AN INTERIM REPORT
SUMMARIZING
2 , 4 - D TOXICOLOGICAL RESEARCH
SPONSORED BY THE
INDUSTRY TASK FORCE ON 2 , 4 - D RESEARCH DATA
AND
A BRIEF REVIEW OF
2 , 4 - D ENVIRONMENTAL EFFECTS

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HISTORY AND USE

The first published article on the use of 2,4–D as a herbicide appeared in 1944 which was also the first year that 2,4–D was sold as a herbicide. Since then, 2,4–D has become probably the most widely used herbicide in the United States, and perhaps the world, because of its effectiveness and low cost. A 1978 scientific review stated that more than 40,000 scientific articles and technical reports had been published at that time. Few chemicals, if any, have ever been researched as thoroughly as 2,4–D.

The major uses of 2,4–D are for selective postemergence weed control of herbaceous, broad-leaved weeds in cereal crops such as wheat, barley, oats, rye, and corn. It is also effective for the control of certain water weeds - like Eurasian water milfoil and water hyacinth. In rangelands, forests, pastures, roadsides and non crop areas, 2,4–D may be used to control some woody plants such as willow, sumac and sagebrush. Its utility for control of dandelions and plantains in lawns and ornamental turf is well known.

INDUSTRY TASK FORCE ON 2,4–D RESEARCH DATA

On April 29, 1980, the U. S. Environmental Protection Agency (EPA) issued a 2,4–D Fact Sheet which announced that many of the studies in their scientific data files, which were used to support the registration of 2,4–D herbicides, did not meet current day standards for toxicology tests. Most of the studies were scientifically valid and showed that the use of 2,4–D did not pose an imminent hazard or unreasonable adverse effect when used as directed on product labels. Nonetheless, EPA felt new data should be generated. Therefore on August 29, 1980, EPA issued an Order and Notice informing registrants of 2,4–D products that significant gaps existed in the data base for 2,4–D, and that additional scientific information would be required from the registrants under Section 3(c) (2) (B) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) if these 2,4–D registrations were to be continued with EPA.

On October 29, 1980, EPA was notified by letter that an Industry Task Force on 2,4–D Research Data had been formed which made a commitment to the Agency to develop the requested scientific data. After several meetings with EPA to clarify test requirements and to identify the appropriate test compounds, protocols were developed to obtain the requested data. As indicated previously, not all the scientific studies requested were to fill data gaps. While earlier test reports containing similar data had been submitted to EPA to obtain registration, the studies had been conducted prior to implementation of current guidelines. EPA apparently felt the studies should be repeated using the latest techniques to confirm the results obtained from the earlier tests. In addition some information was requested that was not required for the original registration.

The Task Force is composed of 13 domestic and foreign companies that manufacture or sell technical 2,4–D acid. The first step for the Task Force was to select a blend of 2,4–D for use in the toxicological testing program. The blend had to be "representative" of the 2,4–D sold by the 13 member companies of the task force. For this reason, the results of this toxicology testing obtained by the Task Force are meaningful only if the end product contains technical 2,4–D manufactured or sold by a member of this Task Force.

SUMMARY OF TOXICOLOGY STUDIES SPONSORED BY THE INDUSTRY TASK FORCE ON 2,4–D RESEARCH DATA

EPA requested eight types of toxicological information which required 30 tests that were scheduled by the Task Force to provide the desired scientific data. These ranged from tests using single oral doses of 2,4–D acid and other derivatives to two-year feeding studies in mice and rats and a multigeneration reproduction study on rats.

Before discussing the results and to assist in better understanding these studies, the Toxicology Background Section of EPA'S 2,4–D Fact Sheet of April 29, 1980, is quoted below:

IV. Toxicology Background

The potential hazard of a chemical is usually measured in laboratory animal tests. Animals are given doses of a chemical over a specific time period. Scientists attempt to derive from most of these tests a "no observable effect level" (NOEL) -- the dose level below the dosage where effects are first observed. From the animal tests and NOEL's, the potential effects on humans and other animals can be estimated. A set of brief definitions is provided below to permit better understanding of the subsequent discussion of toxicological findings.

