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AGENT ORANGE FACT SHEET:

AN HISTORICAL PERSPECTIVE

The following information was compiled in 1979. It was designed to bring an awareness of AGENT ORANGE and related herbicides to the American public.

Herbicides were developed during the Second World War, initial work being done at the University of Chicago and later moved to Fort Detrick, Maryland. Although they were first considered for military use at the end of the War in the Pacific, the first application (of 2-4-D) was for domestic weed control in the US.

The first recorded military use took place in Malaysia in the 1950s where the British used 2-4-5-T to clear communication routes. The first US field tests were conducted in Puerto Rico, Texas, and Fort Drum in New York (1959).

In 1960 the South Vietnamese government requested that the U.S. government conduct trials of these herbicides for use against guerrilla forces. Further tests were conducted in Thailand by Fort Detrick personnel before the chemicals were given to the RVN.

The herbicides involved were known by their code names, Orange, White and Blue. There were several others, such as Purple.

AGENT ORANGE is a 1-124-1 mixture by weight of the n-butyl esters of 2-4-5-trichlorophenoxyacetic acid (2-4-5-T) and 2-4-dichloro-phenoxyacetic acid (2-4-D).

Agent White is a 3-882-1 mixture by weight of tri-iso-propanolamine salts of 2-4-dichlorophenoxyacetic acid (2-4-D) and 4-amino 3-5-6-trichloropicolinic acid (pico-lorum).

Agent Blue is a 2-663-1 mixture by weight of na-dimethyl arsenate (na cacodylate) and dimethyl arsenic (cacodylic acid). Agents

Orange and White are used as defoliants and Agent Blue as a desiccant.

Agent Blue was produced by Ansul Chemical Company which has divested itself of this line prior to selling the company. Agents Orange and White are still being produced. The most widely produced and dispensed of the herbicides in both Vietnam and the U.S. is AGENT ORANGE (2-4-5-T and 2-4-D).

Adverse effects of the chemical 2-4-5-T and its chemical precursors on the workers engaged in their production had been observed as early as 1949. At that time a Monsanto-owned plant manufacturing 2-4-5-T in Nitro, West Virginia, had an explosion, and 228 workers developed Chloracne.

Chloracne symptoms include skin eruptions on the face, neck, and back, shortness of breath, intolerance to cold, palpable and tender liver, a loss of sensation in the extremities, damage to peripheral nerves, fatigue, nervousness, irritability, insomnia, loss of libido and vertigo.

Chloracne was also found in 1953 among the male workers and many of their wives, children and pets at a BASF (Badischer Anilin & Soda Fabrik)-owned 2-4-5-T plant at Ludwigshafen am Rhein in Germany.

The factory experienced an explosion months after the appearance of Chloracne among the workers. In medical examinations following the explosion, some workers were found to have severely damaged internal organs including the liver. Heightened blood pressure, myocardial degeneration, severe depression, memory and concentration disturbances were also observed. Fifteen years later some of these workers were still suffering from Chloracne and its symptoms despite treatment and no subsequent exposure. One death from intestinal sarcoma was attributed to the explosion

In 1963 another explosion occurred in a 2-4-5-T factory owned by Philips Duphar in Amsterdam, Holland. Fifty workers developed Chloracne and suffered internal damage and serious psychological disturbances as a result, and the factory was closed. In 1973 the plant was still so contaminated with Dioxin that it had to be dismantled, embedded in concrete, and buried at sea.

Dow Chemical, the largest producer of AGENT ORANGE in the U.S. experienced an outbreak of Chloracne among its workers in 1964 in one of their 2-4-5-T manufacturing plants. Over seventy workers were affected, 12 of them severely.

Dow's director of its Midland Division, Dr. Benjamin Holder, described the symptoms as fatigue, lassitude, depression, blackheads (prevalent on the face, neck, and back), and weight loss. Heavy exposure, Dr. Holder said, could lead to internal organ damage and nervous system disorders.

In 1970, Julius F. Johnson, Director of Research and Development, appearing before the Hart Sub-Committee of the U.S. Congress, described Chloracne as "a skin disorder mostly prevalent of the face, neck, and back. It is similar in experience to severe acne of the kind suffered by teenagers".

