

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

MICHAEL NEWTON^A and LOGAN A. NORRIS^B

^AProfessor of Forest Ecology, Oregon State University, Corvallis; ^BChief Research Chemist, USDA Forest Service, Corvallis, Oregon

ABSTRACT

Potential Exposure of Humans to 2,4,5-T and TCDD in the Oregon Coast Ranges.¹ Newton, M. and Norris, L.A. (1981). *Fundam. Appl. Toxicol.* 1:339-346. Research on the use of 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) contaminated with 2.5×10^8 parts 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in forests of the Oregon Coast Ranges permits estimates of human exposures for both compounds. Estimated total exposure of nearby ($\geq 1/8$ mile distant) residents during the first week after application is 0.0039 mg/kg of 2,4,5-T for a 70-kg adult. Exposure to TCDD in the same episode would be 1.9×10^{-10} mg/kg. Nearly half the total exposure, i.e. 0.0019 mg/kg 2,4,5-T and 5.0×10^{-11} mg/kg TCDD would occur the first day. Based on published and unpublished acute no-effect estimates of 40 mg/kg for 2,4,5-T and 0.0001 mg/kg for TCDD, the smallest safety factors for the two chemicals are 20 000:1 for 2,4,5-T for 1 day and 1 000 000:1 for TCDD for 1 week. Applicators are far more heavily exposed, with daily maximum actual intake for helicopter loaders (the highest exposure group if they do not wear gloves) of 0.063 mg/kg per day 2,4,5-T and 1.6×10^{-9} mg/kg per day TCDD. Minimum safety factors for the most heavily exposed workers based on these data are estimated at 635:1 for one-time exposure to 2,4,5-T; 83 333:1 for one-time exposure to TCDD; 318:1 for daily exposure to 2,4,5-T; and 625:1 for daily exposure to TCDD. Nearly all exposure to 2,4,5-T in forestry operations is through dermal contact. Inhalation appears minor. Urine is a reliable indicator of exposure to 2,4,5-T if collected within 1 to 4 days of exposure (depending on the degree of exposure). Human skin exposed to a concentrated spray mixture containing 38.4 g 2,4,5-T per liter, as the ester, transmitted 0.0013 mg/cm² per hr during the period of saturated contact.

