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This report is: ☐ INTERIM ☒ FINAL and mainly: ☒ NEW ☐ REVIEW

DESCRIPTIVE SUMMARY WITH CONCLUSIONS: (Include in this space references to data books, and to earlier related reports, patents and publications.)

The Environmental Protection Agency's Rebuttable Presumption Against Registration (RPAR) for products containing 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) was triggered in part by their conclusion that exposure to this herbicide could be hazardous to women of child bearing age.

EPA's evaluation is based on "worst case" estimates for contamination of applicators using various types of equipment, and on a margin of safety much higher than for every-day exposure to known teratogens such as table salt, vitamin A and caffeine. Data from studies with 2,4,5-T itself in humans demonstrate that EPA's estimates are orders of magnitude too high. In actual practice, the hazard is extremely slight from exposure to this useful herbicide, even for pregnant women who might be employed "as pesticide applicators, operators of highway construction and maintenance equipment, foresters, and chemical formulators."

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REALISTIC EVALUATION OF HUMAN EXPOSURE FROM APPLICATION OF 2,4,5-T SPRAYS

by

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Submitted to U.S. Environmental Protection Agency
in Response to the
Rebuttable Presumption Against Registration
of Pesticide Products
Containing 2,4,5-trichlorophenoxyacetic acid (2,4,5-T)

August 4, 1978

REALISTIC EVALUATION OF HUMAN EXPOSURE FROM APPLICATION OF 2,4,5-T SPRAYS

TABLE OF CONTENTS

SUMMARY

EPA's Rebuttable Presumption Against Registration (RPAR) for products containing 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) was triggered in part by their conclusion that exposure to this herbicide could be hazardous to women of child bearing age (Position Document, April 21, 1978).

> (3) *Exposure Analysis.* In order to determine whether a rebuttable presumption should be issued based on reproductive and fetotoxic effects, pursuant to § 162.11(a)(3)(ii)(B), the Working Group must determine whether or not an ample margin of safety exists between the levels of 2,4,5-T and/or TCDD which produce reproductive and fetotoxic effects, and the level(s) to which humans can reasonably be anticipated to be exposed.
>
> The cancellation of uses of 2,4,5-T on food crops intended for human consumption and for use around the home, recreation sites, aquatic areas, and ditch banks in 1970 was thought to have eliminated the potential exposure to that portion of the population at risk (women of child bearing age).
>
> Social changes over the last few years, however, have given women the opportunity for employment in areas that once were considered open only to men. Since women of child-bearing age are now employed in occupations such as pesticide applicators, operators of highway construction and maintenance equipment, foresters, and chemical formulators, they have become part of the population at risk with potential exposure to 2,4,5-T and/or TCDD.
>
> In order to determine whether an ample margin of safety exists, the Working Group must first determine how much 2,4,5-T a woman could be exposed to through oral, dermal, or inhalation exposure. For each of these analysis, the Working Group assumes a woman to weigh 60 kg. The following calculations are based on an exposure analyses for 2,4,5-T and TCDD performed by EPA's Criteria and Evaluation Division [CED] (*164*).

EPA's evaluation is based on "worst case" estimates for contamination of applicators using various types of equipment, and on a margin of safety much higher than for everyday exposure to known teratogens such as table salt, vitamin A and caffeine. Data from studies with 2,4,5-T itself in humans demonstrate that EPA's estimates are orders of magnitude too high. In actual practice, the hazard is extremely slight from exposure to this useful herbicide, even for pregnant women who might be employed "*as pesticide applicators, operators of highway construction and maintenance equipment, foresters, and chemical formulators.*"

EPA ESTIMATES FOR EXPOSURE TO 2,4,5-T

EPA estimated effective doses for women applying 2,4,5-T by extrapolating data from direct measurements of contamination in workers applying chemically dissimilar pesticides under different application conditions. EPA also assumed that the woman would spend 8 hours each day actually applying the herbicide with a hand-pressured backpack sprayer, or operating a "tractor-mounted low-boom sprayer", or standing in an open area directly under the spray path of an aircraft applying the herbicide.

Table 1 lists EPA's estimates for daily exposure in a 60-kilogram woman under these conditions as calculated by their Criteria and Evaluation Division (EPA #164). In each case they assumed that the woman was using a commercial product containing 4 pounds of 2,4,5-T acid equivalent (a.e.) per gallon diluted 10-fold with water (a spray containing about 4% 2,4,5-T a.e.). The 2,4,5-T was assumed to contain 0.1 ppm of the trace contaminant 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), resulting in effective doses of TCDD 10 million times less than those estimated for 2,4,5-T.

The complete text of this portion on Exposure Analysis in the RPAR Position Document is attached for ease of reference.

Table 1. SUMMARY OF EPA ESTIMATES OF EXPOSURE TO 2,4,5-T AND TCDD IN A 60 KG WOMAN

Equipment; Location.	Treatment Conditions	Contamination per 8 Hours	2,4,5-T mg/kg/day	(Margin of Safety) vs 20 mg/kg	TCDD µg/kg/day	(Margin of Safety) vs 0.03 µg/kg
Backpack sprayer; for rights-of-way, spots in pasture or rangeland	4 lb a.e./gal diluted 10-fold with water; applied to wet	0.18 pint (1/3 cup or 86 ml) on bare skin	6.8 (dermal) 0.2 (inhalation)	(3)*	0.0007 (dermal) negligible (inhalation)	(40)*
Tractor mounted low boom sprayer; for rights-of-way, rangeland.	4 lb a.e./gal diluted 10-fold with water; applied to wet	0.048 pint (3/4 fl. oz or 23 ml) on bare skin	1.8 (dermal) 0.05 (inhalation)	(11)*	0.00018 (dermal) negligible (inhalation)	(170)*
Aerial application on person directly beneath spray path, in the open with very light clothing, and who remains there all day.	4 lb a.e. in 10 gal water per acre as medium to coarse spray.	3.1 mg on bare skin	0.051 (dermal)	(400)*	5×10^{-6} (dermal)	(6000)
		0.34 mg by inhalation in 2 hr.	0.023 per 8 hr (inhalation)	(870)*	2×10^{-6} (inhalation)	(15000)
			0.074 (cumulative)	(270)*	7×10^{-6} (cumulative)	(4300)

*According to EPA, these estimated exposures do not offer an adequate margin of safety when compared to dosage levels which caused no effect when administered daily during the critical stage of pregnancy in mice for 2,4,5-T, or in rats for TCDD.

EPA also assumed that she was wearing very light clothing with no protective equipment and that 10% of all active ingredient in spray falling on bare skin was absorbed before any was washed off. They also assumed that 2% of an aerial spray was in droplets small enough to be inhaled (less than 60 microns in diameter), and that exposure by inhalation would amount to 3% of that by dermal contamination when using ground equipment. In either case, 100% of the active ingredient in the inhaled material was absorbed.

Margins of safety for each situation have been calculated by comparison of these estimated exposure rates with levels which caused no adverse effect in pregnant animals or their offspring, even when administered daily for as long as half the gestation period. Based on data from many studies, EPA concluded that no-effect-levels had been established for 2,4,5-T at 20 milligrams per kilogram of body weight per day (mg/kg/day) and for TCDD at 0.03 micrograms per kilogram of body weight per day (µg/kg/day). It should be noted that higher doses caused embryotoxic or fetotoxic effects in several species of animals, but teratogenic effects were observed only in mice, a specie which is known to be very sensitive to any kind of stress during pregnancy (Golberg 1971, Dow #46).

Although the Position Document (see excerpt above) states that "*the Working Group must determine whether or not an ample margin of safety exists between the levels of 2,4,5-T and/or TCDD which produce reproductive and fetotoxic effects and the levels to which humans can reasonably be anticipated to be exposed*" (emphasis added), EPA has not indicated what levels would produce such effects, nor what margin of safety would be considered ample.

Using these "worst case" estimates for potential exposure, EPA concluded that the margins of safety were not adequate for 2,4,5-T and/or its TCDD contaminant when applied by ground equipment. In the case of aerial application, the margin of safety was deemed adequate for exposure to TCDD (calculated as 6000-fold for skin absorption, 15000-fold for inhalation, and 4300-fold for cumulative dermal and inhalation exposure compared to the no-effect level of 0.03 µg/kg per day). However, the margin of safety was deemed to be inadequate for 2,4,5-T itself (calculated as 400-fold for dermal, 870-fold for inhalation and 270-fold for cumulative exposure, compared to the no-effect level of 20 mg/kg/day in mice). It should be noted that many products used daily by pregnant women (such as aspirin, vitamin A, or caffeine), have very low margins of safety for effects of much greater consequence

than those produced in laboratory animals by considerably higher doses of 2,4,5-T containing traces of TCDD. (See Dow Rebuttal Document, Section III, C.1. Teratogenic/fetotoxic effects).

DIRECT AND INDIRECT MEASUREMENT OF EXPOSURE TO PESTICIDES

As discussed by Durham et al. (1962, EPA #163) both direct and indirect methods can be used to measure exposure to pesticides in applicators. Direct measurement of a pesticide in samples collected during spraying is frequently easier than measurement of the same compound or its derivatives in tissues or other biological materials. It provides an estimate of the total potential exposure but does not give information on the portion of contacted material that is actually absorbed.

EPA's estimates for 2,4,5-T are all based on direct measurements for potential exposure in applicators using other pesticides under dissimilar conditions, and are greatly exaggerated due to a series of erroneous assumptions as discussed in Part I below.

On the other hand, EPA has not considered available data from indirect measurements on 2,4,5-T and related compounds in humans including studies conducted in their own

laboratory (Shafik et al. 1971, EPA #33). Such data provide a more realistic estimate of exposure to humans under actual use conditions for this herbicide, as discussed in Part II herein.

I. ESTIMATES BY EPA BASED ON DIRECT MEASUREMENTS

Most of the studies on exposure to applicators have been conducted by a government research group located in Wenatchee, WA, who were formerly associated with the Communicable Disease Center of the Public Health Service, Department of Health, Education and Welfare (HEW), and later incorporated into the Office of Research and Monitoring of EPA. A number of these studies were cited in EPA's 2,4,5-T RPAR Position Document (Wolfe et al. 1959, EPA #145; Task Group on Occupational Exposure to Pesticides 1974, EPA #146; Staiff et al. 1975, EPA #147; Durham et al. 1962, EPA #163; Wolfe et al. 1974, EPA #166; and Wolfe 1972, EPA #179). Other studies by this group also furnish additional pertinent information as discussed herein (Wolfe et al. 1963, Dow #128; 1966, Dow #129; 1967, Dow #130; and 1972, Dow #131).

A. Review of EPA Assumptions

EPA's Criteria and Evaluation Division (EPA #164) utilized data from these studies but made a series of erroneous

"worst case" assumptions which led to greatly exaggerated estimates for exposure of applicators to 2,4,5-T:

(1) They extrapolated linearly from data for contamination with totally different chemicals applied under dissimilar conditions (rate of application, concentration of spray, total volume per acre, solvent, droplet size, pressure, direction of spray, avoidance of spray drift, etc.)

(2) They assumed that all applications of 2,4,5-T were at the high rate of 4 lb/A although virtually all treatments in rice, rangeland, and forests are at 0.5 to 2 lb/A. They also assumed that the dilution rate was 1 gallon of product made to 10 gallons with water although ground applications are generally at 1 to 3 gallons in 100 gallons of water, and many are made in oil or oil/water rather than in water alone.

(3) They assumed that applicators would be wearing very light clothing although many states require pesticide applicators to wear coveralls or similar minimal protection (e.g. California 1977, Dow #135). Calculations by Wolfe et al. (1959, EPA #145) "*indicate that protective clothing such as long-sleeved*

shirt, long trousers, shoes, rubberized gauntlet gloves, and a tropical helmet and veil would decrease potential exposure almost to zero (less than 2% of unprotected value)". The amount of protection required also depends on the job. For example, a training manual for aerial applicator ground crews (Haley 1973, Dow #136) recommends that a flagman wear a jacket or coveralls, whereas a loader would need overboots, an apron or coveralls, rubber gloves, respirator, and goggles.