Dow ran its own study of the effects of ORANGE using 220 workers and 4,600 controls. The range of exposure to 2-4-0 was 30-40/mg/do. Ten of the men were karyotyped, and no rearrangement of genetic material was reported. The 220 men were exposed to 2-8/mg/do of 2-4-5-T. Fifty two men were karyotyped negatively. No difference between the study group and the control group was reported.

Dow's testing indicated that a contaminant of 2-4-5-T (Dioxin) was responsible for the Chloracne and illness experienced by its workers. They conducted tests utilizing animals on 2-4-5-T with varying amounts of 2-3-7-8-tetrachlorodibenzo-p-dioxin.

At levels of 27 ± 8 the chemical was shown to be toxic and fatal to the animals. Cleft palates were observed in further tests. The results were not repeated with 2-4-5-T without the contaminant. Dioxin was found to be one of the most toxic substances known, a fatal dose being 0.022-0.045a in rats and 0.0006 in guinea pigs, LD-50 as milligrams per body weight.

Between 1965 and 1969 a 2-4-5-T production plant near Prague, Czechoslovakia, developed leaks in its processing area. Workers developed Chloracne and exhibited weight loss, libido diminution and insomnia.

Maximum symptoms were observed about one to two years after the initial exposure but lasted over eight years in some of the exposed workers. Several workers died of severe liver damage, and workers' families also became sick. Contaminated equipment was buried in a mine shaft.

Other studies of workers exposed to 2-4-D and 2-4-5-T were conducted by Festisov (1966), Long (1969), Poland (1971), Sundell (1972) and Piper (1973).

These studies showed exposed workers exhibiting symptoms including fatigue, headaches, loss of appetite, stomach and kidney pain, upper respiratory distress, decreased hearing, smell and neurological responses, high serum albumin values, skin and eye irritations and concentrated TCDD (Dioxin) levels in body fat and liver tissue. The studies inconclusive epidemiological results must be re-examined in light of their design deficiencies, such as lack of use of control groups (Festisov, Poland), insufficient follow-up period in a retrospective study (Sundell) and lack of longitudinal studies which would provide adequate evidence of temporary and long-range effects (NAS). Further tests showed TCDD, the contaminant in 2-4-5-T, to be an extremely toxic agent with a slow effect rate and diverse symptomatology including edema, necrotic changes of the liver, gastric hyperplasia and ulceration, hemmoroglus of gastrointestinal tract and other organs, atrophy of the kidneys, thymus and other lymphoid organs and tissues. Later, symptoms appear to lead to decreased immune responses.

AGENT ORANGE (contaminated with Dioxin) and Agent White were authorized for use in Vietnam in November 1961, to improve road and waterway visibility and clear camp perimeters.

Later, **Agent Blue** was authorized to destroy crops and clear areas suspected of harboring enemy base camps or supply routes. The U.S. Air Force created the 309th Air Commando Squadron to conduct the spraying. The operation, originally known as Hades, and became known as Operation Ranch Hand.

In the spring of 1962 the South Vietnamese military conducted large-scale tests of herbicides along 70 miles of Highway 15. In the summer, further tests were conducted using 2-4-D at 1.5 gallons/acre and 2-4-5-T at 3.3 gallons/acre. The herbicides used in Vietnam were applied mostly by twin engine C-123 Provider Transports (Fairchild Hiller) equipped with 3785.1 tanks and an internal defoliant dispenser (Hayes International) with 36 high-pressure nozzles distributed on three booms.

Normal spray time was two minutes, but a full load could be dumped in 30 seconds. Missions usually consisted of three to five aircraft flying in a staggered lateral formation. Single plane runs were known as sorties. Helicopters, UH-1 Huey (Bell Aerospace), trucks, boats and hand spraying equipment were also used to dispense the herbicides in Vietnam.

Targets were selected by U.S. or Vietnamese officers, approved by provincial chiefs, the Vietnamese Army general staff, the U.S. Military Assistance Command and the American Ambassador.