INTRODUCTION

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

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

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

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

METHODS

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

Exposure through dermal contact — applicators

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

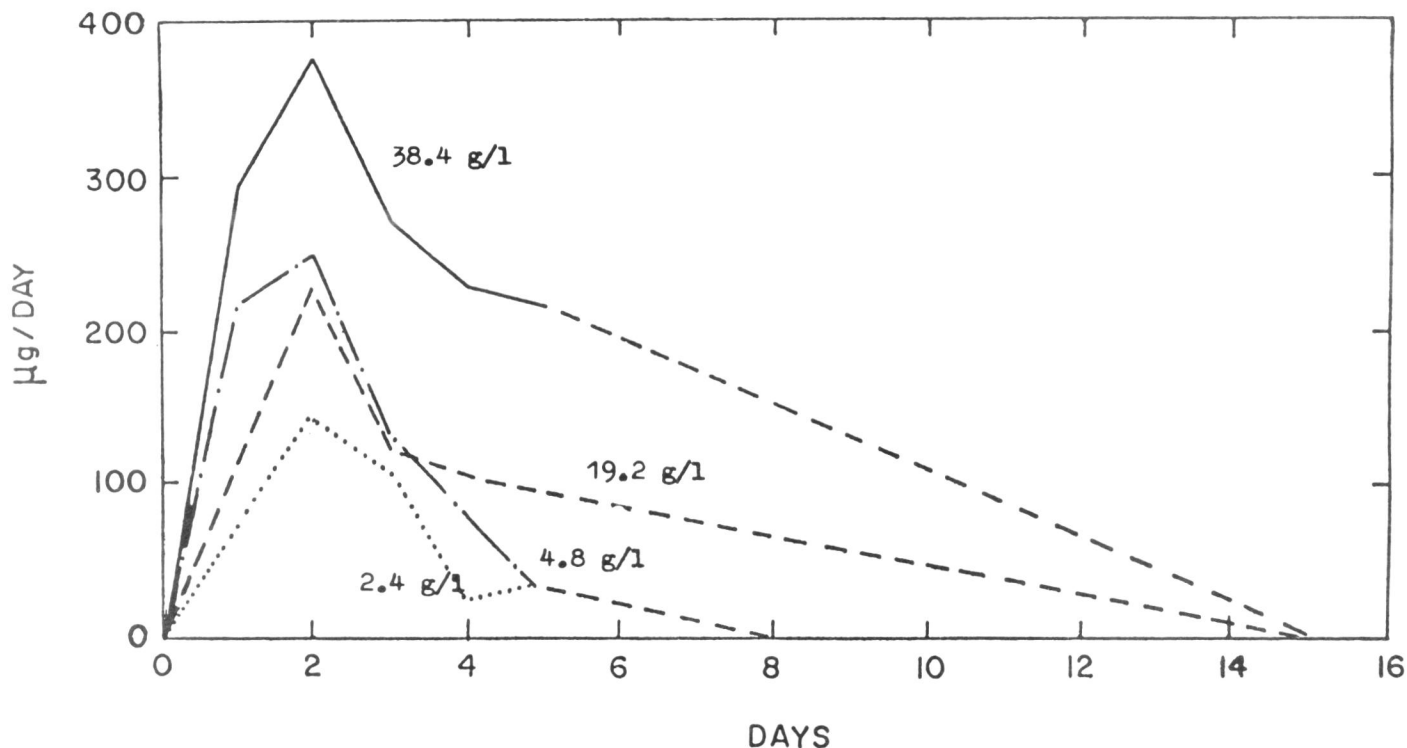


FIG. 1. Micrograms 2,4,5-T per day in urine of humans after 2-hour contact by 2,4,5-T ester emulsions of various concentrations on 900 cm² of skin.

Specific absorption rate by human skin — experimental

Data on the absolute penetration of 2,4,5-T through skin was lacking in the literature. It was therefore necessary to conduct an exploratory controlled experiment to determine the rates at which operationally used mixtures of 2,4,5-T would lead to physiological exposure of humans. An exposure test was run on four volunteers, including one woman. Contact was provided by placement of 900-cm² bleached denim patches on the thigh, at which time 40 mL of 2,4,5-T propylene glycol butyl ether ester emulsion was applied by syringe, saturating the patch to the drip point. Concentrations applied to patches included the range of those in registered use, varying from 2.4 to 38.4 g/liter acid equivalent in the spray mixture (2 to 32 lbs/100 gal).

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

Physiological exposure was measured in terms of recoverable 2,4,5-T in urine. Absorption of 2,4,5-T was measured by analysis of the total amount of herbicide eliminated in the urine, as described by Gehring *et al.* (1973). Urine collection began 24 hours before application of the treated patch, with 24-hour samples being composited for a period of 5 days. Aliquots of the composites were analyzed using a procedure similar to the method of Smith and Hayden (1979) using the macroreticular resin XAD-7.² According to Gehring *et al.* (1973), 2,4,5-T taken by mouth is almost entirely eliminated in

urine within 5 days. According to their calculations, half the 2,4,5-T in plasma disappeared in about 23 hours, suggesting that the total physiological body burden would at no time exceed twice the amount recovered in any 23-hour period.

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

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

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

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

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

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

^BMeasured 2,4,5-T recovered in urine in first 5 days.

^CFrom extended curves as in figure 2. Integrals plotted and values obtained from function: mg eluted = 30X (concentration, aehg) which is a linear approximation of the integrals.

^DSum of measured and estimated postmeasurement amounts.

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

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

^A70-kg body weight.

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

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

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

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

Estimated absorption from discontinuous contact

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

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

Exposure of forest residents through water, food, and air Exposure through drinking water

Our research on levels of herbicide contamination resulting from forest usage near streams extended from 1963 to 1968 continuously, and intermittently to the present. Much of the research was conducted before untreated buffer strips were required along streams to reduce direct stream contamination in Oregon. This program has determined the range of contam-

ination levels likely to be encountered in streams flowing from or through forest areas treated operationally with herbicides for vegetation control with or without streamside buffers. In addition to research, monitoring by public agencies has provided extensive data regarding field-use levels of contamination when buffer strips are used. These monitoring data indicate that contamination levels under practical conditions of herbicide use are substantially below the maximum observed in our research intended to measure "worst-case" situations.