(4) They neglected to consider that the greatest potential for exposure is on the hands, particularly when handling the concentrate during loading and mixing, and can be avoided by simply wearing gloves (Wolfe et al. 1966, 1967, Dow #129, 130). They compounded this error by assuming that values for <u>total</u> exposure to an insecticide concentrate and its very dilute spray solution were due to only the dilute spray, and by extrapolating linearly from the dilute spray (e.g. 0.06% fenthion) to a 4% 2,4,5-T solution. Furthermore, workers tend to avoid excess exposure of hands to the dilute and concentrate liquid sprays materials (Wolfe et al. 1974, EPA #166).

(5) They assumed that exposure would be continuous during 8 hours each day, even for a person using a backpack sprayer to squirt 2,4,5-T on individual trees or patches of weeds and brush, interspersed with frequent trips back to reload the sprayer. Furthermore, exposure with this equipment is mainly on the hand and forearm holding the wand and can be avoided by wearing even one glove.

(6) They assumed that an applicator using a backpack sprayer would get 0.18 pint (86 ml) of spray on exposed skin daily, without considering that the carrier solvent might be diesel oil which is very irritating and soiling (Haley 1973, Dow #136).

(7) They assumed that 10% of the 2,4,5-T and its trace contaminant falling on bare skin would be absorbed on the day of spraying. Although not cited in the Position Document, EPA's Criteria & Evaluation Division (EPA #164) discussed a study in which only 5.8% of the 2,4-D applied to the forearm of volunteers was absorbed over a period of 5 days after exposure, chiefly on the second or third day, if not washed off for at least 24 hours (Feldmann and Maibach 1974, Dow #132).

(8) They assumed that the amount inhaled during applications with ground equipment would be 3% of the dermal exposure such as in applications of insecticides as aerosols in orchards. However, 2,4,5-T is applied at low pressures as a coarse to medium spray to avoid drift, so only a negligible portion of the droplets would be small enough to be inhaled (Wolfe et al. 1967, Dow #130).

(9) They also assumed that aerial spraying of 2,4,5-T would continue for 8 hours each day rather than only when wind velocity, temperature, etc., are within acceptable limits. (See excerpt of label for ESTERON* 245 low-volatile herbicide which follows).

(10) They assumed that a flagger would remain standing directly beneath the spray path for 8 hours each day and that 2% of the spray would be in droplets small enough to be inhaled (less than 60 microns in diameter). However, 2,4,5-T is applied as a coarse to medium spray from a height of generally less than 10 feet above the target area.

*Trademark of The Dow Chemical Company.

Thus EPA appears to have neglected many factors in selecting conditions for their examples, and further compounded the error by using additive "worst case" conditions for each situation. Since 2,4,5-T is a potent broadleaf herbicide, considerable effort is made to avoid off-target drift. For example approved labeling for ESTERON 245 herbicide specifies:

USE PRECAUTIONS

AVOID CONTACT WITH 2,4,5-T SUSCEPTIBLE CROPS AND OTHER DESIRABLE BROADLEAF PLANTS — ESTERON 245 Herbicide is injurious to most broadleaf plants. Therefore, do not apply directly to or otherwise permit even minute amounts to contact cotton, grapes, tobacco, fruit trees, vegetables, flowers, ornamentals or other desirable plants susceptible to 2,4,5-T. Do not use in or near a greenhouse.

DO NOT APPLY IN THE VICINITY OF COTTON, GRAPES, TOBACCO, TOMATOES OR OTHER DESIRABLE 2,4,5-T SUSCEPTIBLE CROPS OR ORNAMENTAL PLANTS.

DO NOT SPRAY WHEN WIND IS BLOWING TOWARDS SUSCEPTIBLE CROPS OR ORNAMENTAL PLANTS

AVOID SPRAY DRIFT — Applications should be made only when there is no hazard from spray drift since very small quantities of the spray, which may not be visible, may severely injure susceptible crops during both growing and dormant periods. Use coarse sprays to minimize drift since, under adverse weather conditions, fine spray droplets may drift a mile or more. The spray thickening agent, NALCO-TROL[1], may be used with this product to aid in reducing spray drift. If used follow all use recommendations and precautions on the product label.

[1] NALCO-TROL — Trademark of NALCO Chemical Company

GROUND EQUIPMENT — With ground equipment, spray drift can be lessened by keeping the spray boom as low as possible; by applying 20 gallons or more of spray per acre; by using no more than 20 pounds spraying pressure with large droplet producing nozzle tips; by spraying when wind velocity is 8 miles per hour or less. Do not apply with hollow cone-type insecticide or other nozzles that produce a fine-droplet spray.

AERIAL APPLICATION — With aircraft, drift can be lessened by applying a coarse spray; by using no more than 20 pounds spray pressure at the nozzles; by using straight stream nozzles directed straight back; by using a spray boom no longer than ¾ the wing span of the aircraft; and by spraying only when wind velocity is less than 6 mph.

DO NOT APPLY BY AIRCRAFT WHEN AN AIR TEMPERATURE INVERSION EXISTS. Such a condition is characterized by little or no wind and with air temperature lower near the ground than at higher levels. The use of a continuous smoke column at or near site of application is suggested to indicate direction and velocity of air movement, and to indicate a temperature inversion by layering of the smoke.

At high temperatures (above 95°F) vapors from this product may injure susceptible plants growing nearby. Do not use in or near a greenhouse. Excessive amounts of this herbicide in the soil may temporarily inhibit seed germination or plant growth.

Such limitations also have a moderating effect on the potential for exposure in applicators. For example, Wolfe et al. (1959, EPA #145) reported that dermal exposure to DDT increased two to three-fold for each 10 psi increase in pressure. At 50 psi, the exposure was about 11 times greater than at 20 psi.

Although dermal exposure may not be greatly affected by the size of droplets landing on the skin, smaller droplets are more likely to drift and contaminate the applicator. Respiratory exposure is greater with smaller droplets, such as when using an air blast machine to penetrate the foliage canopy for insect control in orchards. Wolfe et al. (1966, Dow #129) reported droplet sizes of 20 to >150 microns in diameter for parathion and malathion applied at 0.063 to 1000 gallons of spray per acre. Such sprays would require 10 seconds or more to fall 10 feet and could move 50 to 1000 feet downwind in a 3 mph wind (Warren 1976, Dow #133). On the other hand, 2,4,5-T is applied as a medium to coarse spray, with droplets 240 to 400 microns or more in diameter. These would fall 10 feet in about 2 seconds, and would drift only a short distance (Warren 1976, Dow #133). Thus it is unlikely that a flagger would be inhaling the spray for 8 hours each day.

In a recent study by Dow (Miller 1978, Dow #134) the spray was confined nearly completely to the target area using equipment typically used in rice and rangeland. When ESTERON 245 was applied by air at 0.5 pound 2,4,5-T acid equivalent in 1 to 4 gallons of spray per acre, recovery of active material ranged from 73 to 91% on the target area, and 96 to 99% within the target area plus 165 feet

downwind. Average droplet size ranged from 197 to 397 microns in diameter, and the percent of spray mass under 100 microns ranged from 1.4 to 9.4% depending on the nozzle system used. Equipment used for treatment of rights-of-way is even more restrictive than in this study.

B. Use Pattern for 2,4,5-T

The herbicide 2,4,5-T is an organic acid which is formulated as water soluble amine salts for weed control in rice, and as oil-soluble long-chain amine salts or emulsifiable low-volatile esters for control of weeds and brush in pastures and rangeland, in right-of-way areas and in forests. It is selective in its activity against broadleaf weeds vs grasses, and against deciduous trees vs conifers.

2,4,5-T is a systemic auxin-type herbicide which is taken up from applications to foliage and, to a lesser extent, via the roots from soil. Recommended use patterns depend on the species of weeds or brush to be controlled, and on the site of application. Rice is treated midseason, generally after flooding, by air from a height of no more than 10 feet above the crop to minimize spray drift. Foliar treatments for brush control are more effective in the spring and early summer when the leaves are well developed and the plants are actively growing. Stem and

stump treatments are more effective in late fall or during the dormant period so the 2,4,5-T is available for uptake when growth resumes in the spring. Conifer forests are treated before bud break in early spring or after hardening in late spring or early summer.

The solvent chosen and rate of treatment depend on the species of weeds or trees to be controlled and their stage of growth. For aerial applications, 2,4,5-T is generally applied at a rate of 0.5 to 2 pounds (occasionally 4 pounds) acid equivalent per acre, as a medium to coarse spray from a minimum height above the target area, often with the addition of a drift control agent or with a drift control system to avoid damage in susceptible plants off the target area. As shown in the attached label for ESTERON 245 herbicide, ground applications are made with either high volume sprays (1 gallon of a 4 pound per gallon ester formulation in 100 gallons of water), or low volume sprays (1 gallon in 10 gallons of water, oil/water, or oil alone), carefully directed on the target areas.

The type of equipment used depends on how much of the total area needs treating and on its accessibility. A hand-pressured backpack sprayer could be used by an applicator on foot or on horseback for spot-treating weeds and brush

in pastures and rangeland, and in accessible rights-of-way such as along utility lines or pipelines. Tractor mounted low-boom sprayers could be used along roadsides or railroads, and in relatively level pastures and right-of-way areas, or for forest site preparation. Small fixed-wing aircraft or helicopters equipped with special booms are used for overall treatment of rice paddies and large brushy areas of rangeland and forests. Aerial applications are especially well suited for maintaining cleared strips such as rights-of-way along utility lines and pipelines, or for fire breaks in hardwood forests. No flaggers are needed in such sites because the areas to be sprayed are clearly demarcated. Flaggers are used only occasionally in forests because of the rough terrain and height of the vegetation.

C. Evaluation of Studies Selected by EPA

The three studies selected by EPA do not represent the above conditions for 2,4,5-T. The pesticides used in these studies have different chemical properties, and were applied at different concentrations and volumes, as follows:

(1) Fenthion - O,O-dimethyl-O-[4-(methylthio)-*m*-tolyl] phosphorothioate. An undefined formulation was applied with a hand pressured backpack sprayer as a fine

spray at 0.06% in water for mosquito control (Wolfe et al. 1974, EPA #166).

(2) Paraquat - 1,1'-dimethyl-4,4'-bipyridium formulated as its dichloride. A concentrate containing 2 pounds per gallon was made up at 2 quarts per 100 gallons of water (a 0.12% solution) and was applied with a "tractor mounted low-boom sprayer" at 100 gallons per acre to burn down weeds and grass in an orchard (Staiff et al. 1975, EPA #147).

(3) Malathion - S-[1,2-bis(ethoxycarbonyl)ethyl] O,O-dimethyl phosphorodithioate. An undefined formulation was applied by air from a height of 70 feet above the target area as a fine spray containing 7.5% technical active ingredient, mainly in medium grade diesel oil, at the rate of 0.46 pound malathion per acre (about 1 gallon total spray per acre) to control mosquitoes in a populated area (Caplan et al. 1956, EPA #167).

In each example cited by EPA, the applicators wore very light clothing and took no precautionary measures when loading and mixing the pesticides, nor during actual application. The malathion study was conducted more than 20 years ago when less was known of the potential hazards from exposure to toxic pesticides.

According to EPA's estimates (C&E Division, EPA #164), the hazard from exposure using ground equipment was much greater than during flagging for aerial application, even when the flagger remained directly under the spray path for 8 hours each day. For example, application of fenthion with a hand pressured backpack sprayer caused dermal contamination ranging from 0.1 to 6.3 mg/hour (mean 3.6 mg/hr) with about 80% of the total on the hand and forearm holding the spray wand (Wolfe et al. 1974, EPA #166). Application of paraquat caused dermal contamination ranging from 0.01 to 3.4 mg/hour (mean of only 0.4 mg/hour) with practically all on the hands of the operator (Staiff et al. 1975, EPA #147). Nevertheless, EPA used linear extrapolation of these maximum values (6.3 and 3.4 mg/hour) to estimate potential exposure to 2,4,5-T. In both cases, practically all contamination could be avoided by wearing light coveralls and at least one impervious glove. Cotton gloves should not be worn since occlusion could increase the potential for absorption of concentrate or spray splashed on the gloves (Task Group on Occupational Exposure to Pesticides, EPA #146).

Exposure during application with a tractor-mounted low-boom sprayer would be minimized by staying upwind to the spray, and by being in the cab of the vehicles above the

spray directed at the weeds and brush. Similarly, aerial applications are made upwind to avoid contamination of the aircraft, particularly the windshield. Furthermore, 2,4,5-T is not applied when there is a potential for spray drift, to avoid damaging off-target vegetation, as discussed previously.

