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THE HEALTH RISKS OF HERBICIDES IN FORESTRY: A REVIEW OF THE SCIENTIFIC RECORD

JOHN D. WALSTAD
FRANK N. DOST

COLLEGE OF FORESTRY OREGON STATE UNIVERSITY

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CONTENTS

PREFACE

For more than a decade now, the use of herbicides (especially phenoxy herbicides) in forestry has been the subject of intense controversy. The debate has touched upon many aspects of herbicides, ranging from ecology to economics. But at the center of discussion has been the issue of possible adverse effects on human health. Members of the scientific and medical community have been actively engaged in evaluating the safety of herbicide use. This investigation has been broadened as new questions have been raised or new information has come to light; for example, reports of illness in Vietnam veterans possibly connected with their exposure to Agent Orange, miscarriages in coastal forest dwellers near areas treated with 2,4,5-T, and inappropriate disposal of dioxin-contaminated wastes. Researchers and physicians have also given expert testimony as the debate has moved into the courtrooms.

Enough studies have been completed in the past fifteen years or more that it is timely to publish a review of the scientific record regarding the health risks of using herbicides in forestry. This bulletin also provides a brief introduction to the methods of toxicology and the regulatory control of toxic substances by government. We hope that this information will be helpful to those concerned with the use of herbicides in our environment and particularly in forestry operations.

INTRODUCTION

Herbicides are important tools used by forest managers to sustain the productivity of commercial forests. However, such economic considerations must not take precedence over concerns for public health and environmental safety. Phenoxy herbicides have been the focus of considerable public controversy and scientific scrutiny over the past decade. As a consequence, their safety has been periodically re-examined as new information or concerns have come to light. Such risk assessments are appropriate for any chemical product in order to ensure that its use is not likely to jeopardize human health or the general environment. An overview of the methods of toxicology and regulatory control by government agencies will provide background information for the issue of safety.

The risks to human health from herbicide use in forestry are evaluated in three ways in this report. First, we present calculations of the amounts of various herbicides, especially phenoxies, which an average person would have to ingest in order to meet or exceed certain toxicological points of reference established through testing of laboratory animals. Second, we analyze data from field studies that measured amounts of herbicide in the environment or specific organisms. Third, we review the conclusions of the many medical, scientific, and legal reviews of herbicide safety conducted over the past decade.

One of several misconceptions surrounding the use of herbicides in forest management is that not enough is known about them to evaluate their safety. However, a bibliography compiled by scientists at the Texas Agricultural Experiment Station indicated that even by 1977 there were over 870 scientific articles on the toxicology of phenoxy herbicides (Diaz-Colon and Bovey 1977). Seven other volumes in this bibliographic series cover the literature pertaining to fate in the environment, ecological effects, analytical chemistry, effects on higher plants, dioxins, interrelations with microorganisms, and military uses (Bovey and Diaz-Colon 1977, 1978a, b, c; Diaz-Colon and Bovey 1976, 1978a, b). It is estimated that there are over 40,000 published studies dealing with various aspects of the phenoxy herbicides (Council for Agricultural Science and Technology 1978). Of course, numbers of studies do not necessarily indicate depth of knowledge, but phenoxy herbicides are certainly among the most intensively examined chemical families. Bovey and Young (1980) have synthesized much of the information in their textbook on phenoxy herbicides.

Regardless of the amount of information we have, however, we will never be able to state with absolute certainty that the use of a given herbicide (or any chemical product, for that matter) is perfectly safe. The difficulty arises from several sources:

1. There are practical limits to the size and scope of experiments that can be conducted in testing a chemical, inevitably leaving some possible effects untested.

2. The test results must be extrapolated to different animal species, to larger populations, or to different situations, which always leaves a chance that they will respond differently than the specific test animals.

3. The tests themselves can be flawed, inadequately designed, or misinterpreted.

4. There is always the possibility of some unknown or unanticipated effect arising.

Thus, it is impossible to prove beyond a shadow of doubt that a chemical product is going to be safe under all conceivable uses.

One solution to this dilemma would be to simply forego the use of chemical products and not run the risk of encountering possible adverse effects. But this would mean the elimination of countless materials that have contributed to the overall health and well-being of our society. Antibiotics, crop fertilizers, pest-control chemicals, and household products come immediately to mind. Therefore, a more realistic approach is to conduct enough tests on these materials that a reasonable judgment can be made as to whether or not harmful effects are likely to occur for prescribed uses. Numerous toxicology laboratories and regulatory mechanisms have been established for this purpose of risk assessment.

TOXICOLOGY

In order to provide a reasonable certainty of safety, toxicologists determine the effects of chemicals on vital physiological functions of animals. Observable effects may be found in such attributes as liver and kidney function, reproductive success, nervous system performance, metabolism, growth and development, and survival. Various means of dosage are used, such as oral, dermal, respiratory, or injection. Specific strains of mice and rats that are expected to be quite sensitive are usually selected for study. Some studies may be short in duration, seeking acute effects; others may extend throughout the lifetime of the animal or even into subsequent generations, looking for more subtle chronic or subchronic effects. Acute responses are usually associated with higher doses; whereas chronic conditions are often, but not always, the result of lower doses over a longer time. The effects of a chemical may be both acute and chronic; it also may produce a recoverable effect, such as lung congestion, or produce irreversible effects, such as birth defects (teratogenic), mutations (mutagenic), cancer (carcinogenic), and death (lethal).

The lethal dose of such chemicals is usually expressed as the LD_{50}, the dose that is lethal to 50 percent of the animals treated in a test. Information on the lethal dose is of primary value in evaluating highly toxic chemicals like modern insecticides, where the principal health concern is acute illness from occupational exposure. However, the LD_{50} is also useful as a basis for comparing the relative acute toxicities of various chemicals such as herbicides, insecticides, and household substances (Table 1).

Whether the effects being studied are acute or chronic, the experiments are usually designed to establish the dose-response relationship and to discover the threshold dose below which no effect can be detected.[1] The no observable effect level (NOEL) is another term that is often used instead of the threshold dose when describing toxicological parameters. Although the two terms are semantically different, they merely represent

[1]The threshold concept as it applies to carcinogens is still the subject of much debate (Maugh 1978), because it may be impossible to do the experiments that would establish the validity of the concept for all carcinogens. Nevertheless, it is quite clear that the threshold concept is valid for most toxicological responses, including at least some types of carcinogenesis (Cornfield 1977, Council for Agricultural Science and Technology 1977). There is no question that as the dose of a carcinogen decreases, the probability of a carcinogenic effect decreases. If that probability is low enough, it may be considered as virtually zero. From a priority standpoint, the Carcinogen Policy Group of the Environmental Protection Agency (EPA) has decided not to pursue (for regulatory purposes) any chemical which presents a statistical cancer risk of less than one case in a million lifetimes (Anonymous 1981).

TABLE 1.

ACUTE TOXICITIES OF VARIOUS CHEMICALS.

Toxicity category[1] (Signal word on label)	Chemical substance	Oral LD_{50} (for rats) (mg/kg)	Oral LD_{50} extrapolation (for 60-kg human[2])
IV. Very slight		50,000	6.7L
	Sugar	30,000	(≈ 1.8 gal)
	Fosamine	24,000	
	Ethyl alcohol	13,700	
	Picloram	8,200	
III. Slight (caution)	Asulam, Simazine	5,000	670 mL
	Glyphosate	4,300	(≈ 1.4 pt)
	Table salt	3,750	
	Bleach, dicamba	2,000	
	Atrazine	1,750	
	Aspirin, Vitamin B_3	1,700	
	Hexazinone	1,690	
	Dalapon, Amitrole-T	1,000	
	2,4-DP	800	
	MSMA	700	
	2,4,5-TP, Triclopyr	650	
II. Moderate (warning)	2,4,5-T	500	67 mL
	2,4-D	370	(≈ 0.3 cup)
	Caffeine	200	
	Paraquat	150	
I. Severe (danger-poison)	Nicotine	50	6.7 mL
	Dinoseb	40	(≈ 1 tsp)
	Strychnine (rodenticide)	30	
	Parathion (insecticide)	13	
		5	0.67 mL
			(≈ 11 drops)
	TCDD	0.01	

[1]Categories, signal words, and LD_{50} ranges are based on a classification system used by the EPA for labelling pesticides (Maxwell 1982). Note the logarithmic scale; the range for each category is about 10 times greater than that for the previous category. Pesticide values were generally obtained from the Farm Chemicals Handbook (1982). The TCDD value was obtained from Schwetz et al. (1973). Values for other substances were obtained from the Merck Index (Windholz 1976).

[2]Quantities assume a liquid formulation of commercial herbicide product containing 45 percent active ingredient. See Appendix 1 for procedures involved in calculations.

two ways of viewing a similar portion of the dose-response curve (Fig. 1). The threshold dose is the lowest dose that produces an effect, thereby implying that no effect will appear at any lower dose. The NOEL, on the other hand, is the highest dose with no effect, thereby implying that any higher dose may cause a response. The NOEL, being the more conservative of the two terms, has been used in this report.

Intake of chemicals normally occurs in three basic ways: oral (ingestion), respiratory (inhalation), and dermal (absorption).[2] Of these, the greatest potential for intake of herbicide under occupational conditions is

[2]A fourth route of chemical entry involves direct injection. This mode of administration is usually confined to laboratory situations with test animals, and has little, if any, practical merit for realistic occupational situations.

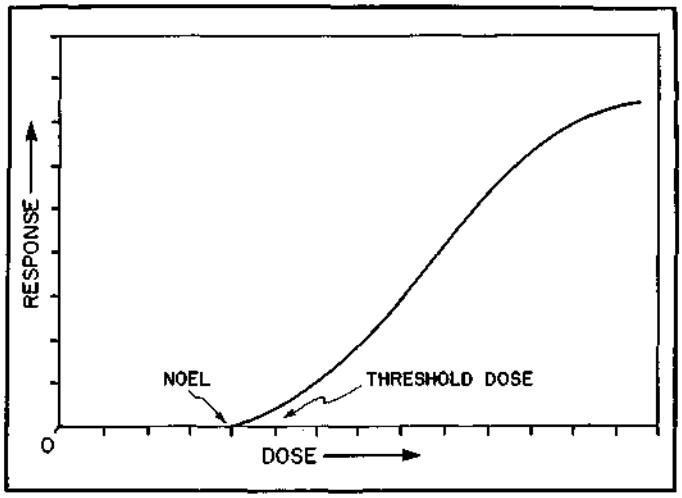

FIGURE 1. CONCEPTUAL DIAGRAM OF THE DOSE-RESPONSE CURVE SHOWING THE RELATIONSHIP BETWEEN THE NO OBSERVABLE EFFECT LEVEL (NOEL) AND THE THRESHOLD DOSE.

through the skin. Instances have occurred of oral intake of herbicides with resulting harm, but such cases have involved either suicidal intent or mistaken ingestion of concentrated material from unlabeled containers. Because most chemicals are more potent when ingested by mouth than when absorbed through the skin, and because of the convenience of adding such chemicals to the feed of test animals, oral administration of doses is often chosen for toxicologic testing. Consequently, most of the data used in this report are derived from studies involving oral dosage.

A cautious evaluation of the risk[3] of any given chemical includes a determination of the safety factor associated with the amount of each dose. The safety factor is a number derived from dividing the NOEL (determined from laboratory animal tests and extrapolated to body weights of human size) by the known or estimated maximum dose for humans exposed[4] in various occupational or environmental circumstances. A safety factor of 100 means that the dose is 1/100th of the NOEL. That figure is generally considered to be the minimum acceptable safety factor for pesticides and is the one used in this report. As a frame of reference, the safety factor (therapeutic index) used for pharmaceutical drugs may be 10 or less. In other words the medication might be used at a dose that is 1/10th (or more) of the harmful dose. Tables 2 and 3 illustrate how safety factors are utilized to evaluate the risks associated with the intake of various herbicide concentrations.

There is little choice but to rely on animal experiments to assess potential human health risks. Fortunately, many other animal species have physiological functions similar to humans, thereby making them reliable indicators of potential problems in humans. Thus, the battery of animal tests conducted nowadays (ranging from mice to monkeys and from acute to chronic effects) has generally been sufficient to detect potential problems before wide-spread use of a given chemical is permitted.

Occasionally, clinical and epidemiological data on human populations exposed in the past can be used in making regulatory decisions, but the discovery of adverse health effects in this manner is tragic. Almost always, such effects have arisen from contact with chemical products that were introduced prior to the present use of broad animal-screening protocols. Failure to follow adequate safety precautions has also been frequently implicated.

The information from toxicologic studies must be coupled with information on the likelihood and degree of human exposure and intake in order to realistically assess the risk inherent in the use of any chemical (Norris 1971a). For example, it is entirely possible to use a highly toxic chemical safely, if intake can be minimized or eliminated. On the other hand, even a relatively innocuous chemical can be dangerous if intake is excessive.

[3]The terms "risk" and "hazard" are sometimes confused. According to Hohenemser et al. (1983), hazard is properly used to indicate threats to human health or things of value. For example, driving an automobile is classified a hazard. Risks, on the other hand, involve a probability of harm resulting from exposure to a hazard. Thus, the lifetime risk of dying in an automobile accident is 2 to 3 percent of all ways of dying.

[4]"Exposure to herbicides" is sometimes erroneously interpreted to mean actual intake or absorption of a dose. "Exposure to herbicides" correctly means a situation of proximity and potential for intake.

TABLE 2.