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

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

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

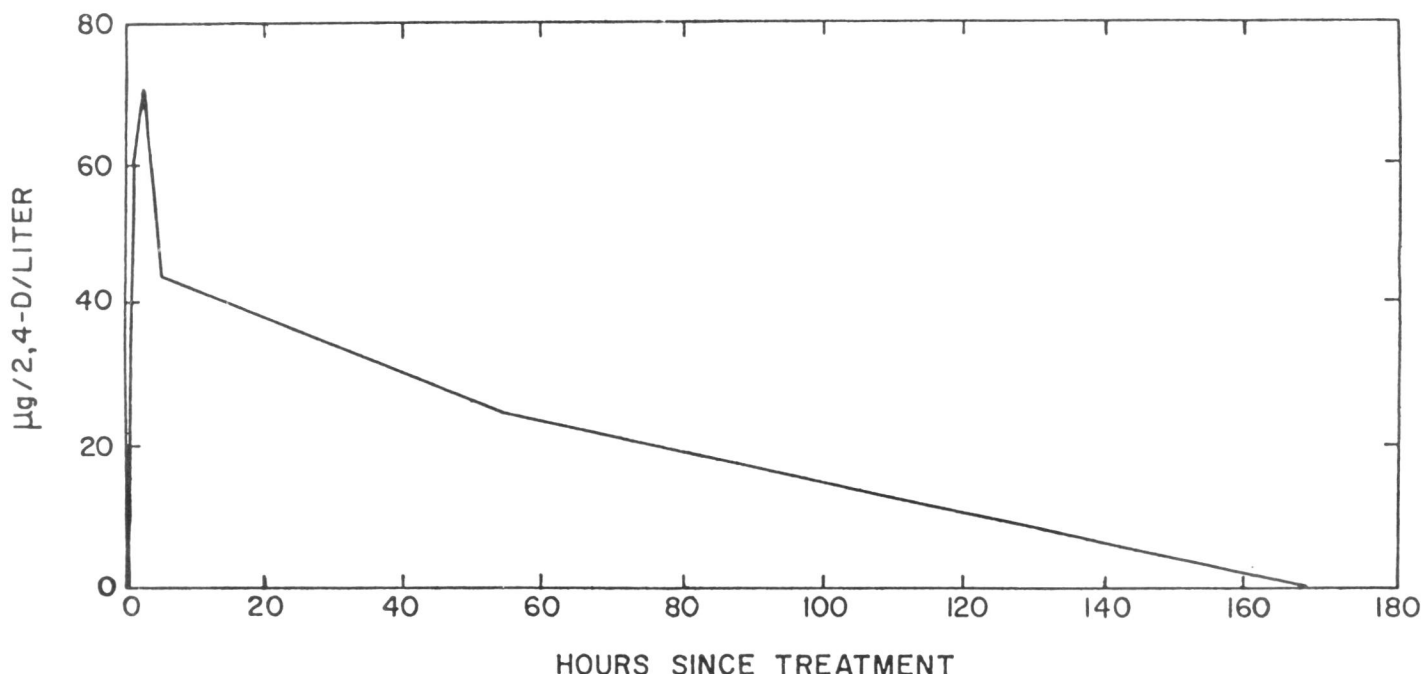


FIG. 2. Herbicide concentration in the most heavily contaminated forest watershed (Hunt Cr., 1965) treated with $2\frac{1}{2}$ pounds 2,4-D per acre without buffer zones.

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

Source	Total		Dose (70-kg person)		Safety factors	
	24 hrs	168 hrs	24 hrs	168 hrs	24 hrs	168 hrs
mg.....	mg/kg.....			
2,4,5-T						
Water (creek)	0.136	0.267	0.0019	0.0038		
Venison	0.0021	0.0095	0.00003	0.00014		
Atmosphere	0.00075	0.00075	0.00001	0.00001		
Total	0.139	0.277	0.0019	0.0039	21 053	35 897
TCDD						
Water (creek)	3.4×10^{-9}	6.67×10^{-9}	4.9×10^{-11}	9.5×10^{-11}		
Venison	5.2×10^{-11}	2.37×10^{-10}		7.43×10^{-14}		3.4×10^{-12}
Atmosphere	1.9×10^{-11}	1.9×10^{-11}	2.7×10^{-13}	2.7×10^{-13}		
Total	3.5×10^{-9}	6.9×10^{-9}	5.0×10^{-11}	9.9×10^{-11}	2 000 000:1	1 010 101:1

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

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

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

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

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

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

The low solubility of TCDD (Anonymous, 1978) suggests that there will be greater differential adsorption of TCDD on sediments in preference to 2,4,5-T, and that the actual exposure to TCDD will be lower than the calculated level (Isensee and Jones, 1975). Although adsorption is reversible, re-

lease of the TCDD into water would be minor because of the extremely low original input and the strong partition in favor of the sediment. Degradation takes place during the period of adsorption, hence total exposure would be reduced both by the adsorption phenomenon and by degradation *in situ*. Thus, our estimate of exposure is not likely to be exceeded, or even used.