Wolfe et al. (1967, Dow #130) reported that potential exposure was 12 times greater during application of parathion with an air blast machine in an orchard than when the same chemical was applied on row crops with a boom-type sprayer that directed the spray downward. Thus, exposure depends in great part on whether the spray is applied overhead, underfoot, or alongside and downwind.

Further evidence for this can be found in a summary paper by Wolfe et al. (1967, Dow #130) which tabulates data from over 80 exposure studies involving more than 5000 measurements of exposures to 23 pesticide chemicals in a variety of formulations and under a variety of methods of application. Many of these studies were done with insecticides applied with air blast equipment in fruit orchards, a practice which causes heavier exposure than when spraying row crops (Wolfe 1966, Dow #129). Table 2 lists eight studies representing conditions resembling

Table 2. SUMMARY OF PUBLISHED STUDIES ON POTENTIAL EXPOSURE OF WORKERS TO PESTICIDES USING DIRECT METHODS

Pesticide Used	Application Equipment	Activity, Location	Spray % ai	Rate lb ai/A	Av. Exposure/Hour Dermal mg	Dermal (ml)*	Inhal. mg	Inhalation vs Dermal %**	Reference Cited
Endrin	High pressure power hand gun directed downward	Spraying orchard cover crops for mouse control	0.05%	1.2	3.1	(6)	0.01	0.3	Wolfe 1967 Dow #130
Endrin	Power air blast on boom sprayer directed downward	Treating orchard cover crops for mouse control	0.05%	1.2	2.5	(5)	0.01	0.4	Wolfe 1967 Dow #130
Demeton	High pressure power hand gun	Driving tractor in nursery	0.05%	1.2	1.9	(4)	0.01	0.5	Wolfe 1967 Dow #130
Parathion	Gasoline powered knapsacker mister	Directed spraying on tomato bushes	0.4%	0.5 (est.)	9.1	(2)	0.29	3.2	Simpson '65 Dow #135
Parathion	Tractor mounted boom ground sprayer	Operating tractor in row crops	0.9%	0.5	4.7	(5)	<0.01	<0.2	Wolfe 1967 Dow #130
Parathion	Air application for insect control	Flagging in fruit orchard	9%	1.5 (est.)	84	(1)	0.02	0.02	Wolfe 1967 Dow #130
Malathion	Air application for mosquito control	Standing outdoors in populated area	7.5%	0.46	0.89	(0.01)	0.055	6.2	Caplan '56 EPA #167
Malathion	Air application for mosquito control	Standing indoors in populated area	7.5%	0.46	0.25	(<0.01)	0.012	4.8	Caplan '56 EPA #167

* ml on exposed skin, calculated from total dermal contamination due to handling concentrate plus dilute spray, as all due to dilute spray.

** Exposure by inhalation was less than 0.5% of dermal exposure except when applied as a mist (parathion), or as a fog for mosquito control (malathion). Exposure to malathion was during a 2-hr spray period and 2 hours afterwards.

those which might be encountered during application of 2,4,5-T. Exposure during use of ground equipment amounted to about 4 to 6 ml per hour actually spent spraying, which is much less than the 86 ml per day estimated by EPA, even for this type of application.

EPA's estimates for exposure of applicators also included "worst case" calculations of the amount contributed by inhalation. They erroneously interpreted the footnote under Table 34 of the Position Document to mean that

Table 34. Cumulative Exposure to 2,4,5-T and TCDD

Situation #1: 2,4,5-T	Situation #1: TCDD
Oral- 0.0007 mg/kg	Oral- -----
Dermal- 6.8 mg/kg	Dermal- 0.0007 ug/kg
Inhal.- 0.2 mg/kg[a/]	Inhal.- negligible[a/]
Cum. = 7.0 mg/kg	Cum. = 0.0007 ug/kg
Situation #2: 2,4,5-T	**Situation #2: TCDD**
Oral- 0.0007 mg/kg	Oral- -----
Dermal- 1.8 mg/kg	Dermal- 0.00018 ug/kg
Inhal.- 0.05[a/]	Inhal.- negligible[a/]
Cum. = 1.85 mg/kg	Cum. = 0.00018 ug/kg
Situation #3: 2,4,5-T	**Situation #3: TCDD**
Oral- 0.0007 mg/kg	Oral- -----
Dermal- 0.051 mg/kg	Dermal- 5×10^{-6} ug/kg
Inhal.- 0.026 mg/kg	Inhal.- 2×10^{-6} ug/kg
Cum. = 0.0777 mg/kg	Cum. = 7×10^{-6} ug/kg

a/ Calculations were made on a worst-case basis as 3% of dermal exposure based on Wolfe (179) who states, "over 97% of the pesticide to which the body is subjected during most exposure situations, and especially to applicators of liquid sprays, is deposited on the skin." TCDD inhalation exposure values were negligible: Situation #1, 21×10^{-6} ug/kg; Situation #2, 54×10^{-7} ug/kg.

exposure by inhalation would be 3% of the dermal exposure during application with a backpack sprayer or a tractor-mounted sprayer (situation #1 and #2, respectively). On

the contrary, available data indicate that only trace amounts of pesticides are likely to be inhaled during application of dilute sprays (Table 2). The respiratory exposure depends in large part on the type of formulation being applied. According to Wolfe et al. (1967, Dow #130), the relative respiratory exposure expressed as the mean percentage of total (dermal plus respiratory exposure) was 0.23% for a dilute spray, 2.87% for an aerosol (fine spray), and 0.94% for a dust. In the study on fenthion (Wolfe 1974, EPA #166), inhalation exposure ranged from <0.001 to 0.067 mg/hr during application using a hand pressure sprayer and <0.001 to 0.092 mg/hr using a power sprayer. Mean values were less than 0.6% of the dermal exposure under the same conditions.

EPA's estimates for inhalation during aerial applications of 2,4,5-T is also erroneous, since it is based on data for malathion applied as a fine spray for mosquito control (Caplan et al. 1956, EPA #167). EPA assumed that 2% of the 2,4,5-T spray droplets would be less than 60 microns in diameter, and that the applicator would be inhaling these fine droplets for 8 hours each day.

Data in Table 2 indicate that inhalation exposure would be negligible for applications resembling how 2,4,5-T

is used. Values approaching 3% were obtained only for aerosol type sprays such as with malathion for mosquito control (study 7) or parathion as a mist in tomatoes (study 4). Furthermore, a person would not be exposed to 2,4,5-T by inhalation for 8 hours per day since coarse droplets fall rapidly (Warren 1976, Dow #133).

D. Conclusions About EPA's Estimates Based on Direct Measurements

EPA appears to have made a number of erroneous assumptions and to have selected poor models for predicting exposure of applicators to 2,4,5-T. Consideration of mediating factors such as clothing worn and care taken during application would seem to be essential for EPA to make reliable estimates of the potential for contamination of applicators by 2,4,5-T. It should also be noted that many of the "worst case" assumptions are contrary to label practice and thus provide a built-in margin of safety which is not accounted for in EPA's numerical derivations.

CAUTION

MAY BE HARMFUL IF SWALLOWED · MAY CAUSE IRRITATION

Avoid Contact with Eyes, Skin and Clothing

Do Not Cut or Weld Container

II. REALISTIC ESTIMATES OF EXPOSURE BASED ON INDIRECT MEASUREMENTS WITH 2,4,5-T

According to Durham et al. (1962, EPA #163) *"any measure of absorption or its necessary sequelae constitutes an indirect measure of exposure. It is not often convenient to measure absorption itself, but measurement of a compound or its biotransformation products in the blood, tissues or excreta gives information on minimal absorption. Such indirect measurements may be used in evaluating the relative hazard of different routes of exposure, different operational procedures and different protective devices* (as described previously for direct measurements). *In addition, they are more useful in relating exposure under observed use conditions to clinical effects".*

In 1962 when the above observation was made, there was not a single pesticide for which the inter-relationships between occupational exposure to different formulations by different routes, the fate of the compound in the body, and its clinical effects were all adequately known. However, more studies have been conducted in recent years on 2,4,5-T and its TCDD contaminant than for most if not all other chemicals. Among these are several controlled studies in humans which have provided much needed information to refute claims of ill effect from exposure to this useful herbicide. Studies have also been conducted on excretion of 2,4,5-T by manufacturing plant workers and by pesticide applicators which show conclusively that EPA's estimates for exposure are grossly exaggerated, as discussed previously herein.

A. Ingestion Studies in Humans (Dow, Japan, India)

Numerous studies on the metabolism of 2,4-dichlorophenoxyacetic acid (2,4-D) and related herbicides have shown that these chemicals are absorbed and distributed rapidly in the body, and are excreted, unchanged, relatively quantitatively in the urine within a week after administration (Leng 1977, EPA #79). Pharmacokinetic studies with 2,4,5-T in rats and dogs (Piper et al. 1973, EPA #67) and in humans (Gehring et al. 1973, EPA #74) corroborated these findings and demonstrated that rates of clearance from plasma and elimination in urine depend on dosage level, animal species, and chemical structure of the phenoxy acid in question (Table 3). Phenol metabolites were detected only in ruminants (Leng 1977, EPA #79) or in trace amounts in urine of rats fed excessively high doses (Shafik et al. 1971, EPA #33).

TABLE 3 *M. L. Leng 1977 (EPA # 79)*

Effect of species on fate of 2,4,5-T in animals.

Species Studied	Rat[1]	Dog[1]	Human[2]
Single Oral Dose, mg/kg	5	5	5
Number of Animals/Tests	6	4	5/7
Duration of Study, Days	4-6	9	4
Peak Plasma Conc., ug/ml	15	20	57
Interval Post-Administration, Hour	12	< 4	7
Volume of Distribution, ml/kg	144	221	80
Number of Body Compartments	1	1	1
Average Rate of Clearance, $T_{½}$, Hour			
from Plasma	4.7	77	23.1
from Body via Urine	13.6	87	23.1
Excretion as Percent of Dose			
in Urine, Total Ether Soluble	83	42	89
(as Altered 2,4,5-T)	(none)	(4)	(little)
in Feces	(little)	20	<1
Total in Excreta as Percent of Dose	83	62	90

[1] Piper et al., 1973. (EPA #67)
[2] Gehring et al., 1973. (EPA #74)

In the study by Dow with 2,4,5-T in humans (Gehring et al. 1973, EPA #74), five male volunteers weighing 73 to 94 kilograms ingested a single dose of 5 mg/kg. Plasma levels attained a peak of about 60 µg/ml within about 2 hours and decreased rapidly with a half-life of about 23 hours. As shown in Table 4, urinary excretion was rapid with a diurnal fluctuation, and a total of about 90% of the dose was recovered largely as free 2,4,5-T within 4 days after administration. It is interesting to note that the fraction

Table 4. Excretion of 2,4,5-T in Urine After Single Oral Dose at 5 mg/kg in Five Male Volunteers[1]

Interval After Ingestion (hr)	(day)	Incremental % of Dose Excreted	Cumulative % of Dose Excreted	Fraction in Daytime Collection[3]
0-12		26.8		
12-24	1	14.1	38.1[2]	0.70
24-36		20.7		
36-48	2	8.7	67.5	0.70
48-60		9.9		
60-72	3	4.4	81.8	0.69
72-84		4.8		
84-96	4	1.8	88.5	0.73
				av. 0.71

[1] Gehring et al. 1973 (EPA #74)

[2] One subject pooled the 0-12 and 12-24 specimens so the mean excretion for day 1 is not the sum of the mean excretions for 0-12 and 12-24 hours.

[3] Calculated from 26.8/38.1 = 0.70; 20.7/29.4 = 0.70; 9.9/14.3 = 0.69; 4.8/6.6 = 0.73.

excreted during the daytime was constant at 0.71 of the total per day.

Similar studies in humans were conducted by Dow with 2,4-D in five males (Sauerhoff et al. 1977a, Dow #140) and with silvex in seven males and one female (Sauerhoff et al. 1977b, Dow #141). The results are compared in Table 5 (Leng 1977, EPA #79).

64 M. L. Leng 1977 (EPA No. 79)

TABLE 5

Fate of three phenoxy herbicides in humans.

