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Report to Rep. Ralph H. Metcalfe; by Henry Eschwege, Director, Community and Economic Development Div.

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Congressional Relevance: Rep. Ralph H. Metcalfe.

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Concerns have been expressed about the Department of Defense's (DOD's) use of Agent Orange, an herbicide, in Vietnam because it contains the highly toxic contaminant dioxin. From August 1965 to 1971, DOD sprayed 11.22 million gallons of Agent Orange in Vietnam, with about 3 gallons per acre sprayed undiluted. DOD has little information available on the number or extent of personnel exposure to herbicides in Vietnam. However, aircraft crews involved in spraying missions were more likely to have been exposed than were others, and their records could possibly be traced. DOD research before herbicide use in Vietnam was concerned with effectiveness more than with health effects. Later DOD ecological studies failed to demonstrate long-term health effects, but the National Academy of Sciences believed that further studies are needed. DOD does not have plans for epidemiological studies related to herbicide uses in Vietnam. (HTW)

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UNITED STATES GENERAL ACCOUNTING OFFICE

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COMMUNITY AND ECONOMIC
DEVELOPMENT DIVISION

B-159451

AUGUST 16, 1978

The Honorable Ralph H. Metcalfe
House of Representatives

Dear Mr. Metcalfe:

By letter dated April 10, 1978, you expressed concern about possible long-range adverse health effects on individuals that were exposed to the herbicide Agent Orange and requested that we examine certain aspects of the Department of Defense use of this herbicide in Vietnam and the Veterans administration handling of disability claims submitted by herbicide-exposed Vietnam veterans. As agreed with your office on June 28, 1978, this report addresses (1) the extent of the Defense use of herbicides and other chemicals in Vietnam, (2) the number of military and civilian personnel exposed to these chemicals, and (3) the Defense-funded studies of the health effects of these chemicals.

Our review of the Veterans Administration handling of disability claims submitted by herbicide-exposed Vietnam veterans is continuing. In addition, the Environmental Protection Agency is currently reevaluating the registered uses of chemical 2,4,5-T, a component of Agent Orange, in this country. We plan to include these matters in a final report to you by January 1979. We expect to work closely with your staff during this period.

In summary:

--Agent Orange, a 50:50 mixture of 2,4-D and 2,4,5-T, was the most widely used herbicide in Vietnam. The component 2,4,5-T contains a contaminant, TCDD (dioxin) that is highly toxic, stable, and persistent, and its use has caused great public concern.

- Defense has little information available on the number or extent of personnel exposure to herbicides in Vietnam. Officials acknowledged, however, that aircraft crews involved in herbicide spraying missions were more likely to have been exposed than others; this group possibly could be traced through military records.
- Defense research before herbicide use in Vietnam was primarily concerned with herbicide effectiveness rather than its health effects. Subsequent Defense ecological studies failed to demonstrate long-term health effects. In its 1974 report, however, the National Academy of Sciences concluded that further extensive studies are needed.
- Defense plans no epidemiological studies related to herbicide uses in Vietnam.

These matters are discussed in greater detail in the following sections.

USE OF HERBICIDES AND OTHER
CHEMICALS IN VIETNAM

Defense field tested herbicides in Vietnam in 1961 and carried out military herbicide operations from 1962 to 1971. The herbicides were used primarily for (1) defoliating trees and plants to improve observation and (2) destroying food crops of hostile forces. Four herbicides were used:

- Agent Orange (a mixture of 2,4-D and 2,4,5-T);
- Agent Purple (a similar mixture of 2,4-D and 2,4,5-T that contained a different form of 2,4,5-T--it was replaced by Agent Orange in 1964);
- Agent White (a mixture of 2,4-D and Picloram);
and
- Agent Blue (cacodylic acid).

The military use of herbicides in Vietnam is detailed in enclosure I.

According to a National Academy of Sciences report, about 18.85 million gallons of herbicides were sprayed during the 1962 to 1971 period. From August 1965 1/ to 1971, Defense sprayed 11.22 million gallons of Agent Orange, 5.24 million gallons of Agent White, and 1.2 million gallons of Agent Blue over about 3.6 million acres of South Vietnam. Out of this area, 66 percent was sprayed once, 22 percent was sprayed twice, 8 percent was sprayed three times, and 4 percent was sprayed four or more times. The quantities sprayed annually and application rates are summarized in enclosure II.