HYPOTHETICAL DAILY INTAKE BY A 60-KG (132-LB) PERSON OF VARIOUS SUBSTANCES CONTAINING HERBICIDES THAT WOULD NOT EXCEED 1/100 OF THE CHRONIC OR SUBCHRONIC ORAL NO OBSERVABLE EFFECT LEVEL (NOEL) DETERMINED FROM LABORATORY STUDIES WITH TEST ANIMALS.[1]

Herbicide	Chronic or subchronic oral NOEL[2] (mg/kg/day)	Substance and concentration of active ingredient: Commercial formulation[3] (concentration as formulated)	Aqueous spray mixture[4] (24 g/L; 2 lb/10 gal)	Stream water[5] (0.1 ppm)	Ambient air[6] (1 µg/m³)	Animal meat[7] (0.1 ppm)
		--------Daily intake in metric units/(English units)-------				
		mL (drops)	mL (drops)	L (gal)	m^3 (yd^3)	kg (lb)
2,4,5-T	10	0.013 (0.2)	0.25 (4)	60 (16)	6,000 (8,000)	60 (132)
2,4,5-TP	20	0.026 (0.4)	0.50 (8)	120 (32)	12,000 (16,000)	120 (264)
2,4-D	20	0.027 (0.4)	0.50 (8)	120 (32)	12,000 (16,000)	120 (264)
2,4-DP	10	0.013 (0.2)	0.25 (4)	60 (16)	6,000 (8,000)	60 (132)
Amitrole	10	0.028 (0.4)	0.25 (4)	60 (16)	6,000 (8,000)	60 (132)
Asulam	40	0.071 (1.1)	1.0 (16)	240 (64)	24,000 (32,000)	240 (528)
Atrazine	50	0.074 (1.2)	1.25 (20)	300 (80)	30,000 (40,000)	300 (660)
Dalapon-Na	50	0.04 g	1.25 (20)	300 (80)	30,000 (40,000)	300 (660)
Dicamba	5	0.007 (0.12)	0.125 (2)	30 (8)	3,000 (4,000)	30 (66)
Dinoseb	5	0.01 (0.16)	0.125 (2)	30 (8)	3,000 (4,000)	30 (66)
Fosamine	30	0.043 (0.7)	0.75 (12)	180 (48)	18,000 (24,000)	180 (396)
Glyphosate	30	0.059 (0.9)	0.75 (12)	180 (48)	18,000 (24,000)	180 (396)

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TABLE 2 (continued)

Herbicide	Chronic or subchronic oral NOEL (mg/kg/day)	Substance and concentration of active ingredient: Commercial formulation (concentration as formulated)	Aqueous spray mixture (24 g/L; 2 lb/10 gal)	Stream water (0.1 ppm)	Ambient air (1 µg/m³)	Animal meat (0.1 ppm)
		Daily intake in metric units/(English units)				
		mL (drops)	mL (drops)	L (gal)	m³ (yd³)	kg (lb)
Hexazinone	25	0.06 (1.0)	0.625 (10)	150 (40)	15,000 (20,000)	150 (330)
MSMA	5	0.006 (0.10)	0.125 (2)	30 (8)	3,000 (4,000)	30 (66)
Picloram	20	0.058 (0.9)	0.50 (8)	120 (32)	12,000 (16,000)	120 (264)
Simazine	50	0.038 g	1.25 (20)	300 (80)	30,000 (40,000)	300 (660)
Triclopyr	30	0.041 (0.65)	0.75 (12)	180 (48)	18,000 (24,000)	180 (396)

[1]The values presented in Tables 2 and 3 are based on oral toxicity data. As such, they represent a "worst case" analysis when compared to dermal routes of exposure. See Appendices 1 and 3 for assumptions and examples of calculations used to derive these values. Note that a 100-fold safety factor has been used in preparing these tables. Also note that calculations in Appendix 1 assume that all of the herbicides listed are partitioned in stream water, ambient air, and animal meat in a similar fashion to the phenoxy herbicides, for which the data base is strongest. Abbreviations and metric/English equivalents used are described in Appendix 6.

[2]Chronic or subchronic oral NOEL = daily oral dose of herbicide which does not exceed the no observable effect level (e.g., for toxicity, fetotoxicity, teratogenicity, oncogenicity, mutagenicity, etc.) when administered orally over a relatively long period of time (e.g., 90 days, two years, life-time, or multi-generations, depending on the test and animal species involved) or during a critical stage of development (e.g., pregnancy). Expressed as mg of herbicide active ingredient per kg of body weight per day. Values used are conservative and are generally at or below the NOELs cited in Appendix 4.

[3]Values for concentration of herbicide active ingredient (ai) derived from the commercial product specifications in Appendix 5.

[4]Assumes an aqueous spray mixture containing 24 g herbicide ai/L spray (2 lb herbicide ai/10 gal spray). This is a typical concentration for most of the herbicide mixtures applied in forestry.

[5]Concentration of 0.1 ppm represents the "worst case" actual amount of phenoxy herbicide (2,4,5-T) that has been detected in stream water. More "typical" amounts found in secondary streams for short periods of time following application are generally 0.04 ppm or less. The "maximum hypothetical" concentration in a shallow stream 10 cm (4 in.) deep that has been directly sprayed would be about 2 ppm. See Appendix 2 for calculations involved and results of actual water monitoring.

[6]The concentration of 1.0 µg/m³ represents the highest estimate of 2,4,5-T in the air downwind from Pacific Northwest forest applications. The safety factor determined for such applications is so large it has been suggested that this avenue of exposure to 2,4,5-T did not constitute a measurable risk (Newton and Norris 1981). For example, a person at moderate labor will have a respiratory ventilation rate of 8-10 m³/day. Therefore, the intake noted for 2,4,5-T in Table 1 is 600 times greater than the daily total respiration and assumes that the material remains suspended in the air at the maximum concentration of 1.0 µg/m³ throughout the exposure period (an unlikely scenario). Recalling that the values given are already 1/100 of the NOEL, the actual safety factor for this situation with 2,4,5-T is at least 60,000.

[7]Residues of phenoxy herbicides have not been detected in venison from the Pacific Northwest, except for 0.021 mg 2,4,5-T/kg body weight found in the liver of one animal (Newton and Norris 1968). Thus, the 0.1 ppm value used here probably represents an amount far greater than amounts actually present.

TABLE 3.

HYPOTHETICAL DAILY INTAKE BY A 60-KG (132-LB) PERSON OF VARIOUS SUBSTANCES CONTAINING TCDD THAT WOULD NOT EXCEED 1/100 OF THE CHRONIC OR SUBCHRONIC ORAL NO OBSERVABLE EFFECT LEVEL (NOEL) DETERMINED FROM LABORATORY STUDIES WITH TEST ANIMALS.

Basis for NOEL for TCDD	Chronic or subchronic oral NOEL[1] (µg/kg/day)	Substance containing TCDD				
		Commercial formulation[2]	Aqueous spray mixture[3]	Stream water[4]	Ambient air[5]	Animal meat[6]
		----Daily intake in metric units/(English units)----				
		mL (drops)	mL (tsp)	L (gal)	m^3 (yd^3)	g (oz)
Rat studies[7]	0.001	0.133 (2.1)	2.5 (0.5)	600 (158.4)	60,000 (78,600)	50 (1.75)
Rat and monkey studies[8]	0.01	1.33 (21.3)	25 (5)	6,000 (1,584)	600,000 (786,000)	500 (17.5)
2,4,5-T RPAR Position Document[9]	0.03	4.0 (64)	75 (15)	18,000 (4,752)	1,800,000 (2,358,000)	1,500 (52.5)

[1]See Table 2 note 2. It has been speculated by some scientists that the effects of a series of sublethal doses of TCDD can accumulate over time within an organism, eventually triggering a toxic response once a certain critical level is reached (Meselson et al. 1978, Streisinger 1978). That is, they suggest that the dose required to elicit a toxic response is the same whether given as a single dose or spread out over an extended period of time. It is true that all chemicals have some degree of cumulative or additive effect in that any injury produced requires some period of time for reversal or repair, and any additional doses added during that interval of time will add to the burden. Nevertheless, the period of time required between doses for reversal or repair to occur is finite, and generally ranges from minutes to many days, depending on the chemical and dose at which it is given.

Therefore, the time over which a chemical can gradually accumulate to the point where it suddenly has a toxic effect is not likely to be infinite, so that the time required for a toxic effect to be manifested is not likely to be strictly proportional to the dosage rate, as Streisinger (1978) speculates. No chemical at the present time is known to have such additive properties over long periods of time (U.S. Department of Agriculture 1978).

Indeed, studies with guinea pigs (Vos et al. 1973) and rats (Vos and Moore 1974) exposed to TCDD have shown the opposite. These species can tolerate about three times the LD_{50} dose of TCDD when the chemical is administered in small doses over several weeks. Thus, the case for additive effects of sublethal doses of TCDD over extended periods of time does not appear to be a strong one.

If the incremental doses of TCDD were perpetually stored in an animal's body, one could perhaps make a stronger case for the plausibility of an additive or cumulative effect having a time frame dependent on the total dose. However, TCDD does not persist in this fashion. The excretion kinetics for TCDD are well defined, showing a half-life pattern in several animal species ranging from 12-35 days (Allen et al. 1975, Fries and Marrow 1975, Rose et al. 1976, Neal et al. 1982).

[2]Assumes a commercial herbicide such as Esteron® 245, which contains 45% 2,4,5-T ae (4 lb 2,4,5-T ae/gal product). The maximum level of TCDD permitted in commercial herbicides (2,4,5-T and 2,4,5-TP) sold in international markets is generally 0.01 ppm on a 2,4,5-T ae basis. This concentration has been used in the calculations. The concentrations detected in present production are routinely less than 0.005 ppm.

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[3]Assumes an aqueous spray mixture containing 24 g 2,4,5-T ae/L spray (2 lb 2,4,5-T ae/10 gal spray) made from commercial herbicide containing 0.01 ppm of TCDD. This is a typical concentration of 2,4,5-T for application of this herbicide in forestry.

[4]Based on a concentration of TCDD in stream water of 0.001 ppt or 1×10^{-6} µg/L (derived from water containing 0.1 ppm of 2,4,5-T, which in turn contains 0.01 ppm TCDD; note that this concentration represents a "worst case" situation).

[5]Based on a concentration of TCDD in ambient air of 0.01×10^{-6} µg/m^3 (derived from air containing an "upper limit" of 1 µg/m^3 of 2,4,5-T, which in turn contains 0.01 ppm TCDD; note that this concentration represents a "worst case" situation). The safety factor determined from such a condition following forestry application is so large it has been suggested that this avenue of exposure to TCDD did not constitute a measurable risk (Newton and Norris 1981). For example, a person at moderate labor will have a respiratory ventilation rate of 8-10 m^3/day. Therefore, the intake noted for TCDD at the lowest NOEL (0.001 µg/kg/day) in Table 3 is 6,000 times greater than the daily total respiration, providing a safety factor of at least 600,000.

[6]Assumes a "worst case" concentration of 60 ppt, the maximum amount that was reported in the EPA beef fat survey (U.S. EPA 1977). This survey was designed to detect TCDD in one of the most likely situations (i.e., lean cattle grazing on pastures recently treated with 2,4,5-T).

[7]Based on long-term toxicological studies with rats (Murray et al. 1979, Kociba et al. 1978, 1979a, 1979b). This level was equivalent to approximately 22 ppt in the diet. Rhesus monkeys have tolerated oral doses of 2,4,5-T containing as much as 0.0005 µg TCDD/kg/day without any adverse effects (Dougherty et al. 1975). Experiments by McNulty (1978) on rhesus monkeys indicated they could tolerate a total dose of 0.2-1.0 µg/kg before exhibiting adverse effects.

[8]Based on toxicological studies with rats (Kociba et al. 1975) and rhesus monkeys (McNulty 1978). McNulty (1978) indicated that in his study this level was equivalent to 200 ppt in the total diet. Leng (1978) clarified this interpretation. She pointed out that in the actual experiment the monkeys were force-fed by stomach tube using 10 mL of corn oil three times per week for three weeks. The actual concentration of TCDD in the corn oil was calculated to be about 15,000 ppt (15 ppb) for this portion of the experiment.

[9]Based on the value used in the 2,4,5-T RPAR Position Document 1 (U.S. EPA 1978b).

REGULATORY CONTROL

Regulatory agencies routinely use the results of toxicologic testing to evaluate the risks of using chemical products under different conditions, whether they involve pesticides, food additives, drugs, industrial chemicals, household cleaners, or pollutants. By balancing potential harm against the anticipated benefits, a rational but admittedly subjective judgment can be made.

The Federal Insecticide, Fungicide and Rodenticide Act (FIFRA, as amended) is the primary federal law for regulating pesticides in the United States. The Environmental Protection Agency (EPA) has the authority for administering and enforcing this act, along with designated state agencies. Product registration is a key factor of this act and is described as follows (U.S. EPA 1982a):

> Under current law, pesticides marketed in this country must be registered with EPA. To register a product an applicant must submit data to the Agency adequate to demonstrate that the proposed use will not pose risks of unreasonable adverse effects on human health or the environment when used according to its approved labeling.

The battery of tests required for initial registration of a pesticide takes many years to complete and costs millions of dollars. Even after a product has been registered, any new factual information which comes to light concerning unreasonable adverse effects on human health or the environment may precipitate re-examination of the product. Finally, the law requires each pesticide product to go through the process of re-registration every five years. This process affords an additional opportunity to incorporate new findings or recommendations into regulatory actions. Proper training of pesticide applicators and adequate enforcement of regulations governing pesticide use are important to ensure that the materials will be used correctly.

