spray system for internal carriage in cargo aircraft. It has been used only in C-123 aircraft but is adapted for use in the C-130.

Prior Status: The 1000-gal tank system used in C-123B aircraft in RANCH HAND operations in RVN since 1962 was modified from the Hourglass or MC-1 system developed in 1953. Calibration tests conducted at Eglin AFB in 1963 led to modifications to achieve 3 gal/acre delivery including the addition of a tail boom. No calibrations were made on this modification of the A/A45Y-1/C-123K system until 1968-69.

Chronology:

May 1967. C/B Division of ATC submitted a test requirement for calibration of the C-123B system in operational use in RVN.

August 1967. Test proposed for calibration of C-123K system.

September 1967. Eglin AFB modifying dissemination system for use in C-123K model with jet engines added.

February 1968. Nine spray flights completed with C-123K aircraft in calibration tests.

June 1968. Engineering development of A/A45Y-1 system passed to Warner Robbins AFB.

Test plan prepared at Eglin AFB for: (1) Calibration of C-123B system in operational use; (2) evaluation of Stull Bifluid vs ORANGE; (3) calibration of C-123K scheduled for use in RVN.

September 1968. Completion of plans for calibration of A/A45Y-1/C-123K system using agents BLUE and WHITE.

January 1969. Engineering development and modification in progress of wing boom system (KMU-327/A), which is externally mounted instead of internal as originally planned.

May 1969. Calibration tests with ORANGE in A/A45Y-1/UC-123K system completed.

Negotiation of contract for engineering and design of optimized wing and tail booms for UC-123K system.

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August 1969. Completion of calibration tests of UC-123K system with ORANGE, BLUE, and WHITE.

January 1970. Flight testing of optimized wing and tail boom for UC-123K system completed in January 1970 shows need for additional engineering work on A/A45Y-1 system.

October 1970. Completion of contractor testing and operational reliability tests of optimized wing and tail boom system.

Requirement for optimized system withdrawn due to reduced operational program in RVN. System turned over to AFLC/WRAMA for future use.

References:

Harrigan, E. T. February 1970. Calibration test of the UC-123K/A/A45Y-1 Spray System. Tech. Rept. ADTC-TR-70-36. Armament Development & Test Center, Eglin AFB, Florida.

Harrigan, E. T. April 1970. Test of the KMU-327/A wing and tail boom/UC-123K defoliant system. Tech. Rept. ADTC-TR-70-79. Armament Development & Test Center, Eglin AFB, Florida.

2. PAU-8/A (TMU-66)

Concept: Modular dispenser for external mounting on high- and low-performance aircraft to provide capability of spraying large and small areas.

Prior Status: System was developed and prototypes built prior to Sep 1967. Suitable for use on F-100, F-105, F-86, and F-4 aircraft.

Chronology:

1968. Ground function tests of TMU-66 spray tank; flight tests and spray missions conducted by contractor.

1969-70. Compatibility and function testing by ADTC, Eglin AFB with F-100, F-105, F-4, and A-1E aircraft using agent BLUE.

Tail fins redesigned in December 1970 and flight compatibility tested in February 1971.

June 1971. Planning for full certification of PAU-8/A on F-4 aircraft. Aerosol testing at Dugway and vibration testing at Picatinny Arsenal are planned for FY 72.

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Reference:

Henry, J. E. November 1969. Test of the TMU-66/A Dispenser. Tech. Rept. ADTC TR-69-187. Armament Development & Test Center, Eglin AFB, Florida.

3. PWU-5/A (MISS) (Modular Internal Spray System)

Concept: Versatile, modular disseminator with internal tank for liquid herbicides, insecticides, and fertilizers designed for civic action operations and military use.

Prior Status: None

Chronology:

July 1969. Development of MISS initiated by FMC Corporation with design review scheduled for January 1970. Modular concept chosen to be compatible with 11 types of aircraft: C-46, C-47, C-54, C-97, C-118, C-119, C-121, C-123, C-130, C-131, and DC-7.

March 1970. System designated as PWU-5/A. C-54 removed from aircraft requirements list.

April 1970. Final design approved.

August 1970. Fit test conducted in C-123K aircraft with two 500-gallon tanks and power module.

May 1971. Following certification of bonding technique at Wright-Patterson AFB, flight compatibility tests were conducted at Eglin AFB with PWU-5/A system in C-123K aircraft. Aluminum hanger pads for boom are bonded to wing with 3M epoxy adhesive, permitting rapid conversion of cargo aircraft.

Aerosol testing is planned for FY 72 at Dugway Test Center.

Reference:

Tactical Air Command. 27 Oct 1969. Required operational capability (ROC) for Modular Aerial Spray System. TAC ROC 49-69. Headquarters Tactical Air Command, Langley AFB, Virginia.

4. PAU-7/B (TMU-28)

Concept: Externally mounted tank for high performance aircraft (F-4).

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Prior Status: Original configuration lacked on-off capability in flight.

Chronology:

October 1969 - January 1970. High-speed defoliation test with ORANGE and flight compatibility trials in F-4 aircraft.