Agent Orange was sprayed undiluted in Vietnam at the rate of about 3 gallons (containing 12 pounds of 2,4-D and 13.8 pounds of 2,4,5-T) per acre. Civilian applications of this herbicide's components are usually diluted in oil or water. A Defense official said that the heavier application was needed to assure success of the herbicide operations.

In October 1969 Defense restricted the use of Agent Orange to areas remote from population. This action was prompted by a National Institute of Health report that 2,4,5-T could cause malformations and stillbirths in mice. Researchers later attributed similar problems to the contaminant TCDD, which is produced during the manufacture of 2,4,5-T. In April 1970 Defense suspended all use of Agent Orange in Vietnam, about the same time that the Department of Agriculture restricted the domestic use of 2,4,5-T because of its possible health hazards.

In 1971 Defense directed the Air Force to dispose of all remaining stocks of Agent Orange. These stocks contained TCDD contaminant levels ranging from less than 0.05 to 47 parts per million and averaging about 2 parts per million. Current manufacturing standards for 2,4,5-T require TCDD levels be less than 0.1 part per million.

1/ About 1.27 million gallons were used before August 1965, but a breakdown of the quantities of individual types of herbicides used was not available.

Defense officials said that the disposal of Agent Orange was completed in September 1977.

Other chemicals

A Defense official said that malathion and DDT were the other principal pesticides used in Vietnam; they were used throughout the war for mosquito control. Malathion was sprayed by aircraft, and DDT was applied by back pack and paint brush. The official said that no information is readily available on the quantities used in Vietnam.

Malathion is still used domestically for insect control. However, in 1972 EPA cancelled all except public health and quarantine uses of DDT because of its persistence, biomagnification, and toxicological effects.

PERSONNEL EXPOSURE TO HERBICIDES

A Defense report shows that about 2.6 million military personnel served in South Vietnam from January 1, 1965, to March 31, 1973. Defense records indicate that the number of United States civilian personnel employed by Defense in South Vietnam ranged from 49 in March 1965 to 1,522 in September 1969--cumulative data on civilians are not readily available. Defense has little information, however, on the number of personnel exposed to herbicides in Vietnam, Defense officials stated that (1) no such personnel records were maintained, (2) it would be difficult to estimate meaningful exposure data because the potential for exposure varied widely among personnel, and (3) only a few military personnel would have been exposed directly to spraying. But some personnel could have been exposed indirectly to low levels of herbicides through ingestion of contaminated drinking water and food and by skin contact.

Defense officials acknowledged that certain groups of personnel such as the herbicide handlers and aircraft crews (particularly crewchiefs and flight engineers) involved in herbicide spraying missions were more likely to have been exposed to herbicides than others. The officials said that, if required, the identity of the aircraft crews possibly could be traced through military records. The herbicide handlers were mostly Vietnamese and it would be difficult to identify and trace them.

DEFENSE-FUNDED STUDIES OF THE
HEALTH EFFECTS OF HERBICIDES

The herbicides used in Vietnam were also used in the United States when the military spraying program began. A Defense official stated that, consequently, military studies made before the program began were concerned primarily with military effectiveness rather than environmental and health effects. Defense subsequently funded several studies of the ecological effects of herbicide use; included was a study made by the National Academy of Sciences, as mandated by the Congress in Public Law 91-441 (Oct. 7, 1970), on the effects of herbicides in Vietnam.

None of the major Defense-funded studies concluded that herbicide use damaged human health; however, the National Academy of Sciences, in a February 1974 report, expressed concern over TCDD because of (1) its very high toxicity to animals, (2) its presence in Agent Orange, (3) preliminary reports of the presence of TCDD in fish in Vietnam, and (4) the lack of any data permitting assessment of TCDD effects in humans. As a result, the Academy recommended that long-term studies be made to obtain a firmer basis for assessing the potential harmful effects on man. More specifically, the National Academy of Sciences stated that:

"Further intensive studies are especially required with reference to the ecological distribution, the pharmacology mechanism of toxicity, possible mutagenicity, and carcinogenicity of TCDD and its possible teratogenicity in man."