Nevertheless, there are occasions when new concerns surface that are sufficient to warrant a special review of a particular pesticide product. Such was the case for 2,4,5-T (2,4,5-trichlorophenoxyacetic acid) when the highly toxic contaminant TCDD (2,3,7,8-tetrachlorodibenzo-p-dioxin) was discovered. Both the EPA and the state regulatory agencies can take action to deal with such developments. Options for the EPA range from internal review by their own staff of toxicologists, chemists, and biologists to the formal proceedings of Special Review (formerly known as Rebuttable Presumption

Against Registration, RPAR), Suspension, Emergency Suspension, and Cancellation. In all of these activities, the agency can call on a wide variety of scientific expertise, including the EPA Scientific Advisory Panel, the Cancer Assessment Group, the Reproductive Effects Assessment Group, the National Cancer Institute, and the National Academy of Sciences.

State regulatory agencies have a concomitant responsibility for ensuring safe pesticide use. They can impose use limitations beyond those specified by the EPA, provided local conditions warrant such action; for example, special drift control measures can be required when applying certain herbicides near sensitive crops.

TOXICITY DATA

Most forestry herbicides are classified in the slight to moderate categories of acute toxicity (Table 1). They fall into the same categories as sugar, baby lotion, ethyl alcohol, table salt, liquid detergent and bleach, aspirin, vitamins, and a number of other common household chemicals. With the exception of dinoseb, an herbicide sometimes used to desiccate forest vegetation prior to prescribed burning, they are not nearly as toxic as the nicotine commonly found in cigarette smoke, or certain insecticides like parathion, or some rodenticides containing strychnine. These latter materials are designed to affect specific animal functions, such as the nervous and circulatory systems of insects and rodents. Therefore, they are inherently more toxic to humans than most herbicides, which are specifically designed to affect plant functions like germination and photosynthesis. In any event, using common sense, being adequately trained, heeding label instructions and warnings, and complying diligently with pertinent regulations are normally sufficient precautions to prevent acute illness when using commercial herbicides, whether concentrated or mixed for application.

From a chronic toxicity standpoint, the greatest risk is associated with exposure to commercial herbicide concentrates (Table 2). For example, only about one drop of a commercial atrazine concentrate would be within the safety tolerance of 1/100th of the NOEL for daily, chronic ingestion. However, once the herbicides have been diluted and applied to the environment, huge quantities of water, air, or food from the area would have to be taken in daily to reach this same dose; for example, an adult would have to drink 300 liters (80 gallons) of stream water per day containing 0.1 ppm (a "worst case" situation) of atrazine.[5]

Since most herbicides used for forestry purposes are applied only during short periods in the spring and fall, the potential for chronic exposure to these materials is quite limited. Furthermore, these materials are usually applied only once or twice during the rotation period of a given forest stand, which is customarily 40 years or more. Precautions taken during application, coupled with factors such as dilution, plant uptake, adsorption, metabolism, and breakdown, preclude the potential for exposure to unsafe chronic and acute dosages. These safeguards apply not only to herbicide applicators dealing with concentrated and formulated materials, but to the general public and other animals in the vicinity of the treated areas as well.

Researchers have summarized the toxicological, medical, and environmental information available on phenoxy and other herbicides used in forestry (Newton and Dost 1981). Detailed reviews of the literature and analyses of the pharmacokinetics (metabolic fate) of phenoxy herbicides in animal systems (including humans) have been prepared by Leng (1977) and Leng et al. (1982). A text by Wagner (1981) discusses clinical and toxicological aspects of phenoxy herbicides and other agricultural chemicals. None of these reports suggests that there is a serious level of risk resulting from the proper application of forestry herbicides.

[5]See Appendix 6 for a description of metric-English equivalents and abbreviations for the units involved.

FIELD STUDIES

Studies have been conducted measuring actual intake of herbicides, particularly phenoxies, by humans, fish, and wildlife in the forest. Without exception, the amounts detected have been far below levels that have toxicological significance. Although the data base is substantial, certain gaps still remain in our understanding of some biochemical mechanisms and the implications of herbicide-induced effects on forest ecology. Most of the reviews listed in the bibliography identify these needs, and current research is addressing many of them.

OCCUPATIONAL CONTACT

Several studies have measured the dose received by forestry workers applying 2,4-D (2,4-dichlorophenoxyacetic acid) and 2,4,5-T (Lavy 1979a,b, 1980a,b; Lavy et al. 1980a,b, 1982a,b; Newton and Norris 1981). The Lavy studies involved three common methods of application: backpack spraying, tractor mist blowing, and helicopter spraying. The types of personnel sampled were backpack sprayers, pilots, mechanics, mixers, flaggers, supervisors, and observers. Because phenoxy herbicides are excreted intact in urine relatively soon after intake, it was possible to determine the actual dose of herbicide received by analysis of the urine.[6] Air sampling devices and cloth patches attached to the workers' clothing were used to determine possible routes of intake.

These studies found that the intake of herbicides from forestry applications is primarily restricted to those individuals intimately involved in the operation: mixers, backpack sprayers, pilots, and mechanics. Supervisors, flaggers, and observers rarely showed any herbicide dose in these studies. Contact was minimized when protective apparel was worn, such as rubber gloves, rubber boots, and disposable coveralls, and when hygienic precautions were taken, such as washing hands before rest breaks.

Lavy (1979a) found amounts of 2,4,5-T in the air ranging from non-detectable (< 0.004 µg/L, or 4 µg/m^3) to 0.169 µg/L (or 169 µg/m^3) on sampling devices placed in the breathing zone of workers applying this herbicide via backpack and mist blower methods. The herbicide was rarely detected in air samples collected near the breathing zone of workers involved in aerial application. Similar results were obtained in a study involving aerial application of 2,4-D (Lavy 1980a). Aerial traces of the herbicide were rarely detected on the sites after the completion of spraying.

Where 2,4-D and 2,4,5-T were detected in the urine of crew members, the doses calculated were less than 0.1 milligrams per kilogram of body weight per day (Lavy et al. 1980b, 1982a). Comparable amounts of 2,4-D have also been detected in the urine of agricultural workers applying this herbicide to wheat fields (Nash et al. 1982). Toxicological interpretations by Ramsey et al. (1979, 1980) indicate that these doses are far below the NOEL established for laboratory animals; calculated safety margins ranged from the hundreds to thousands (Hall 1979, 1980).

Humans have experimentally ingested single doses of silvex and 2,4,5-T as high as 1 and 5 mg/kg, respectively, without any immediate adverse effects (Sauerhoff et al. 1977, Gehring et al. 1973). As much as 0.5 g 2,4-D/day was ingested by one man over a 21-day period without observable ill effects (Kephart 1945). There have been several suicide attempts with 2,4-D, at least three of which were successful (Nielsen et al. 1965, Geldmacher et al. 1966). Two individuals have survived suicide attempts in which the doses, as judged by blood and urine concentrations, were estimated to be about 100 mg/kg and 400 mg/kg, respectively (Young and Haley 1977). Additional known cases involving exposure of humans are discussed in Newton and Dost (1981), Leng et al. (1982), and Wagner (1981).

Leng et al. (1982) reviewed several studies of occupational contact with phenoxy herbicides and determined that the maximum acquired dose of 2,4,5-T, for example, is not likely to exceed 0.1 mg/kg of body weight per work day. This worst-case dose is considerably above the acceptable daily intake (ADI) of 0.003 mg/kg/day temporarily adopted for 2,4,5-T at the 1979 Joint Meeting on Pesticide Residues of the Food and Agricultural Organization and the World

[6]Recent work by scientists at the USDA Agricultural Research Service (Sell et al. 1982) has shown that 2,4-D is also excreted via the sweat glands. Since the 2,4-D study by Lavy et al. (1982a) was conducted in the early spring when temperatures were relatively cool and under conditions where physical exertion was not very great, loss of 2,4-D through perspiration was not likely to have been very significant.

Health Organization (Commission to the Council of the European Economic Community 1982). This same dose of 2,4-D is well below the ADI of 0.3 mg/kg/day established by the World Health Organization (Vettorazzi 1979). In any event, it would be prudent for routine applicators of herbicides to follow the precautions found beneficial by Lavy et al. (1982a).

EPIDEMIOLOGICAL STUDIES

Epidemiology is the science that studies the distribution of disease in a population. Since chemical applicators and their immediate families are much more likely than the general population to be harmed by pesticides, any medical problems associated with pesticide contact should be apparent in that occupational group.

Epidemiological surveys of chemical applicators in the U.S. (Roan 1980, Carmelli et al. 1981, Honchar 1982, Williams 1983) and New Zealand (Smith et al. 1981, 1982a) have been unable to establish any link between occupational exposure to pesticides (including 2,4,5-T) and human reproduction problems. The same lack of a correlation between herbicide use and birth defects has also held true for the general population of Hungary, of which a relatively large percentage of the population is involved in agriculture and forestry, with a high rate of pesticide use (including 2,4,5-T) per capita (Thomas 1980).

However, another study (Field and Kerr 1979) found a significant correlation between the amount of 2,4,5-T usage in Australia and certain congenital disorders, such as anencephaly and meningomyelocele (neural-tube birth defects) in the general population of New South Wales. A similar epidemiological analysis of population birth defects in New Zealand (Hanify et al. 1981), while it found no association between 2,4,5-T use and such neural-tube defects, did find a positive association between 2,4,5-T use and human talipes malformation (club foot). These positive associations are somewhat puzzling in light of the laboratory studies done on animals that indicate that other types of birth defects are more commonly associated with 2,4,5-T or TCDD, notably cleft palate and cystic kidney disease (Courtney and Moore 1971). The results are also puzzling in light of the negative findings cited previously with respect to applicators and their immediate families--individuals with a much greater likelihood of contact than the general populations studied by Field and Kerr (1979) and Hanify et al. (1981). In any event, both these researchers stressed the fact that even where 2,4,5-T use and congenital disorders appeared to be linked in their studies, they did not establish a cause-and-effect relationship; nor were any correlations linked with actual or estimated doses.

The possible association of cancer to prior contact with herbicides is more ambiguous. Studies done in Sweden on railroad workers (Axelson et al. 1979), forest workers and sawmill/pulpmill operators (Hardell and Sandstrom 1979, Hardell 1981), and a sample of patients selected from the Swedish Cancer Registry (Erikkson et al. 1979) suggest the possibility of an association between substantial occupational exposure to phenoxy herbicides or chlorophenols and subsequent soft-tissue sarcomas[7] (Milby et al. 1980). It is hard to draw firm conclusions from these studies for several reasons: the determination of actual contact and resultant dose based on recall by patients and incomplete records; the difficulty of singling out one chemical or group of chemicals as the causal agent when exposure has occurred to a variety of chemicals; and the diverse nature of the cancers involved, which suggests more than one type of causal agent. Nevertheless, additional health risk studies are warranted, and several are currently under way. These are described in several documents: National Forest Products Association 1981, JRB Associates 1981, Shepard 1982. Other health risk studies are being planned; for example, the National Institute for Occupational Safety and Health is investigating soft tissue sarcoma epidemiology in the U.S.

Other studies have failed to establish a link between cancer or other illnesses and occupational exposure to phenoxy herbicides and TCDD during manufacturing (Cook et al. 1980, Ott et al. 1980, Zack and Suskind 1980, May 1982, Suskind 1982, Townsend et al. 1982) or spraying (Riihimaki et al. 1978, 1982; van Houdt et al. 1982; Milham 1982; Smith et al. 1982a). Even the heavy use of TCDD-

[7]Sarcomas are malignant growths arising from nonepithelial tissues of mesodermal embryonic origin (e.g., muscles, connective tissues, bone, cartilage, lymphoid tissue, and reproductive, circulatory and excretory organs). Therefore, soft-tissue sarcomas refer to those sarcomas not associated with bone, cartilage, and other structural material.

contaminated Agent Orange by U.S. military forces in Vietnam has been calculated by Stevens (1981) to be an unlikely cause for the systemic illnesses experienced by Vietnam veterans or for birth defects in their children, as claimed by Bogen (1979). Tentative support for this view comes from an epidemiological study conducted by the U.S. Air Force of military personnel engaged in actually mixing and aerially applying Agent Orange in Vietnam from 1962-1971, an operation conducted under the code name "Ranch Hand." Thus far, the study has not detected any increase in soft tissue sarcoma, mortality, organ abnormalities, or major birth defects in offspring of the "Ranch Hand" group when compared to a similar group that was not exposed to Agent Orange (Brown 1982, Assistant Secretary of Defense 1984).

The issue of possible adverse health effects from Agent Orange is still unresolved, however, due to the difficulty of establishing a single causative relationship when so many confounding factors (e.g., contact with other chemicals, use of drugs, stress-related syndromes) are involved, and much of the information regarding dose levels is lacking. A comprehensive study has been launched to investigate whether Agent Orange has caused medical problems for Vietnam veterans. The study, mandated by Congress in 1979, is sponsored by the Veterans Administration and is being conducted by the federal Centers for Disease Control; definitive results are not expected before 1987.

PUBLIC CONTACT

In a two-year survey conducted at several agricultural sites by the EPA, 0.49-10.53 percent of 2,479 air samples contained phenoxy herbicides, but only at very small, mean concentrations (0.1-4.1 ng/m^3) (Kutz 1978). Earlier surveys support these findings (Bamesberger and Adams 1966). Even when sampling was done during the spraying season in the wheat-growing region of Washington (a heavy-use area for 2,4-D), the average concentration of 2,4-D detected in the air was only 0.1 µg/m^3 (Adams et al. 1964).