June 1970. TAC tests of PAU-7/B system at Eglin CB Grid using BLUE and WHITE in F-4 at 100, 200 and 300 ft altitude and airspeed of 550 knots.

September 1970. Project temporarily suspended for lack of firm requirements.

Reference:

Harrigan, E. T. April 1970. High-speed defoliation test with a modified TMU-28/B (PAU-7/B) tank. Tech. Rept. ADTC-TR-70-74. Armament Development & Test Center, Eglin AFB, Florida.

5. A/B45Y-2 Biological Anticrop

Concept: Elevated line source, dry antiplant (anticrop) agent spray tank for use on high performance aircraft.

Prior Status: All development work on the A/B45Y2 system was completed by October 1967 except operational training tests.

Chronology:

June 1968. Procurement of 103 A/B45Y-2 tanks authorized.

August 1968. Operational training and evaluation test (USAF 68-43) in progress.

January 1969. Flight testing completed. Nondestructive tests of tanks showed structural failure of some components.

August 1969. Redesign of spray tank completed by Litton Industries involving paddle shaft assembly, drive shaft and gear box housing.

December 1969. Centrifuge and vibration testing completed at Picatinny Arsenal.

March 1970. Flight testing of redesigned A/B45Y-2 tank completed at Eglin AFB. No further work contemplated due to retraction of requirement.

B. NAVY

1. PAU-5 (XN-1), formerly GRANDAP, Granular Dispersal Apparatus (Equivalent to Army's Dispenser, Insecticide, Solid, Rotary Wing Aircraft).

Concept: Internally mounted pressurized tank and boom system for aerial dispersal of solid granules, pellets or dust-type materials from UH-1 type helicopters.

Prior Status: The system is somewhat similar to an AGAVENCO unit but it has a motorized air supply, and the system was made for military usage by the Disease Vector Control Center. It is very easily modified for defoliant dissemination.

Chronology:

September 1968. Modification of Navy design of GRANDAP by Army Medical Equipment Research Development Laboratory (MERDL) at Fort Totten, New York. Service tests conducted in Panama.

September 1969. Type A classification by Army of MERDL modification of GRANDAP.

Reference:

Recommendation for type classification of Dispenser, Insecticide, Solid, Rotary Wing Aircraft, Task No. 3A643324D820 01 14 as Standard A, US Army Medical Equipment R&D Laboratory, Fort Totten, N. Y. 1969.

2. Systems Tested for Feasibility

a. OVIOA Aircraft

Feasibility study conducted in 1968 by North American on spray system for Mohawk or OVIOA aircraft, principally for dissemination of insecticide. System includes a 375-gallon unit or without observer the aircraft could accommodate a 462-gallon tank.

Status: No further development planned (February 1968).

b. HUSS (Helicopter Underslung Spray System)

Okanagan Copter Sprays, Ltd. of Richmond, British Columbia, Canada has developed a slung system with tank, pump, and boom suspended and jettisonable in flight.

6698

Status: Marine Corps Development and Education Command has obtained several units for evaluation (February 1968). Navy tests with a CH-46 helicopter indicated need for redesign to meet military application requirements.

c. Operation DOUCHE for Riverine Craft

High pressure pump (6000 gpm) mounted on riverine craft for high volume application of defoliant.

Status: Tests conducted in RVN. Units in RVN have been turned over to local forces.

Reference:

Naval Ship Research and Development Laboratory, Annapolis, Md. Confidential Report dated 10 June 1970 on Defoliation DOUCHE, NRDU-V Project 88-68 (U).

C. ARMY

1. UH-1B/D Helicopter Spray System (AGRINAUTICS)

Concept: The AGRINAUTICS (Formerly AGAVENCO) spray unit is a self-contained unit suitable for use in the UH-1B/D Army helicopters, the Navy UH-1E and the Air Force UH-1F types. The 200-gallon fiberglass tank and boom system can be readily installed or removed and no aircraft modifications are required.

Prior Status:

The AGRINAUTICS system for herbicides has been in operational use in RVN since 1967. Earlier models equipped for application of insecticides were used by the Army Medical Corps in RVN in 1966.

Under field conditions, some difficulty has been experienced with ORANGE on contaminated aircraft surfaces in softening the paint. Preventive measures consist of coating the aircraft with grease or lard and follow-up rinsing with diesel fuel or kerosene.

Some structural weaknesses in the boom assembly have been found under field conditions.

Chronology:

Fall 1967. Eight AGRINAUTICS systems equipped for herbicide applications were shipped to RVN by Army Mobility Equipment Command for use in the four Corps Tactical Zones.

January 1969. Twenty-one additional AGRINAUTICS spray systems were ordered for Army aircraft.

Reference:

Agricultural Aviation Engineering Company. 1968. Operation and maintenance instructions for sprayer-pesticide helicopter-mounted UH-1B/D. FSN 3740-999-2405. Model 3090. Agric. Aviation Engrg. Co. (now AGRINAUTICS), Las Vegas, Nev.

2. Dispenser, Insecticide, Solid, Rotary, Wing Aircraft

See Sec. III.B.1.

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