Defense-funded studies are summarized in enclosure III; the National Academy of Sciences summary of the physical and biological characteristics of the herbicide components used in Vietnam is in enclosure IV.

Defense officials believe that no firm link has been made between long-term adverse health effects and exposure to herbicides in Vietnam. They stated that Defense (1) has no plans to conduct epidemiological studies on the possible

ill health effects of herbicide use in Vietnam and (2) has not issued any instructions to its medical facilities to monitor complaints of illness possibly resulting from herbicide exposure.

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As agreed during the June 28, 1978, meeting with your Office, we discussed the matters in this report with Defense officials and incorporated their comments where appropriate. As also agreed we are providing copies of this report to the House Committee on Veterans Affairs. Unless you publicly announce its contents earlier, no further distribution of this report will be made until 30 days from the date of the report.

Sincerely yours,



Henry Eschwege
Director

Enclosures 4

THE MILITARY USE OF HERBICIDES IN SOUTH VIETNAM 1/

Military herbicide operations began in South Vietnam (SVN) in early 1962 and were phased out in 1971. After a relatively slow buildup from 1962 to 1965 the operations increased rapidly to a peak in 1967; declined but only slightly, in 1968 and 1969; and dropped sharply in 1970. According to information from Defense the last herbicide spraying by fixed-wing aircraft occurred on January 7, 1971. After this, herbicide operations were limited to spraying around fire base perimeters, on enemy cache sites, and along land and water communication routes; all were carried out by helicopter or on the ground. The last helicopter spraying operation under United States control was flown on October 31, 1971.

THE HERBICIDAL AGENTS USED

The herbicidal agents used in SVN were identified by code names that referred to the color of bands painted on the containers of the chemicals: Orange, White, Blue, and Purple.

Agent Orange is a 50:50 mixture of the n-butyl esters of 2,4-D ([2,4-dichlorophenoxy] acetic acid) and 2,4,5-T ([2,4,5-trichlorophenoxy] acetic acid). Each gallon of Orange contains 4 pounds of 2,4-D and 4.6 pounds of 2,4,5-T on an acid equivalent basis 2/. Agent Orange was used most extensively in Vietnam until its use was terminated on April 15, 1970, because of concerns of its possible teratogenicity and its contamination with the highly toxic TCDD.

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- 1/ Information excerpted from "The Effects of Herbicides in South Vietnam," National Academy of Sciences, February 1974.
 - 2/ Acid equivalent is the weight of the acid form of the chemical. This is used because the weights of various ester or amine formulations vary. Expression in terms of acid equivalents provides a uniform basis for comparison of different formulations.

Agent Purple is a 50:30:20 mixture of the n-butyl ester of 2,4-D, and n-butyl and isobutyl esters of 2,4,5-T. It was used only until 1964, and was then replaced by Agent Orange.

Agent White is a mixture containing 2 pounds of 2,4-D and 0.54 pounds of picloram (4-amino-3,5,6-trichloropicolinic acid) per gallon on an acid-equivalent basis. It is a formulated product containing 2,4-D and picloram as the triisopropanolamine salts, with the addition of surfactants and water.

Agent Blue is formulated as the sodium salt of cacodylic acid (hydroxydimethylarsine oxide). It contains a minimum of 21-percent sodium cacodylate with additional free cacodylic acid for a total dimethylarsinic acid equivalent of not less than 26 percent on a weight basis, or 3.1 pounds of cacodylic acid and about 1.7 pounds of arsenic per gallon with 5-percent surfactant and 0.5-percent antifoam agent.

All agents were for use at a rate of 3 gallons per acre (28 liters per hectare), except that in the earlier operations and on rare occasions thereafter only half of this dose was used. The herbicides were applied by fixed-wing aircraft (UC-123), helicopter (UH-1), from trucks, from river boats, and from backpacks. Aircraft were outfitted with special spraying equipment consisting essentially of a container and a spray boom with nozzles. The container of the plane spray system had a 1,000-gallon capacity and normally flew at 150 feet with a delivery speed of 130 to 140 knots. The spray-on time of 3 1/2 to 4 minutes permitted approximately 950 gallons of herbicide to be distributed at the rate of 3 gallons per acre. The capacity of the helicopter spray system container was 200 gallons but the helicopter could carry only 100 gallons because of weight limitations. Herbicide spraying from tanker trucks used 50-gallon or 100-gallon drums. Spraying by river boats was done directly from the agents original 55-gallon drums; backpack sprayers had 3-gallon drums. The great majority of the herbicides were sprayed by plane--at least into the later part of 1970, from which time helicopter herbicide operations increased and gradually became the only aerial means of herbicide delivery.