Contamination of wildlife

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

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

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

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

If a forest resident consumes 454 g (1 pound) of deer liver with the maximum level of contamination (0.021 mg/kg 2,4,5-T) during 1 week, total exposure from that source will be 0.0095 mg of 2,4,5-T. TCDD from the same source cannot be estimated precisely, because detectable residues of TCDD in livers of deer, cattle, or rodents have not been reported in the scientific literature³ at detection limits down to 3 ng/kg (3 parts per trillion) (Newton and Snyder, 1978). If TCDD were present at 2.5×10^{-8} times the amount of 2,4,5-T, the total amount of TCDD would be 2.375×10^{-10} mg per 454 g liver. In view of the compensatory tendencies of TCDD to be retained in liver more than 2,4,5-T, but to degrade more quickly on forage, we believe the ratio of TCDD to 2,4,5-T given is reasonable in the short term and generous in the long term.

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

Atmospheric exposure

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

Phenoxy herbicide esters have low but measurable vapor pressures. Air vapor content varies with temperature and area treated. Vapors move downhill as air cools during the evenings of hot days. Only low-level exposure upwind will occur. The vapor load carried by air has been summarized for various esters of 2,4-D by the National Research Council of Canada (Anonymous, 1978). The maximum concentration in air reported for a low-volatile ester of 2,4-D was 0.0031 mg/m³ at unspecified distances downwind from large-scale applications of 2,4-D in wheat. Forest spray units are usually widely scattered and seldom more than 40 ha (100 acres). Given that 2,4,5-T is less volatile than 2,4-D (USDA, 1979), that conditions are unfavorable for evaporation, and that mass effect of treating range areas is absent when applications are made to scattered patches in the cool forested areas of the Coast Ranges, a reasonable upper limit for the level of 2,4,5-T in air might be about 0.001 mg/m³. This figure compares with a range of 0.000012 to 0.000895 mg/m³ in a 2,4,5-T treated forest area reported by Cheney *et al.* (n.d.) and 0.00004 to

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

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

^ANo-effect levels: 2,4,5-T - one exposure 40 mg/kg, daily exposure 20 mg/kg per day

TCDD - one exposure 0.0001 mg/kg, daily exposure 0.000001 mg/kg per day

0.0036 mg/m³ observed by Young *et al.* (1978) from a volatile point source of concentrated 2,4-D and 2,4,5-T.

The volume of air inhaled has been variously reported as 0.9 to 1.8 m³/hr (USDA, 1979; USEPA, 1978). If the average human breathes 1.5 m³ of air during a 1-hour drift exposure, and absorbs all the 2,4,5-T, respiratory exposure may be estimated from the integral of the total breathed air in which the concentration increases from zero to 0.001 mg/m³ then decreases from 0.001 mg/m³ to zero, to be a total of 0.00075 mg of 2,4,5-T. Acknowledging that there are major uncertainties in the above assumptions of drift, it is evident that the total exposure via this route is exceedingly small, even in a worst-case situation. Because of the very low volatility of TCDD, respiratory exposure via vapor is regarded as negligible. If TCDD were vaporized proportional to its concentration in the 2,4,5-T formulation (2.5×10^{-8}), exposure would be 1.87×10^{-11} mg TCDD. Although the possibility of occurrence in fine droplets cannot be excluded, degradation would be extremely rapid in the presence of oil, 2,4,5-T, or other solvents in the presence of light (Crosby and Wong, 1977).

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

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

2,4,5-T

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

TCDD

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

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

For applicators, Table 4 illustrates the safety factors (number of exposures that must be encountered simultaneously to

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

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

CONCLUSIONS

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

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

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

REFERENCES

- Anonymous (1978). *Phenoxy herbicides — their effects on environmental quality*. National Research Council of Canada, Ottawa. Rept. NRCC 16075, 440 p.
- Cheney, H.V., Walby, C.M. and Shields, R.E. (n.d.). Impact of 2,4,5-T on Blodgett Forest. I. Description of an experimental aerial application of 2,4,5-T. Undated report, Environmental Monitoring and Pest Management. Calif. Dept. Food Agric., Sacramento. 189 p.
- Clark, D.E., Palmer, J.S., Radeleff, R.D., Crookshank, H.R. and Farr, F.M. (1975). Residues of chlorophenoxy acid herbicides and their phenolic metabolites in tissue of cattle and sheep. *J. Agric. Food Chem.* 23:573-578.
- Crosby, D.G. and Wong, A.S. (1977). Environmental degradation of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Science* 195:1337-1338.
- Gehring, P.J., Kramer, C.G., Schwetz, B.A., Rose, J.Q. and Rowe, V.K. (1973). The fate of 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) following oral administration to man. *Toxicol. Appl. Pharmacol.* 26:352-361.