A. General terms

1. Acute oral toxicity (LD50) - this test determines the dose level which produces death in half the test animals after a single oral dose (short-term test). Used to predict the near-term toxicity of the chemical immediately upon contact with people or other non-target animals.

2. *Chronic feeding tests - animals are fed for most their life span (usually greater than 18 months in rodents) in order to determine the dose level which shows no toxic effect in test animals. This is the test from which the NOEL is (usually) derived.*

3. *Oncogenicity testing - animals fed relatively large doses of the test chemical for their life span (usually 18 months to 2 years in rodents) to try to induce tumors. These tests are used to predict whether the chemical may pose a cancer hazard.*

4. *Reproductive testing - these tests evaluate the effects of the chemical on the fertility of both the male and female parents by exposing the animals for a period of time before breeding. The tests also measure the possible effects of the chemical on the pregnant female and the fetuses through several generations. (The test with rodents through 3 generations runs approximately 14 months.)*

5. *Teratology testing - these tests evaluate the effects of the chemical on fetuses by exposing pregnant females during the short period of time that the fetus is most susceptible to congenital malformation. Teratogenic effects include cleft palate, central nervous system deformities, eye and limb deformities, and internal organ malfunction. These are considered to be life-threatening effects that put the animal at a disadvantage for surviving in its environment.*

6. *Fetotoxicity - fetotoxic effects can be seen in either the reproduction or teratology tests. Toxicity may be seen in the extreme form as fetal death or as less severe problems, such as delayed formation of bones, reduced body weights at birth, or edema (abnormal fluid accumlation in the tissue). Most fetotoxic effects appear to be reversible once exposure to the test chemical is curtailed. Therefore most fetotoxic effects are considered to be less serious than teratogenic effects, with the exception of fetal death.*

The results of the new toxicological research studies conducted for the Industry Task Force on 2,4–D Research Data are briefly summarized herein.

Acute Dermal Toxicity

The acute dermal LD_{50}[1] using rabbits was more than 2,000 mg/kg for 2,4–D acid, its sodium salt, dimethylamine salt, isobutyl ester, butyl ester, butoxyethanol ester, and isooctyl ester. Compounds having dermal LD_{50} values of 2,000 mg/kg or more are considered to have low dermal toxicity. According to EPA guidelines, when compounds have such low dermal toxicity, further investigations of dermal toxicity are unnecessary. The low dermal toxicity of 2,4–D is very important as this is the most usual route of human exposure during application.

Acute Oral Toxicity

These results show that 2,4–D acid and its derivatives have moderate to low acute oral toxicity. The acute oral LD_{50}[2] values using rats for various derivatives of 2,4–D are given in Table I.

Table I

ACUTE ORAL LD50'S FOR SEVERAL 2,4–D COMPOUNDS WITH FISCHER 344 RATS

Compound	LD_{50} (mg/kg)*
2,4–Dichlorophenoxyacetic acid (technical)	699
Sodium salt of 2,4–Dichloro-phenoxyacetic acid	997
Butyl ester of 2,4–Dichloro-phenoxy acetic acid	695
Dimethylamine salt of 2,4-dichlorophenoxyacetic acid	949
Isooctyl ester of 2,4–Dichloro-phenoxyacetic acid	896
Isobutyl ester of 2,4–Dichloro-phenoxyacetic acid	618
Butoxyethanol ester of 2,4-dichlorophenoxyacetic acid	850

*Milligrams of test substance per kilogram of body weight of the test animal.

Acute Inhalation

The acute inhalation LC_{50}[3] for rats (Sprague-Dawley) after a four-hour exposure was determined to be greater than 1.79 mg 2,4–D acid per liter of air. This amount was the maximum obtainable concentration of 2,4–D in air. Since no deaths occurred at this dosage and a higher concentration cannot be obtained, an LC_{50} cannot be calculated. The results show that 2,4–D has a low inhalation toxicity.