MILITARY CLASSIFICATION OF THE
HERBICIDE OPERATIONS IN SVN

The herbicide operation objectives were (1) defoliation (the use of herbicides to cause trees and plants to lose their leaves to improve observation) and (2) crop destruction (the application of herbicides to plants to destroy their food value), directed at crops of hostile forces. Herbicides were also used, although on a much smaller scale and only by helicopter or on the surface (ground or water), for clearing vegetation around the perimeter of fire support bases and other military installations, on landing zones and enemy cache sites, and along lines of communication. Thus, there were essentially two military objectives of all herbicide operations--defoliation and crop destruction.

APPLICATION OF HERBICIDES IN THE VIETNAM WAR

<u>Agent</u>	<u>1962- July 1965a/</u>	<u>Aug- Dec. 1965</u>	<u>1966</u>	<u>1967</u>	<u>1968</u>	<u>1969</u>	<u>1970</u>	<u>1971</u>	<u>Total</u>
	-- -- -- -- -- (millions of gallons) -- -- -- -- --								
Orange		.37	1.64	3.17	2.22	3.25	.57	.00	11.22
White	--	0	.53	1.33	2.13	1.02	.22	.01	5.24
Blue	--	<u>0</u>	<u>.02</u>	<u>.38</u>	<u>.28</u>	<u>.26</u>	<u>.18</u>	<u>.00</u>	<u>1.12</u>
TOTAL	1.27	.37	2.19	4.88	4.63	4.53	.97	.01	18.85

a/ Detail by type of herbicide not available

HERBICIDES USED IN SVN 1965-1971

<u>Agent</u>	<u>Active chemical components</u>	<u>Military application rate (lb./acre)</u>	<u>Millions of gallons used, Aug. 1965 to 1971</u>
Orange	2,4-D	12.00	
	2,4,5-T	13.80	11.22
White	2,4-D	6.00	
	Picloram	1.62	5.24
Blue	Cacodylic acid	9.30	<u>1.12</u>
Total			<u>17.58</u>

Source: "The Effects of Herbicides in South Vietnam,"
National Academy of Sciences, Feb. 1974.

SUMMARY OF DEFENSE-FUNDED STUDIES WHICH DISCUSS
POSSIBLE HEALTH HAZARDS FROM MASSIVE AND REPETITIVE
APPLICATIONS OF HERBICIDES

Available Defense studies of the health effects of the herbicides used in Vietnam are discussed in this enclosure. These studies were made after concern was raised about the potential ecological and environmental hazards of spraying.

ASSESSMENT OF ECOLOGICAL EFFECTS OF
EXTENSIVE OR REPEATED USE OF HERBICIDES
(FINAL REPORT 15 AUGUST - 1 DECEMBER 1967)

The contractor, the Midwest Research Institute (Kansas City, Missouri) conducted a survey to assess the ecological consequences of the extensive and repeated use of herbicides, including herbicides in Vietnam. The scope included an examination of over 1,500 pieces of scientific literature, and interviews with over 140 experts on herbicide use and animal and plant ecology.

The contractor reported that only one generation had passed since chemical herbicides began to be widely used, and no articles or books had addressed the long-term ecological effects of herbicides on flora and fauna, rangeland, forests, other nonagricultural lands, waterways, lakes, and reservoirs. The authors hoped that their study would lead to a deeper study based on the additional research that is needed.