During this time, Air America also sprayed defoliants for the CIA in combat operations against Thai insurgents on the Isthmus of Kra. The drift of herbicides involved in these operations was estimated at an average of 20%.

AGENT ORANGE, the main herbicide dispensed in this period, was applied at up to 25 times the rate of use in the U.S. Entire tank loads were also jettisoned over one area.

Schedules of the herbicide spraying missions were recorded on HERBS tapes, a computerized record of time, place, geographic location of beginning, end and flight line of the mission, amount and type of herbicide and the military purpose of the operation. The tapes cover the period from August 1965 to February 1971. The HERBS tapes were studied for accuracy by the NAS Committee, which traveled to Vietnam, and were found to contain inaccuracies. Even so, they may offer one source to check individual dose exposure in the period covered when 85% of the missions were flown.

As early as 1964, while the spraying was increasing in Vietnam, reports circulated of increased miscarriages stillbirths and birth defects among exposed Vietnamese women and animals. Because of the war conditions collecting data to corroborate this was difficult.

Records from 1970 for Saigon's leading maternity hospital showed a monthly average of 140 miscarriages and 150 premature births in 2,800 pregnancies, but the hospital would not disclose whether or not this was an increase.

In 1966 the U.S. government started studies on the teratogenic effects of 2-4-5-T. These studies were conducted by Bionetics Research Laboratories of Bethesda, Maryland, for the National Cancer Institute.

The findings were released in 1969. Rats and mice used in the study were given 21.5 mg/kg doses of 2-4-5-T during early gestation. Almost all the offspring were born dead or with cleft palates, no eyes, cystic kidneys and enlarged livers. At 4.6 mg/kg, 39% of the offspring were born deformed. Based on these findings Dr. Lee Du Bridge, Presidential Advisor, said that the use of the chemical in populated areas and on food crops should be restricted.

Dow objected to the findings saying the sample of the 2-4-5-T was used unrepresentatively because of an abnormally high amount of TCDD (Dioxin). As a result, new tests were ordered by Dr. Burger, Dr. Du Bridge's technical assistant, and 2-4-5-T was left in use.

Other tests were run by Dr. Jackie Verett of the FDA Toxicology Lab in Washington, D.C., Dr. Matthew Meselson of Harvard, the National Institute. Dr. Verett used a .50 parts per million Dioxin solution obtained from chemicals used in Vietnam in chicks and found resultant cysts, necrotic livers, slipped tendons, cleft palates and beak deformities.

She then used a .25 parts per trillion solution and observed the same effects. Further tests of 2-4-D and 2-4-5-T without Dioxin still produced dead and deformed offspring. English tests had demonstrated AGENT ORANGE to contain as many as 17 or more contaminants.

Dr. Meselson was the head of an American Association for Advanced Science project. His concern was Dioxin activity and the unknown results of its behavior. "The tetrachloro-dioxin re-presents just one of the 12 or 13 ways the chlorine atoms arrange themselves on a benzene ring to form Dioxin molecules. How do we know about hexa, hepta and octychlors or about how persistent the tetrachlor itself is? Moreover, I am very concerned about the Dioxin that might be formed by unreacted trichlorophenol (2-4-5-T's precursor) when the product is exposed to heat. If it were taken up by plants or wood and these were burned, you'd get more Dioxin. Finally, I'm bothered by the bizarre mental effects suffered by German workers making 2-4-5-T. I say, when in doubt, stop it."

The National Institute of Environmental Health Ser-vices Study used samples of 2-4-5-T which were far less contaminated with Dioxin than the 2-4-5-T used in the Bionetics Study. The results showed 2-4-5-T to have significant teratogenic effects on the study of animals.

Based on this study, on April 15, 1970, Dr. Jesse L. Steinfield, Surgeon General, and David Packard, Secretary of Defense, announced government action limiting the use of 2-4-5-T in the U.S. and suspending its use in Vietnam.

The National Cancer Study conducted by Courtney showed 2-4-5-T adversely affecting the development and viability of mouse and rat fetuses.