Studies have also monitored the ambient air in or near reforestation units treated with 2,4-D or 2,4,5-T. Cheney et al. (not dated) detected amounts of 2,4,5-T ranging from 0.012 to 0.895 µg/m^3 in the air over a fall-treated reforestation unit in the Sierra Nevada of northeastern California (application rate of 3 lb/A, or 3.36 kg/ha). The levels declined sharply by the third day after application and were non-detectable (< 0.008 µg/m^3) by the third week. Within about one kilometer of a forest site in western Oregon that was aerially sprayed with 2,4-D, 2,4,5-T, and picloram in May, air samples collected beginning at one hour after spraying and for the next 57-hour period contained less than 0.2 µg/m^3 of the various herbicides (Norris 1980a). A closer sampling station located at 152 meters from the treated area briefly recorded a maximum of 1.8 µg/m^3, but none of the test tomato plants (very sensitive to herbicides) here or at the farther station were markedly damaged. Furthermore, the results of a long-term air monitoring study in the general vicinity of forestry herbicide applications in western Oregon indicated that widespread contamination of air from such operations was not occurring (Norris 1980a). Only one sample collected during a six month period (May-November) contained any herbicide (0.002 µg/m^3 of 2,4-D), and this was collected long after the normal forestry spray season had ended, suggesting a source other than forestry applications.

Thus, the amounts of 2,4-D and 2,4,5-T detected in or near agricultural and forest sites treated with these materials have generally been in the nanogram to microgram range or less per cubic meter of air. These levels are more than 1,000 times less than the 10 mg/m^3 threshold limit value (8-hr time-weighted average) adopted for 2,4-D and 2,4,5-T in the work place by the American Conference of Governmental and Industrial Hygienists (1977). They are also generally below the levels causing injury to non-target plants, such as crops and ornamentals.

In another two-year EPA survey (Kutz 1978) conducted in major agricultural river basins of the U.S., less than 0.4 percent of the 2,500 water samples contained phenoxy herbicides, again at very low concentrations (maximum of 1.9 ppb). The amounts detected, if consumed by humans, would still be well below the acceptable daily intake (ADI) recommended by the Safe Drinking Water Committee of the National Academy of Sciences (National Research Council 1977). A recent nation-wide survey of rural drinking water

supplies by Cornell University researchers found virtually no 2,4-D, silvex, or insecticides (Francis et al. 1983).

Concentrations of phenoxy herbicides greater than 0.01 ppm are seldom found in streams following conventional forestry applications (Norris 1977, 1981). Concentrations as high as 0.1 ppm have occasionally been detected, but these were recorded before the advent of strict regulations governing application procedures. Most water samples collected nowadays do not contain any detectable amounts at the detection limit of 1 ppb. Any minute amounts which are present dissipate within 24 hours due to dilution, adsorption, and breakdown (Norris 1981). These processes preclude intake by the general public of significant amounts of herbicides from aquatic sources.

Phenoxy herbicides are only rarely detected in agricultural products such as rice, beef, and milk, and then in only insignificant amounts (Council for Agricultural Science and Technology 1978, Bovey and Young 1980). Nor have herbicides generally been found in forest game animals in the Pacific Northwest (Newton and Norris 1968). The maximum residue detected thus far in the edible tissue of game animals has been 0.021 mg/kg of 2,4,5-T in the liver of one deer. The low exposure to and rapid excretion of herbicides by game animals probably prevents contamination of wild meat to any significant extent.

The limited exposure of the general population to phenoxy herbicides[8] is further borne out by preliminary results of the National Human Monitoring Program, a cooperative effort between the EPA and the National Center for Health Statistics of the U.S. Public Health Service. Only trace amounts ($\leq$ 3.2 ppb) of phenoxy herbicides have been detected in a fraction ($\leq$ 0.2 percent) of the human urine samples collected thus far from the general population (Kutz 1978, Kutz et al. 1978).

[8]The only noteworthy exception to this statement is a study done by Dougherty and Piotrowska (1976). A limited survey of human urines and seminal fluids in Florida suggested contamination at the parts per billion level with 2,4,5-T and other chlorophenoxy compounds. However, the authors used unconfirmed methodology and stated that their analytical procedures could not distinguish between various isomers of the chlorophenoxy compounds. In fact, some of the organic polychloride chemicals detected in the study (and for which the molecular structure was given) have never been marketed. False positives due to interferences from other substances are also possible at low levels of detection, particularly when using unproven methodology.

FISH AND WILDLIFE CONTACT

An EPA publication by Newton and Norgren (1977) specifies recommended maximum concentrations of silvicultural chemicals (including herbicides) permissible in forest streams. The recommendations are based on a detailed analysis of the sensitivity of aquatic and terrestrial animals, as well as plants, to various concentrations of silvicultural chemicals in water. As mentioned earlier, concentrations of herbicides in forest streams have rarely exceeded 0.01 ppm following forestry applications. Depending on the herbicide, this is at or well below the maximum concentrations recommended for safe use of water by aquatic and terrestrial animals (Newton and Norgren 1977, Newton and Knight 1981).

The intake by terrestrial animals of phenoxy herbicides is most likely to result from consumption of or contact with recently treated vegetation (Norris 1977). However, data from Norris et al. (1977) indicate that the average amount of herbicide measured immediately after application of 2.24 kg 2,4,5-T/ha (2 lb/A) was about 50 ppm on the foliage, with much less present on the forest floor ($\approx$ 36 mg/m^2) or in the soil (< 0.01 ppm). The herbicides rapidly disappear due to a variety of natural processes, such as volatilization, runoff, leaching, degradation, weathering, absorption, growth dilution, metabolism, excretion, and adsorption (Norris 1981). This dissipation, coupled with the typically reduced palatability of the treated vegetation as it dies, precludes significant chronic exposure of roving animals to harmful amounts of phenoxy herbicides (Norris 1977). Additional information on herbicide residues in water, vegetation, forest floor, and soil can be found in recent reviews by Shearer and Halter (1980), Ghassemi et al. (1981, 1982), Norris (1981) and other pertinent articles cited in the bibliography.

The review by Norris (1981) also summarizes the cases where a search was made for phenoxy herbicides in the bodies of wildlife such as mussels, fish, birds, and other mammals. In the scattered instances of positive results, the amounts have generally ranged from < 0.01 to 10 mg/kg (ppm of sample weight). As indicated in the section of this report dealing with toxicity studies, consumption of these amounts by carnivorous animals would be well

below the chronic or subchronic (NOEL) toxicity levels established for laboratory animals.

Toxic effects on wildlife populations following herbicide application in forest management have not been scientifically documented, though there have been a few unpublished cases, such as rabbits allegedly affected by a routine application of dinoseb (Newton and Dost 1981) and several snowshoe hares thought to have been poisoned by MSMA (Norris 1974). Other than such cases, any tangible impacts have been limited to changes in habitat--an unavoidable result of any silvicultural treatment (chemical as well as non-chemical) which favors one form of vegetation over others. Such effects can be beneficial to certain species of wildlife and detrimental to others. The effects can also be of relatively short or long duration, depending on the situation. Additional information on this topic can be found in Carter et al. (1976), Newton (1975), Newton and Norris (1976), Newton and Dost (1981), and Newton and Knight (1981).

TCDD (DIOXIN)

Much of the concern about herbicide use has arisen from a highly toxic chemical called TCDD (2,3,7,8-tetrachlorodibenzo-p-dioxin)--often simply called dioxin--that is a contaminant only in 2,4,5-T and silvex; it is not in 2,4-D. Because the contamination is so slight, it is not possible to obtain a dose of TCDD that constitutes a risk to human or animal health from conventional agricultural and forestry applications of 2,4,5-T or silvex (Kenaga and Norris 1983). In fact, the TCDD applied in such treatments probably represents less risk than the 2,4,5-T or silvex accompanying it (Newton and Norris 1981); for example, compare the values in Table 2 with the corresponding values in Table 3. This conclusion is supported by the preponderance of scientific opinion on the subject (Turner 1977, Council for Agricultural Science and Technology 1978, Ramel 1978, Bovey and Young 1980). However, because of the controversy surrounding this highly toxic substance, and because it behaves differently in the environment than its parent herbicides, TCDD warrants special attention (McConnell et al. 1978a,b; Schwetz et al. 1973).

One of the difficulties in studying TCDD is detecting it. Because it is so toxic, even parts per trillion levels in environmental samples are cause for concern. Only a handful of laboratories in the world are equipped with the analytical capability to detect such minute amounts of TCDD. Even with this capability, however, one would still not expect to detect TCDD from a conventional forestry application of 2,4,5-T. The amounts would simply be too small to measure. For example, the conventional forestry application rate of 2,4,5-T is 2 kilograms of acid equivalent per hectare (≅ 2 lb ae/A). If there were 0.01 parts TCDD per million parts 2,4,5-T,[9] then no more than 0.02×10^{-6} kg TCDD/ha (20 µg/ha) would be applied. Studies involving much higher concentrations of TCDD detected no measurable toxicological impact (Young et al. 1978).

Based on water monitoring studies showing a maximum concentration of 0.1 ppm 2,4,5-T, the TCDD concentration in streams following forestry application would not exceed 0.001 ppt if a similar pattern of distribution is assumed (see Appendix 3). This would be well below known levels of biological significance to aquatic or terrestrial organisms. For example, Miller et al. (1973) determined that a TCDD concentration in water of from 0.054 to 0.54 ppt did not affect the survival of young coho salmon tested for a 96-hour period. The dose-response relationship was affected by both the size of the fish and the duration of the test. Data for other fish species and several aquatic invertebrate species living in TCDD-contaminated water are also available (Miller et al. 1973, Norris and Miller 1974, Hawkes and Norris 1977, Norris 1981, Kenaga and Norris 1983). As a general rule, TCDD has low solubility in water (maximum of 200 ppt) and an affinity for binding to soil particles, silt, and other substrates; therefore, its mobility and presence in water is so restricted (Council for Agricultural Science and Technology 1978) that actual concentrations in water would be even less than calculated.

[9]The actual concentrations detected in present production of 2,4,5-T and silvex are routinely less than 0.005 ppm.

An accidental explosion at an ICMESA chemical plant on July 10, 1976 resulted in the contamination of about 18,000 ha of a densely populated area near Seveso, Italy (Pocchiari et al. 1983). Concentrations as high as 212 g TCDD/ha were found in the soil in Zone A-North near the plant (Reggiani 1977). This is over ten million times the concentration that might result from a conventional forestry application of 2,4,5-T. It was estimated that in the immediate vicinity of the plant an average TCDD level of 30 mg/ha (Zone B) and 500 mg/ha (Zone A) was deposited on the ground. This is 1,500-25,000 times the amount that might result from a conventional forestry application. Despite these relatively high concentrations of TCDD near the plant, detailed medical examinations of the exposed human population did not reveal any serious short-term adverse health effects beyond temporary reactions such as chloracne, the most definitive human symptom of exposure to TCDD. Several studies indicate the possibility of long-term effects on kidney function, blood lipids, and the peripheral nervous system, but the relationship to TCDD exposure is still ambiguous (Bruzzi 1983b). These potential effects notwithstanding, there has been no discernible increase in the frequency of spontaneous abortions, cytogenetic abnormalities, clinical diseases, or mortality (De Carli et al. 1977, Tuchmann-Duplessis 1977, Reggiani 1978, 1980, Homberger et al. 1979, Bruzzi 1983b).

No clear pattern has yet emerged with respect to the possibility of birth defects associated with the Seveso accident. Initial reports indicated no apparent increase in major types of birth deformities (De Carli et al. 1977, Tuchmann-Duplessis 1977, Reggiani 1978 and 1980, Homberger et al. 1979). More recent analyses suggest an increase in certain types of defects, but a decrease or no change in others (Bruzzi 1983a). Further studies are needed before definitive conclusions can be drawn. Meanwhile, it is obvious that TCDD is not a strong teratogenic agent, or there would have been a more consistent trend in the number and type of birth defects observed (Tuchmann-Duplessis 1983).

The inappropriate use or disposal of waste petrochemical by-products contaminated with high levels of TCDD has led to some unfortunate situations in Missouri, Illinois, New York, and elsewhere. One notorious incident occurred in 1971 and involved the application of TCDD-contaminated waste oil sludge to the dirt floor of a horse arena in eastern Missouri. A soil sample taken from the arena and analyzed by the federal Centers for Disease Control indicated a TCDD level of 33,000 ppb (Sun 1983). Before the problem was diagnosed and the source of TCDD determined, 45 horses died from the toxic effects of TCDD, and two children who played in the area suffered a variety of disorders including chloracne (Carter et al. 1975). The children reportedly recovered (Beale et al. 1977), but the episode was tragic, nevertheless. Some of the levels recorded from oiled roads at Times Beach, Missouri have ranged from 100 to 900 ppb (Anonymous 1982b). By comparison, a conventional forestry application of 2,4,5-T would deposit less than 0.02 mg TCDD/ha. Assuming this was all deposited and contained within the top 1.0 cm of bare soil having a density of 1.0 g/cm^3, then the concentration of TCDD would be less than 0.2 ppt. Thus, the amounts found at Times Beach are from 500,000 to 4.5 million times greater.

It is encouraging to note from the incidents at Seveso and Missouri that no irreversible human health problems have occurred despite relatively massive levels of exposure to TCDD. Similar findings to those of Seveso and Missouri have been reported for several other industrial accidents involving TCDD (Coulston and Pocchiari 1983, Dunagin 1983). Exposure to TCDD resulting from forestry applications of 2,4,5-T or silvex would not be expected to have any adverse effects whatsoever, since the amounts of TCDD applied and potentially internalized would be infinitesimal in comparison. Furthermore, TCDD as a contaminant of 2,4,5-T degrades rapidly after application unless it is somehow incorporated in the soil and protected from photochemical degradation (Crosby and Wong 1977, Norris 1980a).