The report concluded that the aerial spraying of herbicides in Vietnam caused little or no toxicity hazard to people or animals. The report stated:

"The possible toxic hazards involved in the aerial spraying of herbicides in Vietnam are of concern to scientists and to the public.*** After examining the voluminous toxicity data and the actual rates at which these chemicals have been applied we can make the following observations: (1) the direct toxicity hazard to people and animals on the ground is nearly nonexistent, (2) destruction of wildlife food and wildlife habitat will probably affect wildlife survival more than any direct toxic effects

of the herbicides, (3) the application of Orange or White alongside of rivers and canals or even the spraying of the water area itself at the levels used for defoliation is not likely to kill the fish in the water, (4) food produced from land treated with herbicides will not be poisonous or significantly altered in nutritional quality (we use herbicides in large amounts on cropland in this country); if residues of a more persistent herbicide such as picloram should carry over to the next growing season it would retard plant growth rather than concentrate some toxic residue in the crop, (5) toxic residues of these herbicides (Orange, White, and Blue) will not accumulate in the fish and meat animals to the point where man will be poisoned by them, and (6) the primary ecological change is the destruction of vegetation and the resulting ecological succession in the replacement of this vegetation."

CONGENITAL MALFORMATIONS HYDATIDIFORM
MOLES AND STILLBIRTHS IN THE
REPUBLIC OF VIETNAM, 1960-1969

A medical team representing the U.S. Military Assistance Command, Vietnam, and the Ministry of Health, Republic of Vietnam (RVN), made a cooperative study of data on about 499,000 birth from 1960 to 1969 in 22 Saigon, provincial, and district hospitals to determine whether 2,4,5-T could be shown to increase developmental abnormalities in humans.

The December 1970 report describes the incidence of recorded congenital malformations, stillbirths, and hydatidiform moles in RVN before (1960-65) and after (1966-69) larger-scale military use of herbicides. The study failed to show any influence of herbicides on birth defects.

The report noted, however, that the study had several biases because:

--Nearly all the information was derived from population centers and the large hospitals.

- Data was restricted almost exclusively to ethnic Vietnamese. For example, Montagnards as a rule did not enter district or province hospitals, but delivered at home.
- Many records had been destroyed.
- Some hospitals admitted to incomplete reporting of birth defects during the earlier part of the 1960s.

THE EFFECTS OF HERBICIDES IN SOUTH VIETNAM

In response to public concern about the possible effects of herbicide use on the environment and people, the Congress directed Defense to contract with the National Academy of Sciences for a study of the ecological and physiological effects of the widespread use of herbicides in South Vietnam. (Public Law 91-441, Oct. 7, 1970.) The report was issued in February 1974.

A NAS committee spent about 1,500 man-days in South Vietnam during the course of the study. The study noted that (1) long-term field studies were virtually impossible because of the security conditions in South Vietnam and (2) safe access to large areas of the country was denied to the field teams, thereby frustrating their efforts to secure critical data.

The NAS committee could not gather any definitive indication of direct damage by herbicides to human health. The committee, however, was unable to visit the Montagnards in their own locales to verify common and consistent reports of serious illness and death, especially among children, after exposure to herbicide sprays. The committee concluded that although no independent medical studies of exposed populations were available from the time of spraying against which reports of illness and death could be confirmed or refuted, the reports on the Montagnards were so consistent that they could not be dismissed and should be followed up as promptly as possible by intensive studies which should include both medical and behavioral science approaches.

Because of (1) the very high toxicity of TCDD (dioxin) to animals, (2) the presence of this substance in Agent Orange, (3) preliminary reports of TCDD in fish in Vietnam, and (4) the lack of any data permitting assessment of TCDD effects on humans, the committee recommended long-term studies to obtain a firmer basis for assessing the potential harmful effects of TCDD on man. The committee made several other pertinent recommendations which largely depended on data to be subsequently obtained from Vietnam.

ECOLOGICAL STUDIES ON A HERBICIDE-EQUIPMENT
TEST AREA (TA C-52A) EGLIN AFB RESERVATION,
FLORIDA, FINAL REPORT: JANUARY 1967
TO NOVEMBER 1973

The Air Force Systems Command studied the ecological consequences of repetitive applications of massive quantities of herbicides from 1962 to 1970. The Command studied approximately one square mile at the Eglin Air Force Base Reservation in Florida. During this period, 346,117, pounds of herbicides (including 160,948 pounds of 2,4,5-T) were spread on the test area because of aerial spray equipment testing programs. The January 1974 report was authored by Capt. Alvin L. Young, Ph.D; Associate Professor of Life Sciences, United States Air Force Academy.