"I suggest that the teratogenicity of 2-4-5-T is such that even its use in such apparently innocuous domestic matters as clearing brush near power lines is undesirable. Such chemicals could find their way into water supplies and could be ingested in teratogenic-doses", (statement of Dr. Arthur Galston, Yale University, December, 1969, to the Subcommittee on National Security Policy and Scientific Development of the Committee on Foreign Affairs, House of Representatives).

Autopsies of 600 reindeer in northern Sweden which had consumed foliage sprayed with AGENT ORANGE showed a significant residue of the herbicide in the kidneys and liver of the deceased animals.

The Piper Study (1973) also showed Dioxin concentration in the liver and body fat of exposed workers up to ten times the normal concentration.

In 1975 the CDC in Atlanta studied AGENT ORANGE and issued a report showing that exposed animals suffered appetite loss, vascular lesions, Chloracne and gastric ulcers.

More recent tests indicate Dioxin may be concentrated in fatty tissue and released into the blood stream after the initial exposure. Vietnamese epidemiologists have indicated a four-fold increase in liver Cancer in Vietnam in the last ten years.

Despite these tests and world-wide evidence of the effects of AGENT ORANGE, it has remained in use on rice crops in Arkansas, range land in the West and Southwest, national forests and along railroad and power lines. In 1973 Matthew Meselson and Dr. Robert Boughman refined an analytical system for detecting the presence of Dioxin in parts per trillion instead of billion.

Using their system, they found Dioxin residues in Vietnamese crustaceans, indicating that Dioxin had entered the food chain as a result of earlier 2-4-5-T use.

Dow's scientists continued to maintain that 2-4-5-T, when used as directed, presents inconsequential hazards to the environment, animals and man.

The evidence shows that AGENT ORANGE was dispensed in Vietnam in amounts far in excess of previous use; thus, the exposure of U.S. soldiers and the Vietnamese was not as directed. Soldiers in Vietnam sprayed one another with AGENT ORANGE in spray fights as they were told the chemical was harmless.

While U.S. government departments were and were not dealing with 2-4-5-T, on July 10, 1976, another factory had an explosion. The factory, located in Seveso, Lombardy, Italy, was owned by ICMESA with a Swiss parent company.

The explosion produced a cloud of Dioxin which settled over several adjacent communities. The people exposed became nauseated, experienced eye and throat irritations, developed burn-like sores on exposed skin, headaches, dizziness and diarrhea -- the same symptoms recorded by exposed Vietnamese and Cambodian populations. In the next two days, small animals in the area began to die. Most of the small animals in Zone A of the exposed area died or had to be destroyed. Post mortems showed that they died of Dioxin poisoning and had extensive liver damage.

Because of the publicity on the teratogenicity of Dioxin, abortions were made available to the exposed women.

Studies of the situation at the ICMESA plant revealed that Dioxin was probably escaping periodically from the plant over a two-year period prior to the explosion. Two and a half months after the explosion, children and young people began to develop Chloracne.

A year later 130 people had confirmed Chloracne. Symptoms included nervousness, irritability, loss of appetite and sexual drive. Spontaneous abortions appeared to double; the level of birth defects could not be determined because of the abortions. In 1977 it was discovered that 280 children in an area north of the contaminated area were suffering from Chloracne.

Deaths among workers exposed to Dioxin contamination should be examined, as they are among the earliest exposed, and evidence indicates delayed onset of fatal chronic conditions.

In 1958 a worker was assigned work on or near the reactor that was involved in the 1953 explosion in the Badischer Anilin & Soda Fabrik 2-4-5-T factory. The reactor had not been used since the explosion, and the worker used protective clothing which included a face mask. He removed the mask several times during the work. Four days later he was suffering from headaches and had developed hearing loss and Chloracne. Within six months he developed pancreatitis and an upper abdominal tumor. The man died three months later.

Another worker at the same plant who spent two hours working on the reactor wall in 1958 also developed a severe case of Chloracne. One year later a large x-ray opaque area appeared on one of his lungs. Five years after the initial exposure, the worker suffered acute psychosis and committed suicide.