Phenoxy Herbicide Administered	2,4,5-T[1]	2,4-D[2]	Silvex[3]
Single Oral Dose, mg/kg	5	5	1
Number of Subjects/Tests	5/7	5	8
Duration of Study, Days	4 - 6	4	6
Peak Plasma Concentration, ug/ml	57	25	6
Interval Post Administration, Hour	7	4	2 - 4
Volume of Distribution, ml/kg	80	>200, 83	115, 107
Number of Body Compartments	1	1 or 2	2
Average Rate of Clearance, $T_{½}$, Hour			
from Plasma	23.1	11.7	3.7, 19
from Body via Urine	23.1	17.7	5, 26
Excretion as Percent of Dose			
in Urine as Free Acid	88.5±5.1	70 - 88	30 - 80
as Conjugate(s)	(little)	0 - 27	15 - 54
in Feces (First 2 Days)	< 1	–	0 - 3
Total Excreted as Percent of Dose	≈90	88 - 106	67 - 95

[1]Gehring et al., 1973
[2]Sauerhoff et al., ~~1970~~ 1977a
[3]Dow, ~~Unpublished~~ 1977b

In an independent study with 2,4,5-T in Japanese volunteers (Matsumura 1970, EPA #73), a peak plasma level of 21.1 µg/ml was reached at 4 hours after ingestion of a single dose of 150 mg 2,4,5-T by a male weighing 68 kg (i.e. 2.2 mg/kg).

As in the Dow study with 2,4,5-T (Gehring et al. 1973, EPA #74), more than 80% of the administered dose was recovered in the urine within 3 days after a dose of 100 mg in two volunteers weighing 68 and 53 kg (Figures 1 and 2). About 45% of the dose was recovered in the first 24-hour urine collection after doses of <2 mg/kg, compared to the average 38% recovered in the Dow study at 5 mg/kg.

Excretion of 2,4,5-T in the Urine (Matsumura 1970, EPA #73)

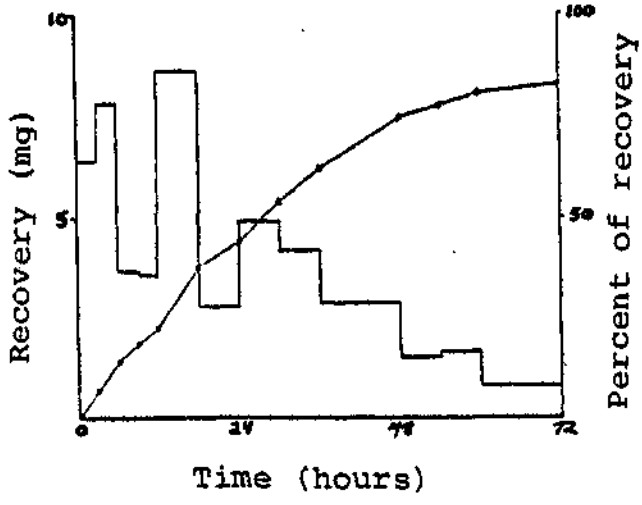

Figure 1. Male, 28 years old, body weight 68 kg, 100 mg 2,4,5-T ingested for dose of 1.5 mg/kg

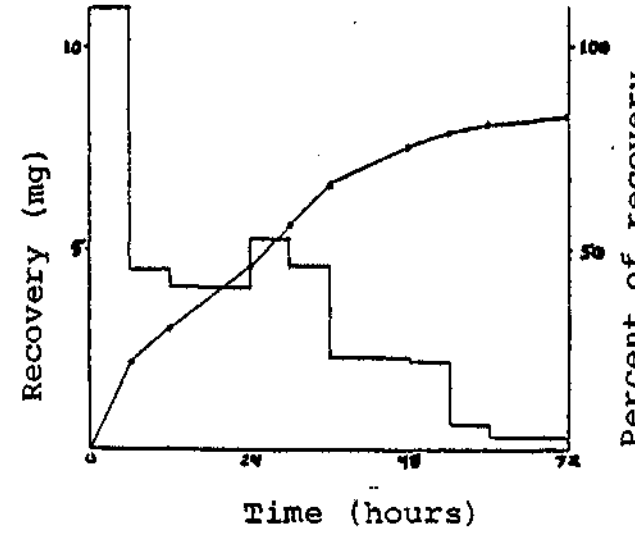

Figure 2. Male, 27 years old, body weight 53 kg, 100 mg 2,4,5-T ingested for dose of 1.9 mg/kg

The fate of phenoxy herbicides in humans has also been studied in India. In their study with 2,4-D (Kohli et al. 1974, Dow #140), a single oral dose of 5 mg/kg was given to six male volunteers. As in the Dow study with 2,4-D (Sauerhoff et al. 1977a, Dow #138), 75% of the administered dose

was excreted unchanged in the urine within 96 hours after administration, but no metabolites were detected. In their study with 2,4,5-T (Kohli et al. 1974b, EPA #75), a total of eight male volunteers received single oral doses of 2, 3 or 5 mg/kg of body weight. Again as in the Dow study (Gehring et al. 1973, EPA #74), the chemical was absorbed readily from the gastrointestinal tract and was excreted rapidly via the kidneys without undergoing any metabolic alteration. The half-life for clearance of 2,4,5-T from the plasma was about 19 hours in the Indian study, compared to 23 hours in the Dow study. Of the total amount excreted in 96 hours, nearly 80% was excreted within the first 48 hours (Table 6).

Table 6. Excretion of 2,4,5-T by Eight Male Volunteers in India (Kohli et al. 1974, EPA #75).

Interval After Ingestion (day)	Cumulative % of Dose Excreted in Urine		
	2 mg/kg (1)	3 mg/kg (1)	5 mg/kg (6)[1]
1	26	57	27
2	48	73	50
3	66	76	60
4	73	79	63

[1] Average for six subjects given oral dose of 5 mg 2,4,5-T per kg of body weight.

Although considerable variation was noted among individuals in each study, particularly those conducted in India, the overall agreement is remarkable. As summarized in Table 7, about one-third of the dose was excreted, on the average, in the urine collected the first day after administration of a single dose. If the dose was 5 mg/kg in a 60 kg person, the total amount administered was 300 mg of which about one-third (100 mg) would be in the first 24-hour urine specimen. Similarly, about one-fourth (75 mg) would be in the second daily sample, and one-tenth (30 mg) in the third daily sample. These data can be used to estimate the effective dosage rate for 2,4,5-T in exposed individuals for whom urinary levels are known.

Table 7. Summary of Excretion Studies with 2,4,5-T in Humans (EPA #73, 74, 75)

Study by	Dosage mg/kg	Number of Subjects	Mean % of Dose in Urine			
			Day 1	Day 2	Day 3	Day 4
Dow	5	5	38	29	14	7
Japan	1.5	1	45	30	5	
	1.9	1	45	30	5	
India	2	1	26	22	18	7
	3	1	57	16	3	3
	5	6	27	23	10	4
Total		15	35[1]	25	11	5

[1]Approximation obtained by taking average of total for all 15 subjects [i.e.(5 x 38)+ 45. . .+(6 x 27)÷ 15].

For example, a concentration of 15 ppm 2,4,5-T in 1500 ml of urine (the normal average 24-hr output for an adult human) amounts to excretion of $15 \times 10^{-6} \times 1500$ ml $\times$ 1000 mg/ml = 22.5 mg 2,4,5-T. Since the average amount of 2,4,5-T excreted in urine in the first 24-hr following a single dose is about one-third of the dose (day 1, Table 7), the 22.5 mg represents one-third of a single 67.5 mg dose. In a person weighing 60 kg, this represents a dose of 1.1 mg/kg. On the other hand, daily dosage results in a steady-state condition wherein the total daily input is equal to the total daily output. Thus, in a daily exposure situation, 22.5 mg 2,4,5-T in a 24-hr urine would result from daily dosage of 22.5 mg/60 kg = 0.4 mg/kg of body weight.

A more sophisticated estimate of the dosage by dermal exposure can be made using a pharmacokinetic model developed for computer analysis of the data generated in the Dow study with 2,4,5-T (Gehring et al. 1973, EPA #74). Estimates of exposure using this model corroborates the above approximation that similar urinary levels would be attained from daily exposure at one-third the single dose rate as from the single dose.

B. Exposure in Workers Manufacturing 2,4,5-T

The Japanese study (Matsumura 1970, EPA #73) also reported finding 0.5 to 3.6 mg 2,4,5-T in urine specimens from eleven workers in a "chemical manure factory" (Table 8). Based on the data for excretion following a single oral dose in the

same study (Table 7), it is estimated that those factory workers had received a single dose of 2,4,5-T ranging from about 0.02 to 0.15 mg/kg[1] during the previous day or two, or about 0.007 to 0.05 mg/kg if they were exposed daily. Their exposure to 2,4,5-T was from working in a room which contained 0.62 to 15.4 mg/m^3 at different locations, and from 0.21 to 0.67 mg/m^3 in their breathing zones in this fertilizer factory (Tables 9 and 10).

Table 8. 2,4,5-T in the urine of workers of a chemical manure factory.

Date	No.	Name	Age	Sex	Urine volume (ml/day)	2,4,5-T (mg/day)	Calc. ppm
Apr. 9	1	A. M.	28	Male	2,060	1.5	0.73
	2	S. S.	50	Male	1,400	—	
	3	Y. I.	60	Male	1,570	—	
	4	T. Ki.	40	Female	1,020	1.3	1.27
	5	S. H.	26	Female	1,020	1.2	1.18
	6	T. T.	20	Male	870	0.5	0.57
Apr. 15	1	A. M.	28	Male	2,000	3.6	1.80
	2	S. S.	50	Male	2,220	—	
	3	Y. I.	60	Male	2,400	—	
	5	S. H.	26	Female	1,260	—	
	7	T. N.	38	Female	1,760	2.7	1.53
	8	S. K.	21	Male	1,400	3.6	2.57
Apr. 16		T. Ki.	40	Female	750	1.0*	
	3	Y. I.	60	Male	1,670	—	
	2	S. S.	50	Male	3,020	—	
	9	S. N.	41	Male	1,470	2.2	1.50
	10	T. Ko.	58	Female	450	3.5*	
Apr. 22	11	Y. O.	38	Female	250	—	
	2	S. S.	50	Male	850	—	
	4	T. Ki.	40	Female	180	1.9*	
	3	Y. I.	60	Male	1,150	—	

* milligrams per liter.

Table 9. Concentrations of 2, 4, 5-T in the surroundings of a chemical manure factory.

Sampling points	Concentrations*
Weighing box	15.4
Inlet of mixer	1.37
Outlet of mixer	0.82
Center of work-room	0.62

* milligrams per cubic meter.

Table 10. Concentrations of 2, 4, 5-T at the breathing location of workers.

Workmen	Concentrations*
A	0.21
B	0.31
C	0.67
D	0.38

* milligrams per cubic meter.

Matsumura 1970 (EPA #73)

[1] $\frac{0.5 \text{ mg in urine}}{45\% \text{ of } 100 \text{ mg in urine}} \times 1.9 \text{ mg/kg b.w.} = 0.02 \text{ mg/kg b.w.}$

$\frac{3.6 \text{ mg in urine}}{45\% \text{ of } 100 \text{ mg in urine}} \times 1.9 \text{ mg/kg b.w.} = 0.15 \text{ mg/kg b.w.}$

In a survey of 204 Dow factory workers (Ott et al. 1978, Dow #28), no adverse effect was noted for exposures ranging from one to ten years at levels estimated to be 0.2 to 0.8 mg/m^3 for 2,4,5-T as the sodium salt. It should be noted that this study covered a period of more than 20 years (from 1950 to 1971) when the exposure to 2,4,5-T was greater than in the current process for making esters, and the TCDD level in the 2,4,5-T was higher than the current limit of <0.1 ppm. Nevertheless, the incidence of cancer in this group of factory workers is less than the national average.

A surveillance study was recently initiated for Dow factory workers currently employed in the manufacture of esters of 2,4-D, 2,4,5-T, and silvex. Preliminary analyses of urine specimens taken during routine physical examinations of three workers indicated the presence of 1.3 to 2.6 ppm 2,4-D, 0.2 to 1.6 ppm 2,4,5-T, and 0.01 to 0.03 ppm silvex. Four months later, urine samples collected from four manufacturing workers contained only 0.27 to 0.52 ppm 2,4-D, 0.17 to 0.54 ppm 2,4,5-T, and 0.004 to 0.023 ppm silvex. Levels in blood samples taken at the same time ranged from 2 to 9 parts per billion for both 2,4-D and 2,4,5-T, while silvex was not detected at a minimum sensitivity of 1 ppb.