An evaluation of the effects of the spray equipment testing program on faunal communities was conducted from May 1970 to August 1973. In a 1973 study liver and fat tissue from 70 rodents from both on and off the test area were analyzed for TCDD. The analysis indicated that TCDD or a chemically similar compound accumulated in the liver and fat of rodents collected from an area receiving massive quantities of 2,4,5-T. On the basis of pathological studies, however, there was no evidence that the herbicides produced any developmental defects or other specific lesions in the animals sampled or in progeny. Lesions were interpreted to be of naturally occurring type and were not considered related to any specific chemical toxicity.

FATE OF 2,3,7,8-TETRACHLORODIBENZO-P-DIOXIN (TCDD)
IN THE ENVIRONMENT: SUMMARY AND
DECONTAMINATION RECOMMENDATIONS

The Department of Chemistry and Biological Sciences, United States Air Force Academy, initiated studies on Agent Orange and TCDD in April 1972, at the request of the Air Force Logistics Command. These studies were to (1) investigate soil incorporation/biodegradation as a disposal method for Agent Orange; (2) investigate the ecological effects associated with past uses of Agent Orange; and (3) investigate the soil persistence and food chain accumulation of TCDD. The October 1976 report was authored by Capt. A. L. Young, Ph.D; Maj. C. E. Thalken, DVM, MS; Lt. Col. E. L. Arnold, Ph.D; Capt. J. M. Cupello, Ph.D; and Maj. L.G. Cockerham, MS.

The report included data on the animal studies conducted at the Eglin Air Force Base Reservation test site (see preceding report summary p. 8). During 1973 and 1974 106 beach mice and 67 fetuses were examined. The authors reported no evidence that the herbicides produced any adverse long-term health effects in the rodents. Specifically, the authors reported that:

- Histopathologic examination in 1973 and 1974 of organs from the 173 adult and fetal beach mice showed only lesions which are normally observed in microscopic surveys of large numbers of field animals.
- Mature animals with liver levels of TCDD from 20 ppt₁/ to 1,300 ppt had no liver lesions. This is most significant in view of the massive quantities of both 2,4,5-T and TCDD that were applied to the test site.

1/ parts per trillion.

--There was no evidence to indicate that TCDD was mutagenic or carcinogenic in the field at the concentrations noted. None of the 34 fetuses examined from animals captured on the test grid showed teratogenic effects.

The authors concluded that these studies suggest that long-term, low-level exposure (less than 1 ppb 2/ to TCDD may in fact not be teratogenic, mutagenic, or carcinogenic.

2/ parts per billion.

CHARACTERISTICS OF HERBICIDES USED IN VIETNAM

The physical and biological characteristics of the components of the herbicides used in South Vietnam as summarized by the National Academy of Sciences in its February 1974 report, are presented below.

Picloram

Picloram, a component of Agent White, is a selective herbicide highly active on many broad-leaved plants. In the form used in herbicide operations in SVN it has a low volatility, making damage by vapor unlikely, but has a high solubility in water and a high stability in soil which may result in problems with herbicide movement in surface and drainage waters.

The acute oral toxicity of picloram and its salts and esters is low for mammals, and chronic toxicity is low for mammals and a variety of other animals including birds, fish, and crustaceans. No toxicity studies in man are known. No teratogenicity was found in rats at 1,000 mg/kg/day. 1/

Cacodylic Acid

Cacodylic acid, the active component in Agent Blue, is a nonselective herbicide that kills many herbaceous plants. It is a nonvolatile, highly soluble organic arsenic compound which is broken down in soil, mostly into inorganic arsenate bound as insoluble compounds which also exist naturally in the soil.

Acute and chronic toxicity studies in a variety of animals indicate a low-to-medium toxicity rating. No teratological studies nor toxicity studies in man seem to have been reported.

1/ Milligrams per kilogram of body weight per day.

2,4-D and 2,4,5-T

2,4-D and 2,4,5-T as the butyl esters, the active constituents of Agent Orange, are moderately volatile and highly insoluble in water; the triisopropanolamine salt of 2,4-D, present in Agent white, is nonvolatile and very soluble in water. Both 2,4-D and 2,4,5-T are stable at ambient temperatures. They are not very persistent within the plant because they are bound into nontoxic complexes or degraded. A highly toxic compound, TCDD, is a contaminant of 2,4,5-T but not 2,4-D (nor picloram).