Generally, TCDD has not been detected in environmental samples taken from within or near 2,4,5-T-treated areas. Using various methods and equipment with minimum limits of detection ranging from 1 to 17 ppt, TCDD has not been found in deer or mountain beaver (Newton and Snyder 1978), fish, water, mud, or human milk (Shadoff et al. 1977, Norris 1980b, U.S. EPA 1980a), bovine milk (Mahle et al. 1977), or beef fat (Kocher et al. 1978). It has also not been found in eagles (Woolson et al. 1973) or waterfowl (Garcia and Rhodes 1979); the limits of detection in

these avian studies were considerably higher (1 to 50 ppb).

Failure to find TCDD in these kinds of samples is not surprising in view of several factors:

1. The minute amounts of TCDD in 2,4,5-T.

2. The rapid photochemical dechlorination and/or volatilization of TCDD, which gives it a half-life of 2 to 12 hours in sunlight (Crosby and Wong 1977, Norris 1980c).

3. The tight bonding of TCDD to soil particles and other inert substances, which makes it relatively immobile in the environment and, therefore, unlikely to leach through soils into ground water or to be taken up by plants to any great extent (Helling et al. 1973).

There have been a few cases where TCDD has been detected following 2,4,5-T applications, but these have usually been the result of exceptional circumstances. For example, the EPA analyzed beef fat from lean cattle grazing on pastures recently treated with 2,4,5-T (U.S. EPA 1977). Three of the 85 samples of fat were definitely positive for TCDD (20 to 60 ppt); five additional samples were suggestive of TCDD contamination, but were below the reliable level of detection (5 to 10 ppt); the remainder had no detectable TCDD. Liver is the preferential organ of TCDD deposition, but, curiously, none of the 43 liver samples contained any TCDD at the level of detection. As another example, Young et al. (1976, 1978) detected TCDD at concentrations ranging from less than 10 up to 1,500 ppt in the livers of some animals collected live from a strip of land at Eglin Air Force Base that was used to calibrate the spraying of Agent Orange (a 50:50 mixture of 2,4-D and 2,4,5-T n-butyl esters) by aircraft destined for Vietnam. The study area had received massive applications (1,120 kg/ha) of 2,4,5-T that contained TCDD in excess of 1 ppm. Analysis of the soil within the treated area indicated TCDD levels from less than 10 to 1,500 ppt 10 years after application. When compared to the maximum concentration of TCDD (<0.2 ppt) that might be expected in bare soil following a conventional application of 2,4,5-T (2 kg/ha), it is evident that the Eglin Air Force Base experience has little, if any, relation to forestry uses of 2,4,5-T.

TCDD has also been detected in fish, particularly carp, collected from Michigan's Saginaw Bay and nearby rivers. Amounts have ranged from 17 to 588 ppt, with most samples in the 100 to 200 ppt range (Anonymous 1983b). The discharge of industrial wastes from plants manufacturing organic chemicals is the most likely source of this TCDD contamination. The U.S. Food and Drug Administration has recommended a tolerance level of 50 ppt in fish destined for human consumption (Anonymous 1983c).

Many studies concerning TCDD in environmental samples are inexplicable, strongly disputed, or remain unconfirmed by the scientific community. This is not a surprising situation, given the trace amounts of TCDD being looked for and the complex analytical chemistry involved. For example, Baughman and Meselson (1973a,b) reported finding concentrations up to 800 ppt in Vietnamese fish collected in 1970 after extensive use of Agent Orange in South Vietnam. However, the level of TCDD in samples gathered in 1973 appeared to be lower by an order of magnitude or more (Baughman 1976). One explanation for the apparent decline in TCDD residues is the fact that spraying of Agent Orange in Vietnam was largely discontinued in 1970; but other possible explanations include differences in sampling procedures between the two dates and the questionable accuracy of the analytical technique, which was highly experimental at that point in time.

In a similar case, Meselson and O'Keefe (1977) claimed to have preliminary indications of TCDD (10 to 40 ppt on a fat content basis) in samples of human milk collected in Oregon and Texas. The Oregon Committee on Synthetic Chemicals in the Environment strongly questioned the validity of the findings, since the analytical procedure did not use EPA confirmed methodology (Hiatt 1977). Furthermore, there are substantial questions about the sample collection methodology used, the proximity of the reported values to the limits of detection, and the unconventional standards used for data evaluation in this study (U.S. Department of Agriculture 1978). Even if the results are accurate, Meselson et al. (1978) concede that, "This possible association (of TCDD residues) with the use of 2,4,5-T does not involve a large enough number of samples to be statistically significant." A more thorough follow-up study by the EPA failed to detect any TCDD in milk samples collected from 105 nursing

mothers in California, Oregon, and Washington (U.S. EPA 1980a). The detection limit in this study was 1 to 4 ppt.

The EPA believed it detected trace amounts of TCDD from a small percentage of forest animal samples (birds and mice) collected from the Siuslaw National Forest in 1973-74. Unfortunately, the analytical methodology used in this study was not precise enough at the time to verify the presence of TCDD in the samples collected (Norris 1981). Furthermore, the two laboratories that did follow-up confirmatory analyses had results that varied widely; thus, there could not be a consistent quantification of the amounts of TCDD which the EPA thought were present (Costle 1977).

These examples illustrate the difficulty of obtaining definitive results when looking for such minute amounts of TCDD. Yet another problem has simply been the potential for human error associated with processing the large number of samples collected for TCDD analysis over the years. In a recent court case an assertion was made that TCDD had been detected at high concentrations in sediments collected by the EPA near Alsea, Oregon. The amounts were uncharacteristically high, in fact not achievable by any imaginable forestry use or misuse, but a great deal of news coverage was nonetheless generated. The discrepancy turned out to be caused by including, for purposes of laboratory efficiency, a few sludge samples from a manufacturing site in Michigan along with the "Oregon batch" when the samples were analyzed. The laboratory report did not fully identify the origin of each sample within the entire batch, thereby creating the false impression that some of the Oregon samples were contaminated with high levels of TCDD. A follow-up check on the sample codes revealed that all of the highly contaminated samples were from the manufacturing site in Michigan and not from Alsea, Oregon (Anonymous 1983d).

A team of scientists with Dow Chemical Company has reported that chlorinated dioxins (including TCDD) are natural products of combustion and can originate from such sources as refuse incinerators, fossil-fueled powerhouses, gasoline and diesel powered automobiles and trucks, fireplaces, charcoal grills, and cigarettes (Dow Communications 1978, Bumb et al. 1980). However, a study by Kimble and Gross (1980) failed to detect any TCDD in the fly ash of a coal-fired power plant, and efforts to resolve such discrepancies over power plant sources of dioxin have not been successful (Crummett 1980). A review by scientists in the Netherlands indicated that several types of polychlorinated dibenzo-p-dioxins (such as TCDD) and dibenzofurans are produced by municipal incinerators (Lustenhouwer et al. 1980). Previous work by Dow scientists had found that minute amounts of TCDD ($\leq$ 1 ppt of TCDD per ppm of 2,4,5-T) were produced when vegetation recently treated with 2,4,5-T was burned (Stehl and Lamparski 1977). Norris and Pierovich (1978) have concluded that the "probability of significant production of TCDD in the field from burning (vegetation treated with 2,4,5-T), however, is vanishingly small."

Additional information on the environmental behavior and fate of TCDD can be found in the reviews by Helling et al. (1973), National Research Council of Canada (1978, 1981), Esposito et al. (1980), Newton and Dost (1981), Norris (1981), Coulston and Pocchiari (1983), and other pertinent articles designated in the bibliography. Compilations of laboratory, clinical, and epidemiological studies concerning TCDD are also available (World Health Organization 1978, Esposito et al. 1980, Kimbrough 1980, JRB Associates 1981, Reggiani 1981, Wagner 1981, Coulston and Pocchiari 1983, Dunagin 1983, and other designated articles in the bibliography).

SCIENTIFIC REVIEWS

The popular press, news media, and other nonscientific literature have carried reports of ill health alleged to be a consequence of herbicide use (see, for example, Nader et al. 1981). Thus, public concern over the safety of herbicides, particularly the phenoxy herbicides, has prompted numerous reviews of the subject over the past decade or more. Recognized authorities in the fields of herbicide toxicology, medicine, physiology, and ecology have investigated a wide assortment of hypothetical and alleged adverse effects

to health and the environment. Although the specific findings in each of these reviews are not identical, the basic conclusion has been consistent: herbicides are safe when used as directed in forestry and agriculture. The following conclusory judgments, excerpted from these reviews, represent a consensus of the expertise that is available on the subject.

In 1969 the President's Science Advisory Committee commissioned a select Panel on Herbicides to conduct an in-depth review of 2,4,5-T. Their report was issued in 1971 and concluded:

> A review of the environmental effects of 2,4,5-T on non-target organisms reveals few harmful consequences of its recommended uses (President's Science Advisory Committee 1971).

In 1971 a review by the Advisory Committee on 2,4,5-T to the Administrator of the EPA concerning alleged effects on human health caused by 2,4,5-T concluded:

> Current patterns of usage of 2,4,5-T and its known fate in various compartments of the environment, including the plant and animal foods of man, are such that any accumulation that might constitute a hazard to any aspect of human health is highly unlikely.
>
> No evidence has been found of adverse effects on human reproduction in three separate locations, namely Vietnam; Globe, Arizona; and Sweden, where pregnant women have allegedly been exposed to high levels of 2,4,5-T.
>
> On the basis of these observations, it is concluded that, as presently produced and as applied according to regulations in force prior to April 1970, 2,4,5-T represents no hazard to human reproduction (U.S. EPA 1971).

In the early 1970's Congress commissioned the National Academy of Sciences to form an international team to investigate claims of birth defects and other adverse effects resulting from the use of Agent Orange (a 50:50 mixture of 2,4-D and 2,4,5-T n-butyl esters) in Vietnam. Their report was issued in 1974 and stated:

> The National Academy of Sciences committee could find no conclusive evidence of association between exposure to herbicides and birth defects in humans (National Academy of Sciences 1974).

The issue of exposure to pesticides (including herbicides) and implications for human health also surfaced in British Columbia in the early 1970's. A Royal Commission of Inquiry into the Use of Pesticides and Herbicides was appointed to look into the matter. Their report was issued in May, 1975 and contained the following statements concerning the evidence regarding herbicides:

> Phenoxy herbicides have been used on roads, rights-of-way, weed control programmes and in agriculture. They have been used in very low doses as a stop drop on apples. The Commission could not find evidence of human injury from these materials (Royal Commission of Inquiry into the Use of Pesticides and Herbicides 1975).

In 1975 the Council for Agricultural Science and Technology commissioned a team of federal and university experts to review the phenoxy herbicides. A report was issued in 1975 and updated in 1978. The most recent edition stated:

> The phenoxy herbicides are predominantly toxic to green plants and are much less toxic to mammals, birds, fish, reptiles, shellfish, insects, worms, fungi and bacteria. When properly used, they do not occur in soils and water at levels harmful to animals and microorganisms. They do not concentrate in food chains and do not persist from year to year in croplands. They are detectable only rarely in food and then only in insignificant amounts.
>
> A highly poisonous kind of dioxin called TCDD is an unavoidable contaminant in commercial supplies of 2,4,5-T and silvex. The amount present in currently produced formulations of 2,4,5-T and silvex is not enough to alter the toxicological properties of these preparations or to endanger human health or to affect plants or animals

in the environment (Council for Agricultural Science and Technology 1978).

In 1977 the Royal Swedish Academy of Sciences issued its conclusions and recommendations concerning the health and environmental risks associated with phenoxy herbicides. The principal findings were:

> There is no evidence that dioxins are formed from phenoxy acid herbicides in the environment.
>
> There is no evidence of bioaccumulation of phenoxy acids. Bioaccumulation of TCDD resulting from normal use of 2,4,5-T is insignificant.
>
> If the levels of TCDD in phenoxy acid herbicides remain below 0.1 ppm, considerations of health risks associated with these products should be based primarily on the potential toxicity of the phenoxy acids per se and not on that of its contaminants (Royal Swedish Academy of Sciences 1977).

Dr. D. J. Turner of the British Agricultural Research Council Weed Research Organization conducted an extensive literature review of 2,4-D and 2,4,5-T. His report, published in a 1977 Bulletin of the British Forestry Commission, summarizes the information as follows:

> The properties, manufacture and uses of 2,4-D and 2,4,5-T are described and the possible side effects of these herbicides are reviewed in detail. While concentrated preparations are moderately poisonous, the diluted solutions which are used for most weed control treatments present little direct hazard to humans and animals. In practice, foodstuffs and water supplies are unlikely to become contaminated. However, if contamination should occur, serious consequences are unlikely. It is pointed out that (1) very large amounts of spray solution or contaminated material are needed to produce toxic effects, (2) the compounds are usually rejected by animals, because of their unpleasant taste and smell, (3) neither herbicide is a cumulative poison, and (4) 2,4-D and 2,4,5-T break down comparatively rapidly in plant or animal tissues, soil and natural water. At the concentrations which will be encountered in forests or on farmland, the herbicides have virtually no effect on most birds, fish, insects, and soil living organisms. Populations of particular insects or soil organisms may sometimes be temporarily reduced but recovery is usually rapid (Turner 1977).