These values indicate that the workers were receiving a low daily exposure of <0.007 mg/kg for each of 2,4-D and 2,4,5-T and considerably less for silvex.

C. Exposure During Actual Application of 2,4,5-T

Several studies have already been conducted on urinary levels of 2,4,5-T in applicators, and others are currently underway. The most complete data available is from a study by Dow in eight field applicators and two controls conducted on a confidential basis for a customer. Air samples and samples simulating skin contact were taken for direct measurement of exposure, while blood samples and 24-hour urine collections provided data for indirect measure of actual exposure in the individuals.

The 2,4,5-T product used was a 59.1% butoxyethanol ester formulation containing 4 pounds of 2,4,5-T acid equivalent per gallon (Amchem WEEDONE T). It was diluted at 3 gal/100 gal with fuel oil (2% 2,4,5-T a.e.) and was applied selectively to the lower 3 to 4 feet of trees and brush in a utility right-of-way using a hand pressured backpack sprayer (2 1/2 gal capacity). The applicators wore short-sleeved shirts open at the neck, long pants, no gloves and no hat. One of the backpacks leaked as evidenced by soaking of the applicator's clothing at the lower back. This latter particular circumstance is considered to be gross misuse and directly contrary to the label precautionary direction: CAUTION! Avoid contact with eyes, skin and clothing.

The results of this study are summarized in Table 11. As expected, urinary levels were higher in the applicators than in the foremen, and were barely detectable in the Dow personnel conducting the study. The highest estimated dose was 0.2 mg/kg/day in applicator L.A. who was wearing the leaking backpack sprayer. This confirms that EPA's estimate of 7.0 mg/kg for cumulative exposure using a backpack sprayer is grossly exaggerated, even for a "worst-case" situation (Position Document, Table 34, Situation #1). It is likely that exposure would be very low (<0.01 mg/kg) if these applicators had worn long-sleeved shirts or coveralls and gloves. Proper maintenance of equipment and better personal hygiene would also have prevented the high exposure experienced by applicator L.A. in this study.

Table 11. 2,4,5-T in Urine of Spray Applicators

Subject	Occupation	kg B.W.	2,4,5-T in Urine ppm	2,4,5-T in Urine mg/24 hr	Dose mg/kg[1]
B.F.	Applicator	73	0.85	1.45	0.02
J.L.	Applicator	73	4.30	7.06	0.10
D.M.	Applicator	59	3.00	3.58	0.06
L.A.	Applicator	68	17.00	13.18	0.20[2]
R.L.	Foreman	77	0.75	1.25	0.02
B.B.	Foreman	87	3.80	4.79	0.06
T.H.	Foreman	70	0.07	0.09	0.001
J.M.	General Foreman	78	0.03	0.08	0.001
R.O.	Ind. Hygienist	75	0.02	0.03	0.0004
E.G.	Clin. Chemist	73	<0.01	<0.03	<0.0004

[1]Calculated from the urinary levels using the pharmacokinetic model for 2,4,5-T excretion in humans (Gehring et al., 1973, EPA #74).

[2]This situation with a leaking backpack which soaked the applicator's clothing is considered gross misuse contrary to label precautionary handling directions. "CAUTION! May be harmful if swallowed. May cause irritation. Avoid contact with eyes, skin and clothing."

Data are also available from an indirect study conducted in 1970 by EPA or its predecessors at the Perrine Laboratory in Florida. Urine samples were collected from people occupationally exposed to 2,4-D and 2,4,5-T, and were analyzed for both the phenoxy acids and their expected phenol metabolites (Shafik et al. 1971, EPA #33). As shown in Table 12, only low ppm levels of the parent compounds were found in the urine of spray operators, and little or none in those whose occupation afforded less direct contact. These samples were collected in 1970 as part of the Community Studies Network in South Dakota, Arkansas and Kentucky (personal communication to M. L. Leng from H. F. Enos, EPA, Athens GA, June 1978).

The samples from Arkansas were collected from four spraymen employed by the Arkansas Electric Cooperative Inc., working out of Fayetteville (personal communication to M. L. Leng from M. L. Anderson, now Chief of Pesticides Technical Assistance Section, EPA, Dallas TX, July 1978). They were applying ESTERON* 245 herbicide (label attached) at 2 gallons in 40 gallons of diesel oil (about 3% 2,4,5-T a.e.) using knapsack equipment to spray around the base of individual trees and up to 2 feet on the trunks. They were wearing jeans and gloves but little care was taken to avoid skin contact. A total of eight urine samples were collected, four in the early morning on July 22 following exposure the

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32 M. T. SHAFIK, H. C. SULLIVAN, AND H. F. ENOS
(EPA #33) Intern. J. Environ. Anal. Chem. 1, 23-33, 1971

To demonstrate the applicability of the method for monitoring occupational exposure, urine from people directly and indirectly involved in the application of 2,4-D and 2,4,5-T derivatives was analyzed. The results, as shown in Table V, indicate a higher degree of exposure for spray operators than those whose occupations afforded less direct contact.

It can be generally concluded that the method suggested for the determination of 2,4-D and 2,4,5-T in urine may be used to determine low levels of exposure to these herbicides. Levels of exposure of 3.75 mcg/kg for 2,4-D and 5.00 mcg/kg for 2,4,5-T in rats can be determined in urine within 24 hr from exposure.

TABLE V2

Results of analysis of urine from people occupationally exposed to 2,4-D and 2,4,5-T[a]

Sample	Exposure compound	Results (ppm) 2,4-D	2,4,5-T	
Spray operator				
1	2,4,5-T	N.D.[b]	1.1	AR
2	2,4,5-T	N.D.	2.8	
3	2,4,5-T	N.D.	2.6	AR
4	2,4,5-T	N.D.	3.6	
5	2,4,5-T	N.D.	3.0	AR
6	2,4,5-T	N.D.	1.3	
Farmer				
7	2,4-D and 2,4,5-T	0.20	N.D.	
8	2,4-D and 2,4,5-T	0.19	N.D.	
Foreman, spray crew				
9	2,4,5-T	N.D.	1.2	AR
10	2,4,5-T	N.D.	0.5	
Herdsman				
11	2,4-D	N.D.	N.D.	
12	2,4-D	N.D.	N.D.	
Farm laborer				
13	2,4-D	N.D.	N.D.	
14	2,4-D	N.D.	N.D.	
15	2,4-D	N.D.	N.D.	
16	2,4-D	N.D.	N.D.	
Pesticide project officer				
17	2,4-D	N.D.	N.D.	
18	2,4-D	N.D.	N.D.	
Spray operator				
19	2,4-D	1.0	N.D.	
20	2,4-D	0.2	N.D.	
Aircraft spray operator				
21	2,4-D and 2,4,5-T	0.4	0.05	
22	2,4-D and 2,4,5-T	1.0	0.05	

[a] The derivative is unknown.

[b] N.D., not detected.

previous day, and four in the afternoon after exposure since 7 a.m. that day. The corresponding samples in Table 12 are 1-2, 3-4, 5-6, and 9-10 for the four members of this crew.

Although 24-hour urine collections were not made, data from Tables 4 and 11 (Dow studies) can be used to estimate the effective dose of 2,4,5-T received by dermal exposure in these applicators. Based on an average 2.0 ppm 2,4,5-T in the eight daytime urine samples (range 0.5 to 3.6 ppm in Table 12), and assuming a daily volume of 1500 ml urine divided equally between 0-12 and 12-24 hours with 0.71 of the total 2,4,5-T in the daytime sample (Table 4), the estimated daily excretion in these applicators was 0.21 mg. This corresponds to an effective dose of about 0.03 mg/kg compared to the average 0.06 mg/kg found in applicators in the Dow study, excluding the one wearing a leaking backpack sprayer (Table 11). In either case, the exposure is at least two orders of magnitude less than the cumulative dose of 7.0 mg/kg estimated by EPA for use of this type of equipment (Position Document, Table 34, Situation #1).

Information has also been obtained recently about the samples collected in Kentucky. According to Edsel Moore of the Kentucky Health Department (personal communication to M. L. Leng, July 1978), their situation also represented a "worst-case". Two groups of people were involved, one inexperienced group of students employed by Western Kentucky

University and one made up of employees of the Kentucky State Department of Agriculture. They were applying 2,4-D or 2,4-D/2,4,5-T with a tractor drawn boom sprayer, or with a tractor drawn "gun nozzle" aimed over a ridge at vegetation growing along a right-of-way. They wore light summer clothing and no protective equipment.

Examination of Table 12 reveals that few remaining samples of urine contained detectable levels of either 2,4-D or 2,4,5-T. Thus, the cumulative dose by both dermal exposure and inhalation must be considerably less than 0.01 mg/kg in applicators using this type of ground equipment, even when no special precautions are taken to avoid contact with the spray. Again, the exposure is at least two orders of magnitude less than EPA's estimate of 1.85 mg/kg for application of 2,4,5-T with a "tractor-mounted low boom sprayer". (Position Document, Table 34, Situation #2).

Additional data will be obtained in a comprehensive study being conducted by the National Forest Products Association. According to the proposed protocol presented to EPA in late July 1978, both direct and indirect measurements of 2,4,5-T exposure will be made during application of the herbicide with backpack sprayers and mist blowers, or by air.

MARGIN OF SAFETY BASED ON DATA FOR 2,4,5-T IN APPLICATORS

Analyses of urine from applicators exposed to 2,4,5-T in various real world situations and comparison with data from known exposures in humans, provide convincing evidence that EPA's estimates are grossly exaggerated. The margin of safety is actually many times greater than calculated by EPA, even for pregnant women, compared to the no-effect level in mice treated daily during organogenesis.

For example, EPA calculated a cumulative exposure of 7.0 mg/kg for a woman using a backpack sprayer to apply 2,4,5-T for 8 hours. Data from the Dow study and the EPA study (Shafik et al. 1971, EPA #33) indicate that the effective dose would be <0.01 mg/kg if the applicator takes even the reasonable precautions as directed by labeling. This would provide a margin of safety at least 2000-fold over the no-effect level in mice and several times that for levels which caused only minor fetotoxic effects in rats.

Exposures using other types of equipment would be even less than with backpack sprayers. Furthermore, increasing awareness of potential problems from exposure to other pesticides has resulted in more specific label precautions and better enforcement of regulations pertaining to wearing of protective equipment and avoiding contact with sprays.

In conclusion, there is little likelihood that a woman of child-bearing age, whether pregnant or not, will suffer any harm from proper use of 2,4,5-T during employment as a pesticide applicator, operator of highway construction and maintenance equipment, forester, or chemical formulator.

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FRIDAY, APRIL 21, 1978
PART II

ENVIRONMENTAL PROTECTION AGENCY

PESTICIDE PROGRAMS

Rebuttable Presumption Against Registration and Continued Registration of Pesticide Products Containing 2, 4, 5–T

(3) *Exposure Analysis.* In order to determine whether a rebuttable presumption should be issued based on reproductive and fetotoxic effects, pursuant to § 162.11(a)(3)(ii)(B), the Working Group must determine whether or not an ample margin of safety exists between the levels of 2,4,5-T and/or TCDD which produce reproductive and fetotoxic effects, and the level(s) to which humans can reasonably be anticipated to be exposed.

The cancellation of uses of 2,4,5-T on food crops intended for human consumption and for use around the home, recreation sites, aquatic areas, and ditch banks in 1970 was thought to have eliminated the potential exposure to that portion of the population at risk (women of child bearing age).

Social changes over the last few years, however, have given women the opportunity for employment in areas that once were considered open only to men. Since women of child-bearing age are now employed in occupations such as pesticide applicators, operators of highway construction and maintenance equipment, foresters, and chemical formulators, they have become part of the

population at risk with potential exposure to 2,4,5-T and/or TCDD.

In order to determine whether an ample margin of safety exists, the Working Group must first determine how much 2,4,5-T a woman could be exposed to through oral, dermal, or inhalation exposure. For each of these analysis, the Working Group assumes a woman to weigh 60 kg. The following calculations are based on an exposure analyses for 2,4,5-T and TCDD performed by EPA's Criteria and Evaluation Division [CED] (*164*).