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

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

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

- Isensee, A.R. and Jones, G.E.** (1975). Distribution of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in an aquatic model ecosystem. *Environ. Sci. Technol.* 9:668-672.
- Murray, F.J., Smith, F.A., Nitschke, K.D., Humiston, C.G., Kociba, R.J. and Schwetz, B.A.** (1979). Three-generation reproduction study of rats given 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in the diet. *Toxicol. Appl. Pharmacol.* 50:241-252.
- Newton, M. and Norris, L.A.** (1968). *Herbicide residues in blacktail deer from forests treated with 2,4,5-T and atrazine.* Proc. West. Soc. Weed. Sci. 1968, p. 32-34.
- Newton, M. and Snyder, S.P.** (1978). Exposure of forest herbivores to TCDD in areas sprayed with 2,4,5-T. *Bull. Environ. Contam. Toxicol.* 20:743-750.
- Norris, L.A.** (1967). Chemical brush control and herbicide residues in the forest environment. In Symp. Proc. *Herbic. and Veg. Manage. in Forests, Ranges and Noncrop Lands*, p. 103-123. Oreg. State Univ., Corvallis.
- Norris, L.A.** (1978). Toxic materials in forest streams. In Toxic materials in the aquatic environment, p. 43-68. *Water Resour. Res. Inst.*, Oreg. State Univ., Corvallis.
- Norris, L.A., and Moore, D.G.** (1976). Forests and rangelands as sources of chemical pollutants. In Non-point sources of water pollution, p. 16-35. *Water Resour. Res. Inst.*, Oreg. State Univ., Corvallis.
- Ramsey, J.C., Lavy, T.L. and Braun, W.H.** (1979). Exposure of forest workers to 2,4,5-T; calculated dose levels. In Project Completion Report to the *National Forest Products Association*. Feb. 14, 1979. (T.L. Lavy, Univ. Ark., Director).
- St. John, L.E., Wagner, D.G. and Lisk, D.J.** (1964). Fate of Atrazine, Kuron, Silvex and 2,4,5-T in the dairy cow. *J. Dairy Sci.* 47:1267-1270.
- Serat, F., Feldman, G. and Maibach, B.** (1973). Percutaneous absorption of toxicants. *Natl. Pest Control Operators News.* Oct., 1973. p. 6.
- Smith, A.E. and Hayden, B.J.** (1979). Method for determination of 2,4-D in urine. *J. Chromatog.* 171:482-485.
- U.S. Department of Agriculture** (1979). Biological and economic assessment of 2,4,5-T. Report of the *USDA/States/EPA 2,4,5-T RPAR Assessment Team*. Washington, D.C.
- U.S. Environmental Protection Agency** (1978). Rebuttable presumption against registration and continued registration of pesticide products containing 2,4,5-T. Position Document 1. *Fed. Regist.*, April 21, 1978. p. 17116-17157.
- U.S. Environmental Protection Agency** (1979a). Decision and emergency order suspending registrations for the forest, rights-of-way and pasture uses of 2,4,5-trichlorophenoxyacetic acid (2,4,5-T). *Office of Pesticide Programs*. Washington, D.C.
- U.S. Environmental Protection Agency** (1979b). Report of the FIFRA Scientific Advisor Panel on proposed Sec. 6(b)(2) notices for 2,4,5-T and silvex. *Office of Pesticide Programs*. Washington, D.C.
- Yates, W.E., Akesson, N.B. and Cowden, R.E.** (1974). Criteria for minimizing drift residues in crops downwind from aerial applications. *Trans. Amer. Soc. Agric. Engin.* 17(4):627-632.
- Young, A.L., Calcagni, J.A., Thalken, C.E. and Tremblay, J.W.** (1978). The toxicology, environmental fate and human risk of herbicide Orange and its associated dioxin. *U.S. Air Force OEHL Tech. Rep.* OEHL TR-78-92.

Purchased by USDA Forest Service, for official use.