In 1977 the "Phenoxy Herbicide Investigation Team" was formed under the auspices of the California Department of Food and Agriculture to investigate a variety of adverse health effects attributed to the use of phenoxy herbicides in the North Coast region of California. Their report, issued in 1978, states the following:

> At the public hearings, allegations were made concerning gross readily apparent effects of the herbicides, and these alleged gross effects were the target of a subsequent investigation by the Phenoxy Herbicide Investigation Team. None of these effects, such as human illness, animal deaths or deformities, plant damage, or environmental damage, could be attributed to or associated with spraying of phenoxy herbicides. Similarly, no substantiation could be provided for any correlation between geographical locations of residents in relationship to the spray site and the etiology of disease. Examination of pesticide illness reports from California physicians by this Department have not revealed any significant health hazards that can be attributed to the phenoxy herbicides as used today in California (California Department of Food and Agriculture 1978).

The New Zealand Department of Health sponsored an investigation of birth defects alleged to be associated with 2,4,5-T in three separate areas in New Zealand. The report was issued in 1977 and concluded:

> In short, the data permit the conclusion that there is no evidence to implicate 2,4,5-T as a causal factor in human birth defects. The accumulated data on 2,4,5-T and its TCDD contaminant are sufficient to give a high assurance of safety in the normal use of this material. This belief is in accordance with the consensus of worldwide scientific opinion (New Zealand Department of Health 1977).

The investigation of a similar set of circumstances in Australia during 1978 by the Consultative Council on Congenital Abnor-

malities for the Minister of Health produced the following conclusions:

> The cluster of babies with birth defects born in Yarram in 1975-76 was not such as to suggest that a specific local cause was operative.
>
> Analysis of all information available showed no evidence that these birth defects were caused by exposure to 2,4-D or 2,4,5-T. The normal agricultural use of 2,4-D and 2,4,5-T has not been shown to cause birth abnormalities in domestic animals nor is there evidence to connect such use with human birth abnormalities (Australian Minister of Health 1978).

An assessment of the toxicologic risk of phenoxy herbicides as used in forest management was conducted by one of the authors of this report while affiliated with the Environmental Health Sciences Center of Oregon State University (Dost 1978). The findings were presented in a report for the USDA Forest Service (California-Pacific Region). Some of the principal conclusions reached were:

> The present knowledge of dioxin effects and behavior is not sufficient to make an unqualified statement of reasonable safety. Several areas of needed research, suggested in a later segment of this report, should improve our level of confidence. Nonetheless, it is my opinion that 2,4,5-T containing less than 0.02 ppm TCDD can be used safely in reforestation if certain protective practices listed later are instituted. In brief, these involve absolute avoidance of spray intrusion across property lines, identification and protection of dwellings and water supplies, reentry discipline and adequate public information programs (Dost 1978).

Despite these numerous reviews of the risk associated with 2,4,5-T, the public concern over the use of this herbicide continued. The controversy continued to emerge in public hearings, news media stories, scientific meetings, courtrooms, and other forums.

In April 1978, the EPA instituted yet another review of 2,4,5-T (and silvex) by filing a "Rebuttable Presumption Against Registration" (RPAR). The RPAR process was intended to be a scientific analysis of both the risks and benefits of particular pesticides which are thought to exceed certain toxicological criteria established by the EPA. In the case of 2,4,5-T and its contaminant TCDD, these criteria were carcinogenicity (causing cancer) and teratogenicity (causing birth defects) (U.S. EPA 1978b). Nevertheless, at that point in time the Agency "does not think current use of the chemical poses an imminent or emergency threat to people or the environment" (U.S. EPA 1978a). User groups, environmental groups, manufacturers, public agencies, universities, and individuals responded to the RPAR on 2,4,5-T.

In December 1978 the EPA contracted with Texas Tech University to synthesize the information contained in some 3,000 documents received by the Agency as part of the RPAR process. The report contained the following summary abstract:

> It seems clear that 2,4,5-T is effective as a selective herbicide, which is of considerable economic value to those who use it. It also seems clear that the major concern is with contamination by dioxins, the principal impurity being 2,3,7,8 tetrachlorodibenzo-p-dioxin (TCDD). This dioxin is unquestionably extremely toxic, but the data concerning several RPAR triggers, i.e., oncogenicity, teratogenicity, and mutagenicity do not appear to present a clear picture. Its presence in 2,4,5-T, in our opinions, should be considered as a potential hazard even when the level is extremely low. However, the precise level at which TCDD presents a threat is not easily defined. It may well be in the range of 0.05 ppm. In general, it seems that 2,4,5-T can be used safely provided that the level of dioxin impurities is subject to good quality control, and that persons likely to receive the greatest exposure, i.e., applicators, take appropriate safety precautions. It would appear that there are many gaps in our knowledge about 2,4,5-T so that more extensive studies, especially on trigger suspects, are warranted (Nau and Associates 1979).

On February 28, 1979 the EPA announced an emergency suspension of the use of 2,4,5-T and silvex for forestry, rights-of-way and pasture uses (U.S. EPA 1979e). Paradoxically, applications to rice crops, sugarcane, and rangelands were allowed to continue. The primary basis for the suspension was an alleged correlation between the

use of 2,4,5-T and a series of miscarriages near Alsea, Oregon (U.S. EPA 1979c). This finding has been carefully reviewed and thoroughly refuted by numerous experts in epidemiology, clinical medicine, toxicology, statistics and other pertinent specialties (Agresti 1979, Australian National Health and Medical Research Council 1979a, Blau et al. 1979, Byerly and Tschirley 1979, Cook 1980, Coulston and Olajos 1980, Lamm 1979, 1980, Mantel 1979, New Zealand Department of Health 1979, Smith 1979, United Kingdom Advisory Committee on Pesticides 1980, Wagner et al. 1979, Woods 1979).

Nevertheless, the EPA elected to proceed with the cancellation process on 2,4,5-T and silvex (U.S. EPA 1979a,b). This decision was made despite the recommendations of the EPA's Scientific Advisory Panel which stated:

> After extensive review of the data we find no evidence of an immediate or substantial hazard to human health or to the environment associated with the use of 2,4,5-T or Silvex on rice, rangeland, orchards, sugar cane, and the noncrop uses specified in the decision documents (U.S. EPA 1979d).

Unfortunately, the EPA's emergency suspension of 2,4,5-T and silvex was widely interpreted by the news media as "proof" that these herbicides caused miscarriages in Oregon. A New York Times article as recent as January 23, 1983 typifies the misconceptions that are frequently conveyed by news articles on this subject:

> The Environmental Protection Agency used emergency powers in 1979 to ban virtually all use of 2,4,5-T in the United States after discovering a higher than normal rate of spontaneous abortions in an Oregon region that had been sprayed (emphasis added) (Biddle 1983).

In March 1979 the Advisory Committee on Pesticides for the United Kingdom conducted a review of the safety of 2,4,5-T. The conclusions of this committee were consistent with the aforementioned reviews:

> On the basis of the available data on acute and chronic toxicity of pure 2,4,5-T, the Advisory Committee concludes that, when used as directed, brushkillers containing the chemical offer no hazard to users or to the general public, because the amounts of 2,4,5-T to which individuals might be exposed as a result of such use are many times less than those which could produce any ill effects. On much the same grounds, the Committee is satisfied that there would be no risk to domestic animals.
>
> The Advisory Committee has evaluated the above evidence on the acute and chronic toxicity of TCDD: whilst accepting that it is certainly one of the most toxic chemicals known, the Committee sees no reason to vary its judgment, first reached in 1970 and subsequently re-examined, that the use of brushkillers containing 2,4,5-T contaminated with TCDD can continue without risk, subject to the observance of a maximum allowable level of TCDD in the trichlorophenol used for its manufacture (0.1 ppm) (United Kingdom Advisory Committee on Pesticides 1979).

In October of 1980, Environmental Health Associates submitted a report to the National Forest Products Association summarizing the recent scientific literature. They found:

> In summary, there is not complete agreement among all scientists regarding the possible risks presented by approved applications of 2,4,5-T. However, results of available field studies, practical worst-case scenarios, and conclusions from several scientific review groups (including the EPA FIFRA SAP) appear to strongly support the notion that there is a substantial and sufficient margin of safety to the community associated with approved application of 2,4,5-T containing no more than 0.05 ppm TCDD (EPA FIFRA SAP 1979) or even 0.1 ppm TCDD (McQueen et al. 1977; Ramel 1977) (Milby et al. 1980).

The Australian government has continued its scrutiny of both 2,4-D and 2,4,5-T. The Queensland Cabinet commissioned an interdepartmental committee in November 1980 to review, once again, the safety of these herbicides. Their report, issued in 1981, contained the following summary statement:

> This Committee has extensively examined the medical and scientific information about 2,4-D, 2,4,5-T and human health, and has found that no evidence exists to suggest that the continuation of present approved use of 2,4-D and 2,4,5-T will in any way harm the health and well-being of any members of the general public (Queensland Cabinet 1981).

The State Pollution Control Commission of New South Wales (Australia) has, likewise, reassessed the safety of 2,4-D and 2,4,5-T. An abstract of their report, issued in November 1981, typifies the confident judgment, tempered by recommendations for additional precautions, that are frequently found in such reviews of herbicide safety:

> It is concluded that if these herbicides are used in accordance with specified recommendations, the risk of adverse environmental impact is slight, provided TCDD concentrations in 2,4,5-T products do not exceed the legal limit of 0.1 mg/kg. However, the high toxicity of TCDD, its propensity to bioaccumulate and the possibility of environmental hazards in particular situations are suggested as reasons for the adoption of a number of control measures, such as the elimination or reduction of TCDD concentrations in 2,4,5-T, closer monitoring of 2,4,5-T products in New South Wales and the replacement of 2,4,5-T by other herbicides for selected uses (New South Wales State Pollution Control Commission 1981).

In December 1980 the United Kingdom's Advisory Committee on Pesticides again reviewed the safety of 2,4,5-T, including the evidence from the Alsea II study by the EPA, and came to the following conclusion:

> What we have had to consider in this Review is whether there is any sound medical or scientific evidence that humans or other living creatures, or our environment, would come to any harm if cleared 2,4,5-T herbicides continue to be used in this country for the recommended purposes and in the recommended way. We have found none (United Kingdom Advisory Committee on Pesticides 1980).

The authors of a text book on the subject of phenoxy herbicides evaluated the environmental and human health implications of using phenoxy herbicides as follows:

> Extensive research indicated the phenoxies are rapidly degraded in the environment and do not accumulate in the food chain. Market basket surveys indicated the phenoxies occur very infrequently in human food and in very small amounts. Phenoxy herbicides are lost from soil, plant, and water sources by volatility, photodegradation, rainfall, dilution, biodegradation, and other means. The phenoxies are essentially nontoxic to soil organisms at normal field rates and the soil microbial population is responsible for their rapid breakdown.
>
> When used according to labeled instructions, human health hazards associated with the worldwide use of phenoxy herbicides have been insignificant (in our search of thousands of scientific articles on these herbicides [spanning a period of 30 years], we found less than two dozen documented medical reports of human intoxication). Poisoning in man has occurred by self-ingestion or when grossly misused, but such occurrences have been rare (Bovey and Young 1980).

In March 1981 the American Council on Science and Health completed another independent review of the 2,4,5-T issue. Their final position statement contained the following conclusion:

> Based on its review of the scientific evidence, the American Council on Science and Health (ACSH) concludes that there is insufficient evidence to support a ban on 2,4,5-T. No scientific reports presented to date have shown any convincing relationship between the traditional use of 2,4,5-T and adverse health effects in humans (Hayes 1981).

In October 1981 the American Medical Association published yet another independent study of the 2,4,5-T issue. Among the conclusions reached in their study is that:

> While 2,4,5-T and 2,4-D pesticides have been used in agriculture, forest management, and commercial and residential landscaping for over 30 years, there is still no conclusive evidence that they and/or TCDD are mutagenic, carcinogenic or teratogenic in man, nor that they have caused reproductive difficulties in the human (American Medical Association 1981).

Despite all of these reassuring reviews of product safety, efforts to resolve the re-registration questions have not succeeded to date. The EPA administrative cancellation hearings were suspended in March 1981 in hopes that a negotiated settlement could be reached between Dow Chemical USA (the primary registrant at the time of products con-

taining 2,4,5-T and silvex) and the EPA. The attempt to reach a satisfactory compromise spanned almost three years and cost Dow in excess of $10 million before it collapsed (Dow Communications 1983). On October 14, 1983 Dow withdrew from the EPA hearings and voluntarily cancelled all of its registrations of 2,4,5-T and silvex. In papers filed announcing its decision to withdraw, Dow stated:

> 2,4,5-T and silvex are safe, effective herbicides that neither pose nor threaten unreasonable adverse effects on the environment and are therefore properly registered under the FIFRA. Scientific panels, regulatory authorities and judicial decision makers in this country and throughout the world, including EPA's own Scientific Advisory Panel in reviewing parts of this proceeding, have reached similar conclusions (Anonymous 1983a).

Dow had been the primary defender of 2,4,5-T and silvex during the cancellation hearings. After Dow's withdrawal, the EPA encouraged the remaining participants in the litigation to also withdraw (U.S. EPA 1983). No decision by the parties involved had been made at this writing, and the hearings were still in abeyance.

At the same time, the EPA announced its intent to cancel all remaining uses of 2,4,5-T and silvex (rice, sugarcane, range, orchards, and miscellaneous non-crop sites) (U.S. EPA 1983). However, other registrants of 2,4,5-T and silvex have requested a hearing over this matter, so the registration status of these products is likely to remain in limbo for some time.