Dermal Sensitization

In preparation for the sensitization test, 0.5 ml of a 0.5% solution of 2,4–D acid in acetone was applied once a week to a clipped area on the back of guinea pigs for three

weeks. Two weeks following administration of these dosages, a challenge dose of 0.5 ml of the same solution was applied the same way. Observations were taken 24 and 48 hours after the test application to assess the effects of this treatment. No redness, swelling or other dermal effects were noted. On the basis of these results, 2,4–D acid would be classified as being a non-sensitizer in guinea pigs. When the results of this test are negative, no further tests on this subject are necessary.

Sub-chronic toxicity

A 90-day feeding study was conducted with rats (Fischer 344 strain) using technical 2,4–D acid at dose levels of 0 (controls), 15, 60, 100, and 150 mg/kg of body weight/day. Various parameters, such as food intake, body weight changes, blood studies and urine analysis, were measured during the in-life phase of the study. At the conclusion of the experiment, both gross and microscopic examinations were made of all tissue and body organs of the animals. At the highest dosage of 150 mg/kg/day, the toxic symptoms were: decreased intake of food, lower body weight gains than untreated animals, and evidence of slight effects on the liver and kidney. These effects were reduced at lower dose levels; however, it was concluded that dose levels of 60 mg/kg/day and above exceeded the Maximum Tolerated Dose (MTD) for rats. At the lowest dosage of 15 mg/kg/day, no adverse effects were noted in female rats, but in male rats this dose level produced a slight increase in relative kidney weight with no microscopic changes.

Since the MTD had been exceeded at most dose levels and a slight effect was still seen on male rats at the lowest dose tested, another 90-day feeding study was conducted with rats at lower dose levels. The diets contained levels of 2,4–D acid which amounted to dietary intakes of 0, 1, 5, 15 and 45 mg/kg of body weight/day and the same parameters were evaluated as in the previous study. The results showed slight compound-related increases in the weights of the kidney and thyroid accompanied by slight visual differences on microscopic examination of the kidney at the 5 mg/kg/day and higher doses. Possible compound-related decreases in enzyme levels in the blood serum were also observed. No compound-related effects were observed with regard to survival, clinical signs, body weights, growth rates, food consumption and eye effects. These results confirmed the effects found in the first study.

Highly purified 2,4–D acid (reported as 100%) was also evaluated at 0, 15, 60, 100 and 150 mg/kg/day in a 90-day feeding study on rats (Fischer 344 strain). The responses were essentially the same as those found when using the technical grade of 2,4–D acid (97.3%). These results showed there was little if any difference in toxicity between the technical grade and the highly purified 2,4–D acid.

A 90-day mouse ($B_6C_3F_1$ strain) feeding study was conducted using technical 2,4–D acid. The dose levels were: 0, 5, 15, 45, and 90 mg/kg/day. The same parameters were evaluated as in the subchronic rat studies. Slight compound-induced changes were noted in the kidneys upon microscopic examination. These were most frequent at the highest dosage and decreased as the dosage was lowered, with effects being minimal at the lower concentrations. Increases in organ weights in the pituitary, adrenals and kidneys (females only) were observed. No compound-related effects were observed in terms of survival, clinical signs, body weights, growth rates, food consumption, eye effects or gross and microscopic pathology.

Teratology

Technical 2,4–D was administered by gavage (stomach tube) daily for 10 days in pregnant rats during the period of most rapid organogenesis (development of organs and main body structures). The dosage levels were 0, 8, 25, and 75 mg/kg/day. Some slight maternal toxicity was shown by inhibition of their body weight gains at the 75 mg/kg/day level but no other maternal and no embryo-toxic effects were observed. The conclusion was 2,4–D is not teratogenic in rats even at dosages that caused toxic symptoms in the dams.