(a) *Oral Exposure.* For purposes of this analysis, the Working Group considered currently registered uses where the possibility of oral exposure to 2,4,5-T and/or TCDD existed. Treatment of range and pasture land could result in oral exposure through ingestion of meat and milk from animals grazing on the treated area. Since actual data on residues of 2,4,5-T in animals grazing on treated rangeland is unavailable, for purposes of the 2,4,5-T oral exposure analysis, the Working Group used residue information obtained in a feeding study (*37*) in which cattle were fed considerably higher amounts of 2,4,5-T than they would normally be exposed to in grazing on treated land. The following calculations are based on the average quantities of food eaten per day (1.5 kg), as reported by Lehman (*144, 165*).

Table 25. 2,4,5-T Oral Exposure Analysis

	Whole Milk	Meat (Beef)
No-adverse-effect level for teratogenicity in mice	20 mg/kg	20 mg/kg
Average level of 2,4,5-T identified	0.103 ppm[a/]	0.2 ppm[a/]
% of food item in total human diet	19.6%	4.6%
Average amount of food eaten per day	1.5 kg	1.5 kg
Exposure to 2,4,5-T per day	0.0005 mg/kg	0.0002 mg/kg

a/ Animals were fed at 300 ppm 2,4,5-T in the diet for 2 to 3 weeks. This is a worst case assumption for cows grazing on freshly-treated pasture without a withdrawal period; all milk and meat was obtained from such cows. Meat (beef) includes muscle, fat, and liver tissues which constitute the major portion of edible meat.

To find the average daily intake of a single food item, multiply the average daily food intake by the percent of that item in the total diet: For milk, 1.5 kg×19.6%=0.294 kg; and for meat (beef), 1.5 kg×4.6%=0.069 kg.

The quantity of 2,4,5-T in the average daily diet equals the average daily intake of each food item multiplied by the level of 2,4,5-T in the food item: For milk, 0.294 kg×0.103 ppm=0.03 mg; and for meat (beef), 0.069 kg×0.2 ppm=0.014 mg.

The theoretical exposure of an average woman equals the amount of 2,4,5-T in the daily diet divided by the weight of the average woman: For milk, 0.03 mg/60 kg=0.0005 mg/kg; and for meat (beef), 0.014 mg/60 kg=0.0002 mg/kg; total exposure from milk and beef products could be 0.0007 mg/kg per day.

Existing data on TCDD residues in animals grazing on treated rangeland are too meager to use for an analysis of TCDD exposure to humans through ingestion of meat or milk from animals so exposed.

The Working Group considers that the difference between the no-adverse-effect level of 2,4,5-T for teratogenic effects (20 mg/kg) and the calculated oral exposure level for 2,4,5-T (0.0007 mg/kg per day) does constitute an ample margin of safety. Since this risk criterion for other chronic adverse effects has not been met or exceeded, a rebuttable presumption does not arise.

(b) *Dermal Exposure.* In order to conduct these analyses, the Working Group must determine the amount of 2,4,5-T and/or TCDD which would come in contact with the skin and the amount that would be absorbed.

(i) *Spray Applicator: Back-pack Sprayer.* For purposes of this analysis, the Working Group assumes the applicator to be a 60-kg woman of child-bearing age, and the site of application either a right-of-way or spot treatment of pasture or rangeland. The equipment is a back-pack sprayer (*166*). The following calculations of exposure are based on dilution for spraying of three pints of formulated product per 32 pints of water. Typical 2,4,5-T formulations, based on inspection of a large number of registered labels (*164*), range from 4 to 6 pounds active ingredient (acid equivalent) per gallon. The product used in this exposure analysis has an assumed concentration of 4 pounds 2,4,5-T per gallon. Label recommendations vary from a recommended dilution of 0.094 to 4 pounds acid equivalent per 32 pints of water. A dilution rate of 1.6 pounds per 32 pints has been selected as representative of a typically-used spray mixture.

Wolfe et al. (*166*) studied dermal exposure to fenthion during hand back-pack spraying for mosquitoes for ten situations. Exposure ranged from 0.1 to 6.3 mg/hr, with a mean value of 3.6 mg/hr (6 ml/hr). Method of application was a hand pressure sprayer, using a 0.06 percent spray. Workers wore short-sleeved, open-necked shirts with no gloves or hat. Based on Wolfe's data, CED (*164*) calculated a dermal exposure of approximately 0.177 pints per day. CED (*164*) also determined that approximately 10 percent of the 2,4,5-T and TCDD coming in contact with the skin of the applicators would be absorbed even after washing, based on absorption studies with other pesticides (*145, 146, 163*).

Table 26. Back-pack Sprayer Dermal Exposure Data

	2,4,5-T	TCDD
Use Dilution rate	3 pints (1.6 pounds 2,4,5-T) per 32 pints water	3 pints (0.00000016 pounds TCDD) per 32 pints water
Amount of diluted material gotten on skin daily	0.18 pint	0.18 pint
% Diluted material absorbed	10%	10%
Exposure level	409 mg	0.0409 ug
Dose level	6.8 mg/kg	0.0007 ug/kg
No-Adverse-Effect level for teratogenic effects	20 mg/kg	0.03 ug/kg

The following calculations (see Table 27 for mathematics) will give the daily dermal exposure for both 2,4,5-T and TCDD: (1) Convert the dilution rate to grams; (2) multiply this figure by 1,000 (for 2,4,5-T) to convert to milligrams and by 1,000,000 (for TCDD) to convert to micrograms; (3) multiply this figure by the daily dermal dose of diluted material; (4) multiply this figure by the percent absorbed; and (5) divide this figure by the weight of the applicator for the daily exposure to 2,4,5-T or TCDD per 8-hour working day.

The Working Group considers that the difference between the no-adverse-effect level of 2,4,5-T for teratogenic effects (20 mg/kg) and this calculated dermal exposure level for 2,4,5-T (6.8 mg/kg), as well as the difference between the no-adverse-effect level of TCDD for teratogenic effects (0.03 µg/kg) and this calculated exposure level for TCDD (0.0007 µg/kg), do not constitute an ample margin of safety. The Working Group therefore recommends issuance of a rebuttable presumption against pesticide products containing 2,4,5-T and/or TCDD pursuant to 40 CFR Section 162.11(a)(3)(ii)(B).

(ii) *Spray Applicator: Tractor-mounted, Low-boom Spray Equipment.* For the purpose of this analysis, the Working Group assumes the applicator to be a 60-kg female of childbearing age clearing brush on either rangeland or rights-of-way. The same product cited above (2,4,5-T at 4 pounds/gal) is being used, and the dilution rate is 1.6 pounds of formulation to 32 pints of water (equal to 4 pounds of 2,4,5-T per 10 gallons of water). Based on exposure studies using similar equipment but a different herbicide (*147*), the Working Group determined that, during an eight-hour working day, the applicator would get 0.048 pints of diluted material on her skin. The Working Group determined that 10 percent of the pesticide on the skin would be absorbed (*145, 146, 163*).

The following calculations (see Table 29 for mathematics) will give the daily dermal exposure for both 2,4,5-T and TCDD: (1) Convert the dilution rate to grams; (2) multiply this figure by 1,000 (for 2,4,5-T) to convert to milligrams and by 1,000,000 (for TCDD) to convert to micrograms; (3) multiply this figure by the daily dermal dose of diluted material; (4) multiply this figure by the percent absorbed; and (5) divide this figure by the weight of the applicator for the daily exposure to 2,4,5-T or TCDD per 8-hour working day.

Table 27

2,4,5-T	TCDD
1) 1.6 pounds/32 pt X 454 g/pound = 22.70 g/pt;	1) 0.00000016 pounds/32 pt X 454 g/pound = 0.00000227 g/pt;
2) 22.70 g/pt X 1,000 mg/g = 22,700 mg/pt;	2) 0.00000227 g/pt X 1,000,000 ug/g = 2.27 ug/pt;
3) 22,700 mg/pt X 0.18 pt = 4,086 mg;	3) 2.27 ug/pt X 0.18 pt = 0.41 ug;
4) 4,086 mg X 10% = 408.6 mg	4) 0.41 ug X 10% = 0.041 ug;
5) 408.6 mg / 60 kg = 6.8 mg/kg per day	5) 0.041 ug / 60 kg = 0.0007 ug/kg per day

Table 28. Dermal Exposure Data (Tractor Mounted Equipment)

	2,4,5-T	TCDD
Use Dilution rate	3 pints (1.6 pounds 2,4,5-T) per 32 pints water	3 pints (0.00000016 pounds TCDD) per 32 pints water
Amount of diluted material gotten on skin daily	0.048 pint	0.048 pint
% Diluted material absorbed	10%	10%
Exposure level	109 mg	0.0109 ug
Dose level	1.8 mg/kg	0.00018 ug/kg
No-Adverse-Effect level for teratogenic effects	20 mg/kg	0.03 ug/kg

Table 29

2,4,5-T	TCDD
1) 1.6 pounds/32 pt X 454 g/pound = 22.70 g/pt;	1) 0.00000016 pounds/32 pt X 454 g/pound = 0.00000227 g/pt;
2) 22.70 g/pt X 1,000 mg/g = 22,700 mg/pt;	2) 0.00000227 g/pt X 1,000,000 ug/g = 2.27 ug/pt;
3) 22,700 mg/pt X 0.048 pt = 1,089.6 mg;	3) 2.27 ug/pt X 0.048 pt = 0.109 ug;
4) 1,089.6 mg X 10% = 108.96 mg;	4) 0.109 ug X 10% = 0.011 ug;
5) 108.96 mg / 60 kg = 1.8 mg/kg per day	5) 0.011 ug / 60 kg = 0.00018 ug/kg per day

The Working Group considers that the difference between the no-adverse-effect level of 2,4,5-T for teratogenic effects (20 mg/kg) and this calculated dermal exposure level for 2,4,5-T (1.8 mg/kg), as well as the difference between the no-adverse-effect level of TCDD for teratogenic effects (0.03μg/kg) and this calculated exposure level for TCDD (0.00018 μg/kg), do not constitute an ample margin of safety. The Working Group therefore recommends issuance of a rebuttable presumption against pesticide products containing 2,4,5-T and/or TCDD pursuant to 40 CFR 162.11(a)(3)(ii)(B).

(iii) *Aerial Application: Exposed Population Directly Beneath Spray Plane.* Caplan et al. (*167*), working with aerially applied malathion in oil sprays applied at 0.48 pounds per 0.76 gallons water/acre, determined a dermal exposure to persons directly beneath the spray plane for bare skin (head, neck, shoulders, forearms, hands, and thighs) of 3.556 mg/day. With these data, an equivalent dermal exposure for 2,4,5-T and TCDD, aerially applied at 4 pounds acid equivalent 2,4,5-T per 10 gallons water/acre, can be determined.

Table 30. Dermal Exposure Data (Aerial Application)

Dermal exposure to aerially applied malathion	3.556 mg/0.46 pounds malathion per acre	
	2,4,5-T	TCDD
Use Dilution rate	4 pounds 2,4,5-T per 10 gallons of water/acre	0.0000004 pounds TCDD per 10 gallons of water per acre
% Diluted material absorbed	10%	10%
Exposure level	3.1 mg	0.0003 ug
Dose level	0.051 mg/kg	5×10^{-6} ug/kg
No-Adverse-Effect level for teratogenic effects	20 mg/kg	0.03 ug/kg

The following calculations (see Table 31 for mathematics) will give the daily dermal exposure for both 2,4,5-T and TCDD: (1) Divide the dermal exposure to malathion by the malathion application rate and multiply by the application rate of 2,4,5-T and TCDD to obtain the dermal exposure: for TCDD, multiply this figure by 1,000 to convert to micrograms; (2) multiply this figure by the percent absorbed; and (3) divide this figure by the weight of the applicator for the daily exposure to 2,4,5-T or TCDD per 8-hour working day.