2,4,5-T continues to be scrutinized on the international level as well. For example, in May 1980 the Council of the European Economic Community directed its scientific committee for pesticides to "review all available evidence to establish a scientific basis for possible community action" concerning 2,4,5-T. The investigation by this committee was completed in July 1981 and summarized in a communique as follows:

> In summary, the Committee was satisfied that the marketing and proper agricultural use of 2,4,5-T is not dangerous for human or animal health or prejudicial to the environment. It made, however, a number of detailed recommendations concerning particularly the maximum permitted level of TCDD in 2,4,5-T (0.005 ppm) and the avoidance of 2,4,5-T residues in foodstuffs (Commission to the Council of the European Economic Community 1982).

Although the registration status of 2,4,5-T is in a state of flux at the present time in the U.S. and a few other countries, most countries still permit its use. For example, the herbicide is currently authorized for use in Australia, Belgium, Canada (on a provincial basis), Finland, France, Germany, Ireland, Luxembourg, New Zealand, South Africa, Spain, the United Kingdom, and most Latin American countries. The registration of 2,4,5-T has been withdrawn in Columbia, Denmark, Italy, Norway, the Netherlands and Sweden. The E.C.C. communique cited earlier contains the following position statement with respect to 2,4,5-T registration:

> The Commission accepts the broad conclusions of the opinion of the Scientific Committee for Pesticides and concludes that on the basis of existing scientific evidence a Community-wide prohibition of the marketing and use of 2,4,5-T herbicides . . . would not be justified (Commission to the Council of the European Economic Community 1982).

The focus of attention has shifted recently from 2,4,5-T to 2,4-D and picloram (an active ingredient in Tordon® products). In an assessment of 2,4-D safety conducted by the Minnesota Department of Health in 1978, the situation was summarized as follows:

> A review of the literature of the toxicology of 2,4-D, the data from the 1977 monitoring programs of the Chippewa and Superior National Forests, and the calculation of the estimated 2,4-D exposure to a "maximally exposed individual," support the conclusion that, although certain adverse health effects are not likely to occur, there is significant doubt about some areas of the toxicology of 2,4-D which precludes an absolute assumption of safety relating to its use in forestry management (Minnesota Department of Health 1978).

The effects listed by the Minnesota Department of Health as unlikely to occur are: (1) acute toxicity, (2) chronic health effects and (3) teratogenesis. The areas in

which an understanding of 2,4-D toxicology was listed as deficient were: (1) mutagenicity, (2) carcinogenicity, (3) contaminants and metabolites, (4) environmental and wildlife monitoring, and (5) acceptable daily intake levels.

A review of 2,4-D conducted by the Department of Health Services and Department of Industrial Relations as part of California's Hazard Alert System made several recommendations:

1. Current work practices are inadequate to protect against potential neurotoxicity. They should be reviewed and corrected.

2. The scientific data are sufficiently suggestive of a carcinogenic effect, and demonstrate a weak teratogenic effect, that 2,4-D use should be restricted to areas in which human exposure can be kept to the minimum. Contamination of open water must be monitored and prevented. Broadcast methods of application that could directly expose the general population should be strongly discouraged. Greater consideration must be given to alternative methods for removing unwanted plants.

3. Products containing 2,4-D should be labeled to warn users of the herbicide's potential for causing neurotoxicity and how to protect against it. Present labels are inadequate. Educational information should be provided for anyone who works with the substance.

4. Home gardeners using products containing 2,4-D should exercise care to avoid skin exposure to themselves or others.

5. Adequate tests in rodents should be conducted following National Cancer Institute protocol to determine the carcinogenicity of 2,4-D. Studies should also be conducted to measure the 2,4-D excretion in urine and peripheral nerve function in exposed workers.

(California Department of Health Services/ Department of Industrial Relations 1980)

In response to these and other concerns, the EPA has requested additional toxicological data in support of continued registration of products containing 2,4-D. While this effort is underway, the agency has taken the following position based on its review of the available information on the potential health effects of 2,4-D.

(a) The presently available information on the potential adverse health effects of 2,4-D does not support a regulatory action to remove 2,4-D products from the market;

(b) Information from scientifically valid studies does not indicate that the continued use of 2,4-D poses an imminent hazard or unreasonable adverse effect when used according to label precautions and directions for use.

(U.S. EPA 1980b)

Despite these reassurances, pressure has continued to build against 2,4-D. In the fall of 1980 the Canadian government announced that it had found dioxins in product samples of 2,4-D (U.S. EPA 1981). Although the dioxins found were of limited toxicity, and none of the highly toxic 2,3,7,8-tetrachloro dioxin (TCDD) was found, these findings nevertheless prompted the Canadian government to ban the sale by basic manufacturers of all such products shown to contain dioxins at or above 1 ppb.

The EPA quickly responded to this development and analyzed several 2,4-D products from U.S. manufacturing facilities. It issued a report in January 1981 which stated:

> EPA is coordinating its review activities on 2,4-D with Agriculture Canada, but the Agency says that there is no justification for regulatory action to change current uses of 2,4-D in the United States because products tested here were either dioxin-free or contained extremely low levels (less than 100 ppb)... Based on the preliminary analyses that the Agency has conducted using available data, the concentrations found in U.S. manufacturing-use products do not appear to pose a health hazard (U.S. EPA 1981).

The EPA is continuing to investigate the safety of 2,4-D. On August 29, 1980 it required all registrants of 2,4-D to supply data concerning chronic health effects. These data are anticipated within one to four years, depending on the type of study

involved. The EPA has also recently determined that the problem of dioxin contamination "appears to result from the manufacturing processes principally used in Canada rather than the United States" (U.S. EPA 1982b). Therefore, no change in the registration status of 2,4-D was called for, and the agency concluded:

> EPA's recent evaluations of 2,4-D do not indicate its currently registered uses pose unreasonable risks to public health or the environment. As with any pesticide chemical, if evidence of such risks does arise, the Agency will take appropriate action to reduce or eliminate those risks (U.S. EPA 1982b).

The current position maintaining the registration of 2,4-D is supported by a recent comprehensive review of 2,4-D by a former pesticide specialist with the Dow Chemical Company:

> Considering the short-lived persistence of 2,4-D in the environment; its rapid excretion unmetabolized in mammals and man; its moderate acute oral toxicity; and that it is not present except occasionally in traces in our environment, it is evident that the approved uses of 2,4-D are not hazardous to people or the environment (Mullison 1981).

The March 15, 1982 issue of Inquiry Magazine carried an article titled, "Agent White: it kills weeds, bushes, trees--and maybe people." Agent White is an herbicide mixture used in Vietnam which contains picloram, an active ingredient also of Tordon® and Amdon® products. The article claims to link the use of picloram with a "siege" of cancer in Cherokee County, N.C. In response to this and similar press articles on picloram, the EPA reviewed the data base and then issued the following statement:

> In sum, the data on short term effects, environmental effects and genetic mutation, as well as one NCI (National Cancer Institute) cancer study, support the current registration of picloram. The registrant is conducting a new rat feeding study to clarify the ambiguous results of (a) second NCI study . . . . We have no current evidence that picloram is posing risks of unreasonable adverse effects to human health or the environment, although more data is needed on long term effects to support this conclusion (U.S. EPA 1982a).

The statements cited in the previous reviews reflect the cautious effort of most scientists and regulatory officials to avoid making categorical pronouncements about herbicide safety which might later be proven false by new information, or which might not apply to circumstances different than those evaluated (such as misuse of herbicides). As discussed earlier in this report, it is impossible to state with absolute certainty that the use of such materials is safe under all foreseeable conditions, no matter how strong the data base. Therefore, it is appropriate to rely on the prudent judgments of qualified experts to establish the likelihood of adverse effects as a result of herbicide use. Suitable action can then be taken to avoid undesirable consequences where they are likely to occur.

LITIGATION

The issue of herbicide use in forestry has been addressed in litigation as well as in scientific and regulatory reviews. In the U.S. the cases to date have been strictly confined to the argument of whether or not federal agencies have complied with the requirements set forth in the National Environmental Policy Act (NEPA) of 1969. The issue of herbicide risk per se has not been debated directly in these cases.

NEPA requires all federal agencies to prepare environmental impact statements prior to initiating major actions that may affect the environment. The interpretation of what constitutes a major federal action and the correct procedure for analyzing such an action in environmental impact assessments has been a source of much legal confusion and ambiguity. Consequently, there have been numerous temporary restraining orders and injunctions against the use of herbicides by federal agencies, pending the preparation of adequate environmental impact statements.

A recent trial in Nova Scotia, Canada did directly address the issue of herbicide safety. This marked the first time that the health risks of herbicide use in forestry were debated and weighed in a courtroom situation. At issue were the risks associated with proposed uses of 2,4-D and 2,4,5-T by Nova Scotia Forest Industries, Ltd. After hearing more than a month of expert testimony, Justice D. Merlin Nunn of Nova Scotia's Supreme Court issued the following opinion:

> I am satisfied that the overwhelming currently accepted view of responsible scientists is that there is little evidence that, for humans, either 2,4-D or 2,4,5-T is mutagenic or carcinogenic and that TCDD is not an effective carcinogen, and further, that there are no-effect levels and safe levels for humans and wildlife for each of these substances.
>
> . . . For this reason I felt it incumbent upon me to set forth this detail of fact and my own observations so as to make clear that all the evidence available has been presented by the parties, and that, based on this evidence, fully weighed and considered, this court is of the opinion that these spraying operations can be carried out in safety and without risk to the health of the citizens of this province (Nunn, 1983).

The status of herbicide product registrations and regulations are constantly changing due to legal and regulatory actions. Prospective users of herbicide products are advised to periodically check on local, state, provincial, and federal regulations governing the application of these materials.

CONCLUSION

Without exception, the amounts of herbicides detected in the environment have been far below the known levels of toxicological significance to humans, fish, wildlife, and livestock. As a consequence, it is not surprising that there have been no substantiated cases of direct, adverse health effects to humans or animals when these materials have been used properly in agriculture and forestry. Similar analyses of the risk associated with TCDD in present production of 2,4,5-T and silvex reveal that this substance is distributed in such small amounts that it, too, does not constitute an appreciable risk to human health. Even when TCDD existed at much higher concentrations in 2,4,5-T and silvex, no adverse effects attributable to this impurity have been confirmed consequent to proper applications.

This bulletin has been based on the most authoritative reviews of which we are aware that evaluate the risks of using herbicides. These evaluations have been remarkably consistent in their determination that registered herbicides are safe to humans, wildlife, and livestock when used as directed. This finding is reassuring in light of the important role that these materials play in sustaining the productivity of agriculture and forestry.

Nevertheless, confidence by the general public in the safe use of herbicides has often been shaken. This is partially the result of incomplete or inaccurate news coverage of related events. Sensationalized reporting has frequently left the public with a distorted view of the actual risks of herbicide use. Such a discrepancy between perceived and actual risks associated with herbicides extends to pesticides in general. For example, a recent survey of college students (Upton 1982) indicated that they ranked pesticides as the fourth most hazardous source of risk among 30 alternatives. Actuarial statistics, however, placed pesticides in 28th position among the 30 choices.

Some of the publications presenting other points of view and additional issues concerned with herbicides, and pesticides in general, are listed in Appendix 7. They are not all pertinent to forestry, nor are they necessarily accurate and comprehensive. Regardless, these references do raise some important questions and provide valuable insight into the complex technical and socio-economic aspects of pesticide use. It is hoped that our report will provide a solid foundation for evaluating the information presented in these alternative accounts of the herbicide issue.

BIBLIOGRAPHY[1]

ADAMS, D.F., C.M. JACKSON, and W.L. BAMESBERGER. 1964. Quantitative studies of 2,4-D esters in the air. Weeds 12:280-283.

AGRESTI, A. 1979. Analysis of association between 2,4,5-T exposure and hospitalized spontaneous abortions. Supplement to: A scientific critique of the EPA Alsea II study and report. Environmental Health Sciences Center, Oregon State University, Corvallis.

ALLEN, J.R., J.P. VAN MILLER, and D.H. NORBACK. 1975. Tissue distribution, excretion, and biological effects of [^{14}C] tetrachlorodibenzo-p-dioxin in rats. Food and Cosmetics Toxicology 13:501-505.

\+ ALTOM, J.D., and J.F. STRITZKE. 1973. Degradation of dicamba, picloram, and four phenoxy herbicides in soils. Weed Science 21:556-560.

AMERICAN CONFERENCE OF GOVERNMENTAL AND INDUSTRIAL HYGIENISTS. 1977. Threshold limit values for chemical substances and physical agents in workroom environment with intended changes for 1977. Cincinnati, Ohio.

* AMERICAN MEDICAL ASSOCIATION. 1981. The health effects of Agent Orange and polychlorinated dioxin contaminants. Council on scientific affairs, advisory panel on toxic substances. Technical Report, Chicago, Illinois.

ANONYMOUS. 1981. EPA group decides cancer risks below 10^{-6} aren't worth chasing. Pesticide and Toxic Chemical News 9(31):3.

ANONYMOUS. 1982a. EPA data show Illinois may also have numerous dioxin-contaminated sites. Pesticide and Toxic Chemical News 11(4):8.

ANONYMOUS. 1982b. New dioxin data show discrepancies; Lavelle refuses data to subcommittee. Pesticide and Toxic Chemical News 11(4):25-26.

ANONYMOUS. 1983a. EPA notes intent to end all uses of 2,4,5-T and silvex. Pesticide and Toxic Chemical News 11(49):10-13.

ANONYMOUS. 1983b. EPA report shows more than 40 pollutants, including dioxin, in Dow wastewater. Pesticide and Toxic Chemical News 11(21):25.

ANONYMOUS. 1983c. GreatLakes dioxin levels. Pesticide and Toxic Chemical News 11(17):2.

ANONYMOUS. 1983d. Samples suspected for TCDD still miscoded, misplaced, not checked. Pesticide and Toxic Chemical News 11(40):28-29.