Metabolism

The metabolic behavior of 2,4–D acid was studied in rats after the oral administration of the sodium salt of ring labeled ^{14}C 2,4–D. It was found that 90% of the 2,4–D was excreted in the urine within 12 hours and 95% within 24 hours after administration of a single oral dose. These results suggest that 2,4–D would not accumulate in rats even after repeated oral ingestion.

The isooctyl ester of 2,4–D was administered to rats to see if the metabolic pathway would be the same as for the acid. The results showed that the isooctyl ester of 2,4–D is quickly converted to 2,4–D acid which is then rapidly excreted in the urine. These results demonstrated that the isooctyl ester of 2,4–D was metabolically equivalent to 2,4–D acid which would also be true for other esters of 2,4–D.

Similarly, the metabolic behavior of 2,4–D was studied after dermal application to rats of ring labeled ^{14}C 2,4–D as the propylene glycol butyl ether ester. The results showed that the ester was absorbed slowly through the skin, and was converted rapidly to the acid in the body. The 2,4–D was excreted in the urine as the acid, with a half-life of 20 hours. Thus, the rate of absorption of 2,4–D ester through the skin was slower than its rate of hydrolysis to 2,4–D acid and its subsequent excretion in the urine. These results suggest that 2,4–D would not accumulate in rats even after repeated dermal exposure.

Mice were also used in a metabolic study of 2,4–D. The metabolic pathway of 2,4–D in the mouse was similar to that in the rat. The 2,4–D was excreted mainly in the urine by the kidney, but at high dosage levels, some elimination of 2,4–D also occurred in the feces.

Neuropathology

Questions have been asked as to whether 2,4–D would cause any neuropathological effects. These are effects on the peripheral nervous system usually manifested by a tingling or numbness of the fingers and toes. A 12% solution of a 2,4–D amine in water was applied dermally to rats for three weeks. Measurements were made of responses of the tail and hind leg rat nerves. Observations also were made of the rat's behavior in a rod rolling test which is similar to a lumberjack's log rolling contest. All the measurements obtained were found to be within the normal range. Microscopic examination of the brain, spinal cord and peripheral nervous tissue showed no adverse effects. These data showed that 2,4–D did not cause neuropathic adverse effects in rats.

Multigeneration Reproduction

A multigeneration reproduction study with rats was conducted at dose levels of 0, 5, 20 and 80 mg/kg/day. Parameters evaluated included effects on mating, gestation, lactation, body weights of parental animals and offspring, as well as gross and microscopic pathological examination of body tissue and organs. During gestation and lactation of the F_0 (original parents) generation, the dams in the 80 mg/kg of body weight/day group actually received a dosage of about 120 mg/kg/day. Adverse effects on the F_0 generation and the F_{1b} pups were excessive, prompting termination of the 120 mg/kg of body weight/day dosage level. The complete reproduction study, therefore, was conducted only at the 0, 5, and 20 mg/kg/day dosage levels. A slight decrease in pup weights was seen throughout lactation at the 20 mg/kg dose level. No reduction in reproduction indices was observed at either level. The NOEL was 5 mg/kg/day in this rat reproduction study.

Chronic Feeding Studies

A chronic two-year feeding study on rats (Fischer 344 strain) has just been completed.[4] Such studies are often considered to be lifetime feeding studies. The dose levels were 0, 1, 5, 15, and 45 mg/kg/day. A NOEL was considered to be 1 mg/kg/day, because minor effects were detected on microscopic examination of kidneys at the 5 mg/kg/day level and higher doses. These effects were not surprising since the kidney is one of the major organs of elimination. A slight, but statistically significant, increase in astrocytomas (brain tumors) was observed in the male rats at the highest dosage of 45 mg/kg/day. Astrocytomas are the most common type of brain tumors found in rats and occur spontaneously. Similar results have been obtained in studies with other chemicals, suggesting that this apparent increased incidence in the high dose males may have been simply due to biological variability among the animals used in this study. Therefore, further clarification was necessary to determine if the tumors in this study were caused by 2,4–D or were due to random variability in the groups of the tests animals.