Persistence of 2,4-D and 2,4,5-T in the soil is limited, and breakdown is largely accomplished by microorganisms. Adverse effects on soil microorganisms are found at concentrations of 100 ppm or more--about four times higher than would have been caused by one Agent Orange mission in SVN.

Extensive toxicological studies have shown 2,4,5-T and 2,4-D to be moderately toxic but are still inadequate to define the pharmacology or mechanisms of pathology. In acute exposures, the LD₅₀ ^{1/} ranges from 100 (pigs) to 2,000 (chicks) mg/kg.^{2/} Chronic doses are better tolerated and there is little cumulative action--e.g., 100 mg/kg/day for a year caused only minor deleterious effects in cattle, sheep, and chickens. A variety of unsatisfactory observations suggest that these findings apply also to man (if effects caused by TCDD are excluded). Acute exposures such as drenching by sprays sometimes produced vomiting, headache, reduced sensory perception, and limb paralysis. Long-term occupational exposure did not produce any consistent signs of toxicity.

2,4,5-T is moderately teratogenic in mice; cleft palates were produced in the offspring of mice treated with 300 to 100 mg/kg/day through day 6 to 15 of pregnancy or a single dose of 150-300 mg/kg on a day 12 or 13.

^{1/} LD₅₀ --Single lethal dose to 50 percent of test population of animals.

^{2/} mg/kg--milligrams per kilogram of body weight.

Kidney anomalies occurred in some strains. Less clear-cut results were obtained in the hamster and rat. No malformations were produced by similar chronic treatments in some rat strains and rabbits, sheep, and rhesus monkeys. The significance of these findings for man, if any, has not been established.

TCDD (2,3,7,8-tetrachlorodibenzo-para-dioxin)

TCDD, a contaminant of 2,4,5-T and thus of Agent Orange, is a very toxic material. Its teratogenicity in mice is well established, though in rhesus monkeys no teratological effects have been found. The toxicity to adults of different animal species varies within wide limits (over 1,000 times), and teratogenicity in mice also varies considerably between strains. The teratogenic dose can be lower than the embryo-lethal dose which, in turn, is somewhat lower than the adult toxic dose. Presence of TCDD in 2,4,5-trichlorophenol and 2,4,5-T was responsible for chloracne outbreaks and other toxic effects in workers involved in the manufacture of those products.

The presence of TCDD in 2,4,5-T has caused great public concern, and TCDD may indeed pose a great environmental hazard. It is a stable and persistent compound, but it seems to be taken up by plants to only a very limited extent and is not transported from early-to late-formed parts. This inability to transport in plants and its low solubility, relatively long persistence, and lack of vertical mobility in soils, makes TCDD more nearly resemble the chlorinated hydrocarbon insecticides in behavior than it does the more biodegradable phenoxy acid herbicides such as 2,4-D and 2,4,5-T, and even picloram. It can be concentrated by aquatic organisms in experimentally designed ecosystems, but to a lesser degree than DDT. Contamination of underground water supplies appears very unlikely.

2,4,5-T is probably the main source of TCDD in the environment. It should, however, be realized that at the present level of less than 0.05 ppm TCDD in the about-5,000,000 pounds of 2,4,5-T presently manufactured annually in the United States the amount of TCDD thus produced is maximally about 4 ounces (110 grams) per year which are spread over several million acres. 2,4,5-trichlorophenol

should not be entirely disregarded as another potential source of TCDD. A closely related compound hexachloro-dibenzo-para-dioxin, toxic at levels about 10 to 30 times higher than TCDD, may be present in or produced from a widely used chemical--pentachlorophenol. All herbicides used in the herbicide operations in SVN are toxic to animals in varying degrees. Some have been found to kill, damage tissue, or malform embryos of exposed pregnant female animals. TCDD is highly toxic and is teratogenic at least in mice. Although all these findings cannot be extrapolated to man, the question of possible harm to human embryos is raised. Further intensive studies are especially required on the ecological distribution, the pharmacology, mechanism of toxicity, and possible mutagenicity and carcinogenicity of TCDD and its possible teratogenicity in man.