Table 31

2,4,5-T	TCDD
1) 3.556 mg/0.46 pounds X 4 pounds = 31 mg;	1) 3.556 mg/0.46 pounds X 0.0000004 pounds = 0.000003 mg X 1,000 = 0.003 ug;
2) 31 mg X 10% = 3.1 mg;	2) 0.003 ug X 10% = 0.0003 ug;
3) 3.1 mg/ 60 kg = 0.051 mg/kg per day	3) 0.0003 ug / 60 kg = 5×10^{-6} ug/kg per day

The Working Group considers that the difference between the no-adverse-effect level of TCDD for teratogenic effects (0.03 μg/kg) and this calculated dermal exposure level for TCDD (5×10^{-6} μg/kg) does constitute an ample margin of safety. The Working Group also considers, however, that the difference between the no-adverse-effect level of 2,4,5-T for teratogenic effects (20 mg/kg) and this calculated dermal exposure level for 2,4,5-T (0.051 mg/kg) does not constitute an ample margin of safety. The Working Group therefore recommends issuance of a rebuttable presumption against pesticide products containing 2,4,5-T pursuant to 40 CFR 162.11(a)(3)(ii)(B).

(c) *Inhalation Exposure: Aerial Application.* There are no studies available on inhalation exposure of 2,4,5-T. There are, however, several studies on inhalation exposure to malathion (167, 168) which CED used as a model for this 2,4,5-T exposure analysis (*164*). Caplan et al. (*167*) determined an air concentration, for unprotected persons directly beneath the spray plane during application and for two hours afterward, of 0.067 mg malathion/m^3 from aerial application of 0.48 pounds AI/gallon per acre. The collection period spanned the course of the actual application time plus two hours thereafter. The authors considered the sampling technique to be equivalent to average inspira-

tion through the nostrils. This inhalation exposure (amount available for inhalation) was 12 percent of the applied malathion. Caplan et al. further reported that the average median diameter (=volume median diameter, or vmd [16]) was 109 microns. Based on work by Akesson and Yates (*168*), CRD (*164*) estimated that the size of the malathion droplets which could be inhaled was under 60 microns. Since 2,4,5-T is typically applied as a medium or coarse spray, while malathion is applied as a fine spray, the percent of 2,4,5-T droplets small enough to be inhaled (under 60 microns) would be less than the percent of malathion droplets small enough to be inhaled. According to Akesson and Yates (*168*), 2 percent of 2,4,5-T spray droplets would be available for inhalation (or ¼ the amount of malathion droplets available for inhalation), on a "worst case" basis.

[16]The vmd is that droplet size which divides the total volume of drops in half, i.e., 50 percent of the volume is in drops above the vmd size and 50 percent below it.

The following calculations (see Table 33 for mathematics) will give the daily inhalation exposure for both 2,4,5-T and TCDD: (1) Multiply the air concentration of malathion by the amount of 2,4,5-T and TCDD applied, then multiply this figure by ¼ for the inhalation exposure to 2,4,5-T and TCDD; for TCDD, multiply this figure by 1,000 to convert to micrograms; (2) multiply this figure by the breathing rate; (3) multiply this figure by eight [8] to get the 8-hour exposure total; and (4) divide this figure by the weight of the applicator for the inhalation exposure to 2,4,5-T or TCDD per 8-hours exposure.

Table 32. Inhalation Exposure Data (Aerial Application)

Air concentration of aerially applied malathion	$0.067\ mg/m^3$ with application rate of 0.46 pounds malathion per gallon per acre	
	2,4,5-T	TCDD
Use Dilution rate	4 pounds 2,4,5-T per 10 gallons of water/acre	0.0000004 pounds TCDD per 10 gallons of water per acre
Lung Absorption Rate	100%	100%
Breathing Rate	$1.8\ m^3/hr$	$1.8\ m^3/hr$
Exposure level	0.34 mg per 2 hr	0.000032 ug per 2 hr
Dose level	0.023 mg/kg per 8 hr	2×10^{-6} ug/kg per 8 hr
No-Adverse-Effect level for teratogenic effects	20 mg/kg	0.03 ug/kg

Table 33.

2,4,5-T	TCDD
1) 0.067 mg/cu m per 0.46 pounds X 4 pounds = 0.58 mg/cu m X 1/6 = 0.097 mg/cu m;	1) 0.067 mg/cu m per 0.46 pounds X 0.0000004 pounds = 0.000000058 mg/cu m X 1/6 = 0.000000009 mg/cu m X 1,000 = 0.000009 ug/cu m;
2) 0.097 mg/cu m X 1.8 cu m/hr = 0.17 mg/hr;	2) 0.000009 ug/cu m X 1.8 cu m/hr = 0.000016 ug/hr;
3) 0.17 mg/hr X 8 = 1.36 mg;	3) 0.000016 ug/hr X 8 = 0.000128 ug;
4) 1.36 mg / 60 kg = 0.026 mg/kg exposure per day	4) 0.000128 / 60 kg = 2×10^{-6} ug/kg per day

The Working Group considers that the difference between the no-adverse-effect level of TCDD for teratogenic effects (0.03 µg/kg) and this calculated dermal exposure level for TCDD (2×10^{-6} µg/kg) does constitute an ample margin of safety. The Working Group also considers, however, that the difference between the no-adverse-effect level of 2,4,5-T for teratogenic effects (20 mg/kg) and this calculated dermal exposure level for 2,4,5-T (0.026 mg/kg [17]) does not constitute an ample margin of safety. The Working Group therefore recommends issuance of a rebuttable presumption against pesticide products containing 2,4,5-T pursuant to 40 CFR 162.11(a)(3)(ii)(B).

(d) *Cumulative Exposure.* The Working Group has also considered the possibility of a single individual being exposed through two or more of the above routes. The results (derived from Tables 27, 29, and 31) are shown in Table 34. The Working Group also notes that possible cumulative exposure to several dioxin-containing pesticides could increase the total body burden and increase total risk from dioxin exposure.

The Working Group considers that the differences between the no-adverse-effect level of TCDD for teratogenic effects (0.03 µg/kg) and the calculated cumulative exposure levels for TCDD in Situations 2 and 3 (see Table 34) do constitute an ample margin of safety. The Working Group also considers, however, that the differences between the no-adverse-effect levels of 2,4,5-T and TCDD for teratogenic effects (20 mg/kg and 0.03 µg/kg, respectively) and the calculated cumulative exposure levels for 2,4,5,-T in Situations 1, 2, and 3 and TCDD in Situation 1 (see Table 34) do not constitute an ample margin of safety. The Working Group therefore recommends issuance of a rebuttable presumption against pesticide products containing 2,4,5-T pursuant to 40 CFR 162.11(a)(3)(ii)(B).

[17]Johnson (63) (see Section I.G.(3)), in a review article, calculated a daily inhalation exposure to phenoxy herbicides of 0.025 µg/kg for a 70-kg adult. The calculations were based on actual air monitoring data of air samples collected in two wheat-growing areas in the state of Washington during spring and summer and analyzed for phenoxy herbicides. The author did not specify how soon after application the samples were taken.

Table 34. Cumulative Exposure to 2,4,5-T and TCDD

Situation #1: 2,4,5-T	Situation #1: TCDD
Oral- 0.0007 mg/kg	Oral- -----
Dermal- 6.8 mg/kg	Dermal- 0.0007 ug/kg
Inhal.- 0.2 mg/kg[a/]	Inhal.- negligible[a/]
Cum. = 7.0 mg/kg	Cum. = 0.0007 ug/kg
Situation #2: 2,4,5-T	**Situation #2: TCDD**
Oral- 0.0007 mg/kg	Oral- -----
Dermal- 1.8 mg/kg	Dermal- 0.00018 ug/kg
Inhal.- 0.05[a/]	Inhal.- negligible[a/]
Cum. = 1.85 mg/kg	Cum. = 0.00018 ug/kg
Situation #3: 2,4,5-T	**Situation #3: TCDD**
Oral- 0.0007 mg/kg	Oral- -----
Dermal- 0.051 mg/kg	Dermal- 5×10^{-6} ug/kg
Inhal.- 0.026 mg/kg	Inhal.- 2×10^{-6} ug/kg
Cum. = 0.0777 mg/kg	Cum. = 7×10^{-6} ug/kg

a/ Calculations were made on a worst-case basis as 3% of dermal exposure based on Wolfe (179) who states, "over 97% of the pesticide to which the body is subjected during most exposure situations, and especially to applicators of liquid sprays, is deposited on the skin." TCDD inhalation exposure values were negligible: Situation #1, 21×10^{-6} ug/kg; Situation #2, 54×10^{-7} ug/kg.

DOW*

SPECIMEN LABEL
REDUCED TO 75%

ESTERON* 245
HERBICIDE

FOR THE CONTROL OF TREES, BRUSH AND BROADLEAF WEEDS

Low-Volatile Brush and Weed Herbicide for
Industrial, Forestry, Rangeland and Pasture Uses

ACTIVE INGREDIENT:	
2,4,5-Trichlorophenoxyacetic Acid, Propylene Glycol Butyl Ether Esters	69.2%
2,4,5-Trichlorophenoxyacetic Acid Equivalent — 4 Pounds per Gallon	45.6%
INERT INGREDIENTS:	30.8%

E.P.A. Registration No. 464-205 E.P.A. Est. 464-MI-1

PRECAUCION AL USUARIO: Si usted no lee ingles, no use este producto hasta que la etiqueta le haya sido explicada ampliamente.
TRANSLATION: (TO THE USER: If you cannot read English, do not use this product until the label has been fully explained to you.)

KEEP OUT OF THE REACH OF CHILDREN

CAUTION

MAY BE HARMFUL IF SWALLOWED • MAY CAUSE IRRITATION
Avoid Contact with Eyes, Skin and Clothing
Do Not Cut or Weld Container

In case of an emergency endangering life or property involving this product, call collect
517-636-4400

AGRICULTURAL CHEMICAL
Do Not Ship or Store with Food, Feeds Drugs or Clothing

18.93 L / 5 GAL

86-1064 PRINTED IN U.S.A. IN APRIL, 1978.
REPLACES SPECIMEN LABEL 86-1064 PRINTED OCTOBER, 1977.
DISCARD PREVIOUS SPECIMEN LABELS.
REVISIONS INCLUDE: (1)EMERGENCY RESPONSE PHONE NUMBER ADDED.
(2)"DO NOT CUT OR WELD CONTAINER" ADDED.

SPECIMEN LABEL
(BACK)
REDUCED TO 75%

DOW ESTERON 245 HERBICIDE

Contains Propylene Glycol Butyl Ether Esters of 2,4,5-T • Acid Equivalent: 4 Pounds per Gallon

DIRECTIONS

ESTERON 245 herbicide is recommended for industrial vegetation control in forest areas; on right-of-ways, such as communication lines, electrical powerlines, pipelines, highways, and railroads; fence rows; and on rangelands and pastures. This herbicide controls herbaceous and woody plants including such 2,4-D resistant species as—ash, black gum, brambles, groundcherry, hawthorn, horsenettle, maple, mesquite, oak, osageorange, palmetto, poison ivy, pricklypear cactus, redbay, salmonberry, sweetgum, wild blackberry, wild rose, and certain species of Ribes. **Do not apply ESTERON 245 where spray drift may contact nearby 2,4,5-T susceptible crops or other desirable plants or may contaminate water intended for irrigation or domestic purposes. Read and follow all Use Precautions given on this label.**

PREPARING THE SPRAY

Use only diesel oil, No. 1 or No. 2 fuel oil or kerosene where oil is recommended in the spray mixture.

Oil Sprays: Add ESTERON 245 to the required amount of oil in the spray tank or mixing tank and mix thoroughly. This mixture can be made at any time before actual use and no separation will occur. Do not let any water, or oil-water mixture sprays get into the ESTERON 245 or into the finished mixture, as it may form a gel.

Water Sprays: Fill the spray tank about half full with clean water, add the required amount of ESTERON 245 and complete filling the tank. Mix thoroughly and continue agitation while spraying. **Caution: See NOTE in paragraph on Oil-Water Mixture Sprays.**

Oil-Water Mixture Sprays: When vigorous agitation is used, 1 gallon of ESTERON 245 will emulsify up to 10 gallons of oil in 100 gallons of spray mixture. First, premix the ESTERON 245 and oil in a separate container. Do not allow any water or mixtures containing water to get into the ESTERON 245 or the premix. Fill the spray tank about half full with water, then slowly add the premix with continuous agitation and complete filling the tank with water. If the premix is put in the tank without any water, the first water added may form a thick "invert" (water in oil) emulsion which will be hard to break. As an alternate procedure, the oil may be added after the ESTERON 245 is mixed in the water; but highly vigorous mechanical agitation is required and a poor emulsion may be formed. The premix method is preferred.