A recognized expert in this field, Dr. Adalbert Koestner, Professor and Chairman of the Department of Pathology, Colleges of Human Medicine, Veterinary Medicine and Osteopathic Medicine at Michigan State University, East Lansing, Michigan, conducted a thorough biological evaluation and analysis of the study results. To demonstrate a cause and effect for astrocytomas, the data must satisfy about 11 known criteria to be a neurocarcinogenic agent. In this case 2,4–D did not meet any of these criteria. After careful examination of the rat brain tissue slides and data, his conclusion was that 2,4–D was not the cause of these astrocytomas, and therefore, it is not a neurocarcinogenic agent. Dr. Koestner's report, as well as a full report of this rat study, is currently under review by the U.S. Environmental Protection Agency and Canada's Ministry of Health and Welfare.

A two-year mouse feeding study is still in progress and will be completed in 1987. The interim progress report after one year of testing reported no significant unexpected results. This companion study will aid in the evaluation of the chronic rat data.

ENVIRONMENTAL FATE REVIEW[5]

It is generally agreed by herbicide scientists that the herbicidal activity of 2,4–D will last one to four weeks in warm moist soil when used at recommended rates. It is also known that 2,4–D will disappear faster in soil that has had repeated applications of 2,4–D. Residues of 2,4–D decline rapidly on sprayed vegetation. An extensive study was conducted with several formulated products containing esters or salts of 2,4–D and other herbicides applied to forage grasses on rights-of-way and rangeland at rates up to 12 pounds acid equivalent per acre (lb ae/A). Residues of 2,4–D in or on forage grasses were 60-140 ppm immediately after application for each pound of 2,4–D applied per acre, and decreased to less than 15 ppm within eight weeks after treatment.

Food

Many countries in all parts of the world are members of the World Health Organization (WHO) and The Food Agricultural Organization (FAO) of the United Nations. Special committees of world scientists are appointed by these two organizations to evaluate pesticide residues in foods and the scientific toxicological data for many commonly used pesticides. After studying the scientific

data, this group can decide on a quantity that would be an acceptable daily intake for a human's lifetime. These quantities are very conservative and include large safety factors. In 1971 these expert panels appointed by WHO and FAO determined that the acceptable daily intake for 2,4–D was 0.3 mg/kg/day. This means that a 132-pound person could eat 18 mg of 2,4–D in his food every day of his life and would have no ill effects. Actual dietary levels are much lower since all registered crops are not treated with 2,4–D, and residues that might be present are often removed by washing, peeling, and processing food. In fact, residues of 2,4–D have seldom been found in food intended for human consumption.

The fact that very little 2,4–D is ever present in our food has been shown by the U.S. Food and Drug Administration (FDA), which has conducted market basket surveys for a number of years to determine the amount of pesticides in our food. The exact procedure has been somewhat modified over time, although it originally represented the basic two-week diet for a 16-19 year old male whose food intake is twice that of an average individual. These food samples are subsequently analyzed to measure the pesticide residues, if any, and to discover whether the amount present is less than the quantity permitted by law. The results of a 1983 report of the FDA and the Association of Official Analytical Chemists (AOAC) show that the average quantity of 2,4–D in the diet for 1965 to 1970 was a negligible trace 15,000 times less than the acceptable daily intake (0.3 mg/kg/day) determined by WHO scientists. For the years 1971 through 1973, an even smaller trace was found which was 300,000 times less than the acceptable daily intake. Finally, for the years 1974 to the present, not even a trace has been found. The acceptable daily intake itself is well below the NOEL determined in chronic feeding studies on laboratory animals. This is an added safety factor. Practically speaking, the general public is not exposed to 2,4–D in their food.