Two British workers at the Coalite factory in Bolsover, England, (which had experienced an explosion in 1968) were exposed to cleaned equipment involved in the explosion three years earlier. Within a month both developed Chloracne. In the next year members of both their families also developed Chloracne.

The Philips Duphar plant in Amsterdam had the problem when workers tried to decontaminate the plant involved in the 1963 explosion six months later.

Although all but one of the workers wore deep-sea diving suits and industrial facemasks, nine of the men contracted Chloracne, and three of them died within the next two years. The worker who was not as well protected was still being treated in 1976 for severe effects and was unable to work.

Studies of these and other exposed workers' morbidity and mortality data would seem essential to construct an overview of the epidemiology of 2-4-5-T exposure, especially to help establish risk factors for exposed populations.

Studies in animals are also being conducted. Dr. James Allen, at the University of Wisconsin, has been running studies on the effects of dioxin-contaminated food on nonhuman primates. This seems particularly efficacious in light of recent evidence that rodents often used in medical research seem to be subject to inherent viruses which could distort test results.

Dr. Allen's studies with animals indicate that dioxin persists and accumulates in the tissue of primates. In his rodent studies Dr. Allen found a significant increase in the development of neoplasms suggesting the carcinogenic potential of the compound TCDD.

Beef cattle grazing on western ranges sprayed with 2-4-5-T a year earlier were found, in 1974, to have sixty parts per trillion Dioxin in their fatty tissue, a significant amount.

Dr. Meselson, who has continued his studies at Harvard, has examined the milk of women exposed to the herbicide in Texas and Oregon, and the results seemed to indicate the presence of Dioxin in parts per trillion in some of their milk. Both these results and the cattle tests indicate that Dioxin, one of the most toxic substances known to man, has entered the human food chain.

The evidence also indicates that the herbicide AGENT ORANGE (2-4-D + 2-4-5-T + contaminants, especially TCDD) has both teratogenic and carcinogenic potential for exposed animals and humans. The teratogenic effects may be checked in cases where pregnant women are exposed, but evidence in Vietnam indicates that the mother may suffer chromatin or chromosomal damage following exposure and pass this damage on to subsequently conceived children. One of the complaints of Vietnam veterans is the high incidence of birth deformities (including monsters) present in their children.

Karyotyping should be done on these veterans and their offspring and all birth defects recorded. (The U.S. has no national register for recording birth defects.)

The carcinogenic potential of 2-4-5-T, or AGENT ORANGE, will be harder to ascertain as it involves the development of chronic disease with diverse symptomatology over an undetermined and lengthy amount of time.

The symptomatology developed by populations exposed to AGENT ORANGE and its components, 2-4-D, 2-4-5-T and contaminants, has been demonstrated around the world over a lengthy period of time. Further examination of the teratogenic and carcinogenic effects have been conducted in different animal experiments.

However, no serious epidemiological study has been done in this country, and the government, for example the VA, has used this to disclaim causality. The argument used is that there is no scientifically proven causality, but no one has designed a study to attempt to establish such a correlation in humans. Dow Chemical, one of the largest producers of AGENT ORANGE and White, has conducted a considerable amount of research, especially on the unavoidable contaminant Dioxin in AGENT ORANGE.

Their most recent conclusion revealed by an 18-member task force after several months of study was that Dioxin is present everywhere in the environment where combustion occurs, and Dow went on to argue against zero effluence limits for Dioxins which the EPA and FDA are interested in.

Dow still argues that these Dioxin levels are so low as to be harmless, especially since they are airborne rather than transmitted through the food chain. The government seems to be moving toward shifting the burden of proof away from itself to the producers with irrefutable defense papers. EPA toxicologist, Lyman Condie, says that this

On March 11, 1979, the Environmental Protection Agency (EPA) took unprecedented steps against the chemical. In the first such emergency ban ever, the EPA ordered the immediate halt to most uses of the herbicide 2, 4,5 T which contains Dioxin, and a similar product used for weather control known as Silvex.

The emergency suspension action was temporary while further facts were gathered, but it was the most drastic measure the EPA could take under the law.

The EPA said it was acting on significant new evidence linking the herbicide 2, 4, 5-T with miscarriages in women in Oregon.