NOTE: ESTERON 245 in water or oil-water sprays forms an emulsion, not a solution, and separation may take place unless sprays are agitated continuously. Mechanical agitation is recommended.

INDUSTRIAL BRUSH AND WEED CONTROL INCLUDING FORESTRY USES

HIGH VOLUME SPRAYS

Foliage Treatment: For control of woody vegetation up to 8 feet tall, apply when foliage is well developed and plants are actively growing. Spraying during prolonged hot, dry weather or after leaves have lost their normal green color and vigor may not give satisfactory control. Use 3 to 4 quarts of ESTERON 245 in 100 gallons of water and apply as a full coverage spray. Usually 100 to 200 gallons per acre will be required, although dense stands of brush may require up to 400 gallons per acre. Completely wet all plant parts including leaves, stems and bark. Poison ivy, some brambles and many broadleaf weeds may be controlled using 2 quarts of ESTERON 245 in 100 gallons of water.

To control grasses as well as broadleaf weeds and woody plants on conifer forest planting sites, ESTERON 245 may be used in a tank mixture with DOWPON* grass herbicide. Consult label directions and precautions for DOWPON to determine recommended use of this product.

Basal Bark Treatment: Brush and small trees can be controlled by spraying the basal parts of brush stems and tree trunks to a height of 12 to 15 inches from the ground line. Use a solution of 3 gallons of ESTERON 245 in 100 gallons (1 pint in 4 gallons) of oil. With certain resistant species, 4 gallons of ESTERON 245 in 100 gallons (1 pint in 3 gallons) of oil, is effective. As only the basal portions of the brush are treated on a spot basis, the total amount sprayed per acre would not be expected to exceed 100 gallons. Knapsack or power equipment may be used, but complete wetting of the indicated area is necessary, particularly at the ground line. This means spraying until run-down or run-off to the ground line is noticeable. Old or rough bark requires more spray than young or smooth bark. Low pressures are desirable. Apply at any time, including the winter months, except when snow, ice or water prevent spraying to the ground line. Often delayed response and killing can be expected.

Dormant Brush: Treat any time after brush is dormant and most of the foliage has dropped. Spray should be concentrated at the base of stems and in addition, the upper parts of the stems should be broadcast sprayed enough to wet them. Under rootsuckering species such as sumac, persimmon, sassafras and locust, also spray the ground area to control small root suckers that may not be readily visible. Mix 1½ gallons of ESTERON 245 in 100 gallons of oil. Brush of average density and 4 to 6 feet high may take up to 150 gallons of spray mixture per acre.

Stump Treatment: Where growth is more than 6 to 8 feet tall, cut it close to the ground and spray the freshly cut stumps and stubs with 3 gallons of ESTERON 245 in 100 gallons (1 pint in 4 gallons) of oil, mixed thoroughly. For more resistant species, use 4 gallons of ESTERON 245 in 100 gallons (1 pint in 3 gallons) of oil. Wet thoroughly all exposed bark, as well as cut surfaces. This means spraying until run-down or run-off to the ground line is noticeable. Old or rough bark requires more spray volume than young or smooth bark. Apply at any time, including the winter months, except when ice, snow or water prevent spraying to the ground line. Best results are obtained on freshly cut stumps two inches across or larger. Adequate coverage normally requires from 10 to 100 gallons per acre depending on density of stumps and stubs.

"Frill" Treatment: For large trees, make a singlehack girdle or "frill" of overlapping axe cuts completely around the tree as close to the ground as feasible. Spray the frill thoroughly using a mixture of 2 gallons of ESTERON 245 in 100 gallons (½ pint in 3 gallons) of oil.

Spot Foliage Treatment: Use ¼ pint of ESTERON 245 in 3 gallons of water and spray to wet all foliage, shoots, stems and bark without runoff.

LOW VOLUME SPRAYS

Apply low volume sprays containing ESTERON 245 when foliage is well developed and plants are actively growing. For best results on woody species, soil moisture should be sufficient to promote foliar growth. Spraying during prolonged hot, dry weather or after leaves have lost their normal green color and vigor may not give satisfactory control. Apply low volume sprays by air or ground equipment only when spray drift will not be a problem—note use precautions.

Right-of-Ways and Forest Site Preparation

Foliage Treatment: Use 1 to 3 gallons of ESTERON 245 in enough water to make 10 to 30 gallons of total spray per acre. If desired, oil can be added to the spray in accordance with directions for "Oil-Water Mixture Sprays" given under PREPARING THE SPRAY.

Use With TORDON 101 Mixture: ESTERON 245 may be used with TORDON* 101 Mixture herbicide in a tank mix combination spray applied by aircraft for improved control of root suckering species and other species often not adequately controlled with 2, 4,5-T. Use 1 to 2½ gallons of ESTERON 245 Herbicide plus 1½ to 2½ gallons of TORDON 101 Mixture per acre by diluting with water to a total spray volume of 10 to 30 gallons per acre. Use the higher rates where resistant species such as red maple, sourwood, ash, oaks, hawthorn and cedar are prevalent and especially during unfavorable conditions for plant growth such as drought. Do not add oil or NORBAK* particulating agent to the spray. Aerial applications of the tank mixture should be made only with a helicopter mounted Microfoil applicator or an equipment system providing equivalent drift control.

Read the directions and all the Use Precautions on both labels before using this tank mix.

Note: Do not plant conifer seedlings on treated areas for at least 6 months after applying 2 gallons or more of TORDON 101 per acre in such a tank mix.

Basal Treatment Using Powered Knapsack Sprayer—Mix 1½ to 2 gallons of ESTERON 245 with fuel oil or kerosene to make 20 gallons of total spray solution. Apply with a portable knapsack mistblower to all sides of lower brush stems including the root collar. Good coverage of the root collar is essential for best results. Run mistblower at ¼ to ½ throttle for best spray delivery and coverage. For maximum drift control use a basal nozzle attachment and do not raise nozzle above the horizontal position.

Forest Conifer Release by Air or Ground Sprays

Oil Spray—Apply 2 to 3 quarts of ESTERON 245 in about 10 gallons of oil per acre to control undesired hardwoods in dormant Douglas fir, true fir, hemlock and spruce. Rates higher than 2 quarts may cause conifer injury. Do not use this spray on pines (note section below for pine recommendation). Apply **before** conifer bud break during late dormancy, usually February and March in the northwest. Application of this spray after conifer bud break can injure the conifers.

Water Spray—Apply 2 to 3 quarts of ESTERON 245 in 10 to 15 gallons of water per acre to control hardwood species in conifers including pines. Apply during the summer after the conifers cease spring growth and have "hardened off". Rates higher than 2 quarts may cause conifer injury.

Consult your State, Regional or Extension Forester for recommendations to fit local conditions.

RANGELAND AND PASTURES

RANGELAND—AIR APPLICATION FOR BRUSH CONTROL

Consult the Agricultural Experiment Station, your local Extension Service Weed or Range specialist for best time to treat and need for re-treatment in your area. Do not use from early boot to milk stage where grass seed production is desired.

Mesquite: Use 1 pint of ESTERON 245 plus ½ to 1 gallon of oil in enough water to make 4 gallons of total spray per acre. Apply 40 to 90 days after first leaves appear.

Sand Shinnery Oak: Use ½ to 1 quart of ESTERON 245 plus 1 gallon of oil in enough water to make 4 gallons of total spray per acre.

Post and Blackjack Oaks: Use 2 quarts of ESTERON 245 plus 1 gallon of oil in enough water to make 4 to 6 gallons of total spray per acre.

PASTURE—FOR BROADLEAF WEED CONTROL

Use 2 to 3 quarts of ESTERON 245 per acre by aircraft or ground equipment in the amount of water needed to obtain uniform application. Apply when weeds are in full leaf and after grass is well established. Do not apply on stoloniferous grasses such as bent and bermuda or on forage legumes because these can be injured or killed. Do not apply on newly seeded areas, and do not use from early boot to milk stage where grass seed production is desired. **Note:** Do not graze dairy animals on treated areas within 6 weeks after application. Do not graze meat animals on treated areas within 2 weeks of slaughter.

USE PRECAUTIONS

AVOID CONTACT WITH 2,4,5-T SUSCEPTIBLE CROPS AND OTHER DESIRABLE BROADLEAF PLANTS—ESTERON 245 Herbicide is injurious to most broadleaf plants. Therefore, do not apply directly to or otherwise permit even minute amounts to contact cotton, grapes, tobacco, fruit trees, vegetables, flowers, ornamentals or other desirable plants susceptible to 2,4,5-T. Do not use in or near a greenhouse.

DO NOT APPLY IN THE VICINITY OF COTTON, GRAPES, TOBACCO, TOMATOES OR OTHER DESIRABLE 2,4,5-T SUSCEPTIBLE CROPS OR ORNAMENTAL PLANTS.

DO NOT SPRAY WHEN WIND IS BLOWING TOWARDS SUSCEPTIBLE CROPS OR ORNAMENTAL PLANTS

AVOID SPRAY DRIFT—Applications should be made only when there is no hazard from spray drift since very small quantities of the spray, which may not be visible, may severely injure susceptible crops during both growing and dormant periods. Use coarse sprays to minimize drift since, under adverse weather conditions, fine spray droplets may drift a mile or more. The spray thickening agent, NALCO-TROL[1], may be used with this product to aid in reducing spray drift. If used follow all use recommendations and precautions on the product label.

[1] NALCO-TROL—Trademark of NALCO Chemical Company

GROUND EQUIPMENT—With ground equipment, spray drift can be lessened by keeping the spray boom as low as possible; by applying 20 gallons or more of spray per acre; by using no more than 20 pounds spraying pressure with large droplet producing nozzle tips; by spraying when wind velocity is 8 miles per hour or less. Do not apply with hollow cone-type insecticide or other nozzles that produce a fine-droplet spray.

AERIAL APPLICATION—With aircraft, drift can be lessened by applying a coarse spray; by using no more than 20 pounds spray pressure at the nozzles; by using straight stream nozzles directed straight back; by using a spray boom no longer than ¾ the wing span of the aircraft; and by spraying only when wind velocity is less than 6 mph.

DO NOT APPLY BY AIRCRAFT WHEN AN AIR TEMPERATURE INVERSION EXISTS. Such a condition is characterized by little or no wind and with air temperature lower near the ground than at higher levels. The use of a continuous smoke column at or near site of application is suggested to indicate direction and velocity of air movement, and to indicate a temperature inversion by layering of the smoke.

At high temperatures (above 95°F) vapors from this product may injure susceptible plants growing nearby. Do not use in or near a greenhouse. Excessive amounts of this herbicide in the soil may temporarily inhibit seed germination or plant growth.

Do not use around the home, recreation areas or similar sites. Do not use on susceptible grasses, such as bent, except for spot spraying, nor on freshly seeded areas until grass has become well established. (Most legumes are usually damaged or killed).

This product is toxic to fish. Keep out of lakes, streams, and ponds. Do not contaminate water by cleaning of equipment or disposal of wastes.

Do not contaminate irrigation ditches or water used for irrigation or domestic purposes. This product can be stored in an unheated building but if exposed to subfreezing temperatures, should be warmed to at least 40°F and mixed thoroughly before using. Do not store near fertilizers, seeds, insecticides or fungicides. Do not reuse containers. To avoid injury to desirable plants, do not store, handle or apply other agricultural chemicals with the same containers or equipment used with ESTERON 245 except as specified on this label.

Rinse equipment and containers and dispose of waste by burying in non-crop lands away from water supplies. Containers should be disposed by punching holes in them and burying with waste or follow official local recommendations for container disposal.

Local conditions may affect the use of herbicides. Consult your State Agricultural Experiment Station or Extension Service weed specialist for advice in selecting treatments from this label to best fit local conditions. Be sure that use of this product conforms to all applicable regulations. Apply this product only as specified on this label.

NOTICE: Seller warrants that the product conforms to its chemical description and is reasonably fit for the purposes stated on the label when used in accordance with directions under normal conditions of use, but neither this warranty nor any other warranty of MERCHANTABILITY or FITNESS FOR A PARTICULAR PURPOSE, express or implied, extends to the use of this product contrary to label instructions, or under abnormal conditions, or under conditions not reasonably foreseeable to seller, and buyer assumes the risk of any such use.

10586-049-7 R278

THE DOW CHEMICAL COMPANY
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