Water

The U.S. Geological Survey made a survey of 11 western streams for 2,4–D, and other pesticides, and found no 2,4–D residues using an analytical method sensitive to 0.1 part per billion. In addition to the rapid degradation in soils previously reported, experiments have shown 2,4–D is degraded in water by sunlight, thus decreasing the likelihood of 2,4–D occurring in surface water. In another study, river water samples were taken from 20 locations in 15 western states over a three-year period. There were 321 samples analyzed for 2,4–D and 87% had no detectable residues. When found, the quantities ranged from 0.01 to 0.35 ppb, with 70% of these positive findings having less than 0.15 ppb.

To date, analyses of well water to determine if 2,4–D is present indicate its presence is rare and, if found, it occurs at very low concentrations. One unpublished survey in a large New England state, conducted specifically to determine whether a problem with 2,4–D residues existed, reported there was no 2,4–D in any of the well waters tested throughout the state.

It should be noted that some 2,4–D formulations are registered and used to control aquatic weeds in lakes and ponds. Several government studies are available indicating that after such a treatment, 2,4–D rapidly disappears from the water. Further, even if a trace (1-5 ppb) of 2,4–D is found in water, it should be remembered that a tolerance of 100 ppb has been established by the U.S. EPA for potable water, which is far above the trace amounts occasionally detected.

Air

There has also been a national air monitoring pesticide program. This survey occurred over a three-year period and 2,4–D was found only 5.64% of the time. Further, the sites where found were potentially the worst possible situations. The average quantities found (18.33 ng/m^3)[7] were toward the lower limit of detection for the analytical method. Practically speaking, this means that the public is not exposed to 2,4–D in air.

Soil

A national soil monitoring program surveyed cropland in 43 states and non-cropland in 11 states. Out of 188 analyses, 2,4–D was found in only three of the samples, and the average level was less than 0.01 ppm. Considering the rapid degradation of 2,4–D in soil under conditions favorable for plant growth, these results are not surprising.

Wildlife

Since there is little residue from 2,4–D in the air, soil, or water, and the possible residues in treated vegetation rapidly declines, exposure of wildlife to 2,4–D would be very low. Therefore, considering the relatively low toxicity of 2,4–D to vertebrates, it is not surprising to learn that direct toxic effects of 2,4–D to wildlife, with the exception of fish, have not been noted. The biggest effect of 2,4–D on wildlife is its effect on changing the habitat by controlling broadleaf weeds and this is similar to habitat changes caused by fire or flooding.

A long-term study on the effects of herbicides (which included 2,4–D) upon food and ground cover on a right-of-way showed many common game species have used the treated areas. Of the larger animals, white-tailed deer, ruffled grouse, wild turkey and rabbits have been particularly abundant. This study has been going on for more than 20 years. It is worth noting that the U. S. Department of Agriculture (USDA), discussing the effects of pesticides on beneficial insects, classifies 2,4–D as being relatively non-hazardous to honey bees.

Birds

Birds are not adversely affected by normal application of 2,4–D. In fact, some dietary experiments gave indications that small amounts of 2,4–D stimulated the growth of young birds. Experiments have also been done spraying bird eggs with 2,4–D with no adverse effects being noted.

Fish

The effect of 2,4–D on fish populations is complicated by the fact that various 2,4–D derivatives vary greatly as to their fish toxicity. For example, some esters of 2,4–D such as the butoxyethanol ester require a fish toxicity warning statement on the label, but the dimethylamine salt is not toxic to fish even when present in water at several hundred ppm. Fish toxicity to pesticides is complicated by the differences in sensitivity to pesticides of cold water species like trout and warm water species like bluegills. In addition, other components in the formulation besides the active ingredient, such as wetting agents and oil carriers, can cause greater toxic effects than the pesticide. Applications of 2,4–D to water weeds are strictly regulated through the permit system administered by state agencies; therefore, the proper use of 2,4–D formulations for aquatic weeds is carefully controlled.

Effect on Soil Microorganisms

Many scientists have found 2,4–D does not appear to adversely affect soil microorganisms. In some cases such as with the nitrifying bacteria, 2,4–D has almost no effect. In other cases, soil populations of bacteria have been temporarily reduced but recovery to normal was rapid. It has been observed that the growth of certain soil microorganisms was stimulated by 2,4–D. There has been one 18-year study during which 2,4–D was applied yearly to the soil, and no changes in the microbial populations were noted.

Worst Case

Data from studies on exposed workers indicate that the maximum dose absorbed was less than 0.1 mg/kg/day spent in the field. In most cases, the absorbed dose was as low as 0.001 mg/kg/day. This is far below the dose levels required to cause detectable effects in test animals, and well below the acceptable daily intake of 2,4–D. Thus, there is an ample margin of safety for workers actually handling 2,4–D. Bystanders and the general public would receive no detectable exposure and would suffer no ill effects from living near treated areas.

CONCLUSIONS

Government regulatory agencies throughout the world have established tolerances for 2,4–D in various crops. This action clearly demonstrates that they have decided 2,4–D can be used without harm to human health and the environment. In the U.S.A., the EPA has established tolerances for residues of 2,4–D in both food and potable water. In 1971, after evaluating the toxicological data on 2,4–D, a panel of scientific experts appointed by the World Health Organization in Geneva, determined that the acceptable daily intake was 0.3 mg/kg/day.

Surveys of food, soil, water and air in the U.S.A. have shown only occasional traces of 2,4–D in our environment and usually none. This is because 2,4–D breaks down in treated vegetation and does not persist long in our environment due to microbial degradation in soil and photolysis in water. Although 2,4–D has moderate acute oral toxicity, it is rapidly excreted unchanged in mammals and man. It does not bioaccumulate. Practically speaking, the majority of people in this country are not exposed to 2,4–D at any level. Considering these facts, it should be apparent that the approved uses of 2,4–D are not hazardous to people or the environment when used according to the product label as registered by the regulatory agencies.

If accidental exposure to high levels of 2,4–D does occur, normal precautions should be taken such as bathing, washing clothes, etc., to remove residues. Considerable evidence and long practical experience show such an exposure would not be hazardous to people. The public, therefore, should be reassured and not overly concerned about accidental exposure to 2,4–D.

To conclude, 2,4–D has been in commerce and a subject for research since 1944. In our modern society 2,4–D has played an indispensable role in the production of food and fiber, in maintenance of our utility supply lines, highway and railroad systems, as well as being a useful tool in creating desirable wildlife habitats. Recently completed toxicology studies support the conclusions of earlier studies and allow establishment of NOEL's for 2,4–D. It is reasonable, therefore, to conclude that 2,4–D can be used according to label directions without causing a health hazard to humans, domestic animals or wildlife, and without causing unreasonable adverse effects to our environment. This conclusion is based on the tremendous amount of research published on 2,4–D as well as more than 40 years of use in the real world. These facts should be very comforting to the public and allay concern regarding 2,4–D.

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FOOTNOTES

(1) The acute dermal LD_{50} is the amount of a material administered as a dermal application that will cause death in 50% of the test animals.

(2) The acute oral LD_{50} is the amount of a material administered in a single oral dose that will cause death in 50% of the test animals.

(3) Acute inhalation LC_{50} is the concentration of the airborne substance administered over a four-hour period that will cause death in 50% of the test animals.

(4) The sources of the 2,4–D used for the chronic feeding studies was a mixture of technical acid from two sources. This mixture was made to insure that the possible toxic effect from any impurity would be tested. An important point is that 2,3,7,8-tetrachlorodibenzo-p-dioxin, commonly referred to as dioxin in media reports, has never been found in any sample of 2,4–D analyzed to date using an analytical method of analysis sensitive to one part per billion.

(5) This brief review is of existing published literature but was not sponsored by the Industry Task Force on 2,4–D Research Data.

(6) One ppm is one milligram per kilogram. One milligram (10^{-3} g) is 1/1000 of a gram. A paper circle punched for a three-ring notebook weighs approximately two milligrams. A kilogram weighs 2.2 lb. One ppb is 1,000 times less than one ppm.

(7) ng = nanogram which is 1×10^{-9} grams and m^3 is a cubic meter.