ASSISTANT SECRETARY OF DEFENSE. 1984. Air Force releases Ranch Hand baseline morbidity study. U.S. Department of Defense news release No. 87-84. Washington, D.C.

* AUSTRALIAN MINISTER OF HEALTH. 1978. Report of the Consultative Council on Congenital Abnormalities in the Yarram District. Melbourne, Australia.

* AUSTRALIAN NATIONAL HEALTH AND MEDICAL RESEARCH COUNCIL. 1978. Statement on 2,4,5-T and the dioxin TCDD. Report of the 85th Session, Canberra, Australia.

* AUSTRALIAN NATIONAL HEALTH AND MEDICAL RESEARCH COUNCIL. 1979a. Re-examination of 2,4,5-T. News release, Canberra, Australia.

* AUSTRALIAN NATIONAL HEALTH AND MEDICAL RESEARCH COUNCIL. 1979b. Report of the ad hoc working party on the use and safety of 2,4,5-T. Appendix VI to Report of the 87th Session, Canberra, Australia.

AXELSON, O., et al. 1979. Updating of the mortality among pesticide exposed railroad workers. Lakarigningen 76:3505-3506.

\+* BAILEY, G.W., and J.L. WHITE. 1965. Herbicides: a compilation of their

[1]Citations designated with an asterisk (*) are review articles or bibliographic compilations dealing with human health aspects of herbicide use. Those designated with a plus sign (+) cover general toxicological and environmental implications.

physical, chemical, and biological properties. Residue Reviews 10:97-122.

BAMESBERGER, W.L., and D.F. ADAMS. 1966. An atmospheric survey for aerosol and gaseous 2,4-D compounds. Pages 219-227 in Organic Pesticides in the Environment. Edited by R.F. Gould. American Chemical Society, Washington, D.C.

BAUGHMAN, R.W. 1976. Tetrachlorodibenzo-p-dioxins in the environment. High resolution mass spectrometry at the picogram level. Dissertation Abstracts International 36(7):3380-B.

BAUGHMAN, R.W., and M.S. MESELSON. 1973a. Abstract 55, Proceedings of the National Meeting of the American Chemical Society, Division of Pesticide Chemicals, Chicago, Illinois.

BAUGHMAN, R.W., and M.S. MESELSON. 1973b. An analytical method for detecting TCDD (dioxin): levels of TCDD in samples from Vietnam. Environmental Health Perspectives Experimental Issue 5:27-35. National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina.

BEALE, M.G., et al. 1977. Long-term effects of dioxin exposure. Lancet 1:748.

BIDDLE, W. 1983. Dioxin's peril to humans: proof is elusive. New York Times, January 23, 1983. p. 1, 36.

BINNS, W., and L. BALLS. 1971. Nonteratogenic effects of 2,4,5-trichlorophenoxyacetic acid and 2,4,5-T propylene glycol butyl esters herbicides in sheep. Teratology 4:245.

BLAU, G.E., et al. 1979. Critique of "Report of assessment of a field investigation of six-year spontaneous abortion rates in three Oregon areas in relation to forest 2,4,5-T spray practices." Dow Chemical USA, Midland, Michigan, and Tabershaw Occupational Medical Associates, Rockville, Maryland.

BOGEN, G. 1979. Symptoms in Vietnam veterans exposed to agent orange. Journal of the American Medical Association 242:2391.

+* BOVEY, R.W., and J.D. DIAZ-COLON. 1977. Selected bibliography of the phenoxy herbicides. II. The substituted dibenzo-p-dioxins. MP-1323. Texas Agricultural Experiment Station, College Station, Texas.

+ BOVEY, R.W., and J.D. DIAZ-COLON. 1978a. Selected bibliography of the phenoxy herbicides. IV. Ecological effects. MP-1360. Texas Agricultural Experiment Station, College Station, Texas.

BOVEY, R.W., and J.D. DIAZ-COLON. 1978b. Selected bibliography of the phenoxy herbicides. VI. Methods of extraction and analysis. MP-1381. Texas Agricultural Experiment Station, College Station, Texas.

+ BOVEY, R.W., and J.D. DIAZ-COLON. 1978c. Selected bibliography of the phenoxy herbicides. VIII. Effects on higher plants. MP-1388. Texas Agricultural Experiment Station, College Station, Texas.

+* BOVEY, R.W., and A.L. YOUNG. 1980. The science of 2,4,5-T and associated phenoxy herbicides. John Wiley and Sons, Inc., New York.

BROWN, P.G. 1982. Air Force health study - Update. Paper presented to Veterans Administration, advisory committee on health-related effects of herbicides. Washington, D.C.

BRUZZI, P. 1983a. Birth defects in the TCDD polluted area of Seveso: results of a four-year follow-up. Pages 271-280 in Accidental exposure to dioxins. Human health aspects. Edited by F. Coulston and F. Pocchiari. Academic Press, New York.

BRUZZI, P. 1983b. Health impact of the accidental release of TCDD at Seveso. Pages 215-225 in Accidental exposure to dioxins. Human health aspects. Edited by F. Coulston and F.

Pocchiari. Academic Press, New York.

BUMB, R.R., et al. 1980. Trace chemistries of fire: a source of chlorinated dioxins. Science 210:385-390.

+* BYERLY, T.C., and F.H. TSHIRLEY. 1979. Scientific dispute resolution conference on 2,4,5-T. American Farm Bureau Federation, Park Ridge, Illinois.

* CAIN, B.F. 1980. Assessment of toxic hazards of the herbicide 2,4,5-T in New Zealand. Royal Society of New Zealand Miscellaneous Series No. 4.

+* CALIFORNIA DEPARTMENT OF FOOD AND AGRICULTURE. 1978. Report on the aerial use of phenoxy herbicides. Phenoxy herbicide investigation team. Sacramento.

* CALIFORNIA DEPARTMENT OF HEALTH SERVICES/DEPARTMENT OF INDUSTRIAL RELATIONS. 1980. 2,4-dichlorophenoxyacetic acid (2,4-D) evaluation of the human health hazards. Hazard Alert System, Epidemiological Studies Laboratory, Sacramento.

CARMELLI, D., et al. 1981. A case-control study of the relationship between exposure to 2,4-D and spontaneous abortions in humans. Executive summary. Center for Health and Environmental Research, SRI International. Menlo Park, California.

CARTER, C.D., et al. 1975. Tetrachlorodibenzodioxin: an accidental poisoning episode in horse arenas. Science 188:738-740.

+ CARTER, M.C., et al. 1976. Impact of chemical and mechanical site preparation on wildlife habitat. Industrial Vegetation Management 8(1):5-9.

CHENEY, H.V., C.M. WALBY, and R.E. SHIELDS (not dated). Impact of 2,4,5-T on Blodgett Forest. I. Description of an experimental aerial application of 2,4,5-T. Environmental monitoring and pest management, California Department of Food and Agriculture, Sacramento.

+* COMMISSION TO THE COUNCIL OF THE EUROPEAN ECONOMIC COMMUNITY. 1982. Comunication from the Commission to the Council concerning the marketing and use of plant protection products containing 2,4,5-T. Official Journal of European Communities No. C 170:6-8.

+ CONDON, P.A. 1968. The toxicity of herbicides to mammals, aquatic life, soil microorganisms, beneficial insects and cultivated plants, 1950-1965. A list of selected references. USDA National Agricultural Library, Washington, D.C. Library List No. 87.

COOK, R.R. 1980. Agent orange and spontaneous abortions. Journal of the American Medical Association 243:1423.

COOK, R.R., et al. 1980. Mortality experience of employees exposed to 2,3,7,8 - tetrachlorodibenzo - p - dioxin (TCDD). Journal of Occupational Medicine 22:530-532.

CORNFIELD, J. 1977. Carcinogenic risk assessment. Science 198:693-699.

COSTLE, D.M. 1977. Letter to John R. McGuire dated October 19, 1977.

COULSTON, F., and E.J. OLAJOS. 1980. Report of panel to discuss the epidemiology of 2,4,5-T. New York City, July 10-11, 1979. Ecotoxicology and Environmental Safety 4:96-102.

+* COULSTON, F., and F. POCCHIARI (eds.). 1983. Accidental exposure to dioxins. Human health aspects. Academic Press, New York.

COUNCIL FOR AGRICULTURAL SCIENCE AND TECHNOLOGY. 1977. Comments on health risk and economic impact assessments of suspected carcinogens: interim procedures and guidelines. CAST Report 73. Ames, Iowa.

+* COUNCIL FOR AGRICULTURAL SCIENCE AND TECHNOLOGY. 1978. The phenoxy herbicides. 2nd edition CAST Report 77. Ames, Iowa.

COURTNEY, K.D., and J.A. MOORE. 1971. Environmental degradation of

2,3,7,8 - tetrachlorodibenzo-p-dioxin (TCDD). Toxicology and Applied Pharmacology 20:396-403.

CROSBY, D.G., and A.S. WONG. 1977. Environmental degradation of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). Science 195:1337-1338.

CRUMMETT, W.B. 1980. TCDD in coal fly ash. Letter to the Editor. Science 207:1148.

DE CARLI, L., et al. 1977. Cytogenetic investigations in individuals exposed to the toxic action of TCDD. The Lombardi Region and the Institute of General Biology of the Faculties of Medicine and Surgery of the Universities of Milan and Pavia, Italy.

+ DIAZ-COLON, J.D., and R.W. BOVEY. 1976. Selected bibliography of the phenoxy herbicides. I. Fate in the environment. MP-1303. Texas Agricultural Experiment Station, College Station, Texas.

+* DIAZ-COLON, J.D., and R.W. BOVEY. 1977. Selected bibliography of the phenoxy herbicides. III. Toxicological studies in animals. MP-1343. Texas Agricultural Experiment Station, College Station, Texas.

+ DIAZ-COLON, J.D., and R.W. BOVEY. 1978a. Selected bibliography of the phenoxy herbicides. V. Interrelations with microorganisms. MP-1379. Texas Agricultural Experiment Station, College Station, Texas.

+* DIAZ-COLON, J.D., and R.W. BOVEY. 1978b. Selected bibliography of the phenoxy herbicides. VIII. Military uses. MP-1387. Texas Agricultural Experiment Station, College Station, Texas.

+* DOST, F.N. 1978. Toxicology of phenoxy herbicides and hazard assessment of their use in reforestation. USDA Forest Service, California Pacific Region.

DOUGHERTY, W.J., M. HERBST, and F. COULSTON. 1975. The nonteratogenicity of 2,4,5-trichlorophenoxyacetic acid in the rhesus monkey (Macaca mulatta). Bulletin of Environmental Contamination and Toxicology 13(4):477-482.

DOUGHERTY, R.C., and K. PIOTROWSKA. 1976. Screening by negative chemical ionization mass spectrometry for environmental contamination with toxic residues: Application to human urines. National Academy of Sciences, Proceedings 73(6):1777-1781.

DOW CHEMICAL USA (not dated). Swedish studies challenged in risk assessment. The bottom line. Agricultural Products Department, Midland, Michigan.

DOW COMMUNICATIONS. 1978. Dow reports dioxins occur everywhere as result of normal combustion processes. Dow Chemical Company news release, November 15, 1978. Midland, Michigan.

DOW COMMUNICATIONS. 1983. Dow Chemical withdraws from 2,4,5-T business in the U.S.; exits EPA policy proceeding on the herbicide. Dow Chemical Company news release, October 14, 1983. Midland, Michigan.

DRILL, V.A., and T. HIRATZKA. 1953. Toxicity of 2,4-dichlorophenoxyacetic acid and 2,4,5-trichlorophenoxyacetic acid. A report on their acute and chronic toxicity in dogs. Archives of Industrial Hygiene and Occupational Medicine 7:61-67.

* DUNAGIN, W.G. 1983. Dioxin effects on human health. Missouri Medicine, March, 1983.

EMERSON, J.L., et al. 1971. Teratogenic studies on 2,4,5-trichlorophenoxyacetic acid in the rat and rabbit. Food and Cosmetics Toxicology 9:395-404.

ERIKSSON, M., et al. 1979. Case-control study on malignant mesenchymal tumors of the soft parts and exposure to chemical substances. Lakartidningen 76:3872-3875.

+ ERNE, K. 1966. Studies on the analytical chemistry and toxicology of phenoxy herbicides. National Veterinary Institute, Stockholm, Sweden.

+* ESPOSITO, M.P., T.P. TIERNAN, and F.E. DRYDEN. 1980. Dioxins. U.S. EPA, Industrial Environmental Research Laboratory, Office of Research and Development, Cincinnati, Ohio.

FARM CHEMICALS HANDBOOK. 1982. Meister Publishing Company, Willoughby, Ohio.

FIELD, B., and C. KERR. 1979. Herbicide use and incidence of neural-tube defects. Lancet 1:1341-1342.

+ FOWLE, C.D. 1980. Workshop on the impact of herbicides on the eastern boreal forest ecosystem. Centre for Research on Environmental Quality, York University, Downsview, Ontario, Canada.

FRANCIS, J.D., et al. 1983. National statistical assessment of rural water conditions. Department of Rural Sociology, Cornell University, Ithaca, New York.

FRIES, G.F., and G.S. MARROW. 1975. Retention and excretion of 2,3,7,8-tetrachlorodibenzo-p-dioxin by rats. Journal of Agricultural and Food Chemistry 23:265-269.

GARCIA, J.D., and M.J. RHODES. 1979. Residues of 2,4,5-T in the American coot (Fulcia americana). Bulletin of Environmental Contamination and Toxicology 23:231.

GEHRING, P.J., et al. 1973. The fate of 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) following oral administration to man. Toxicology and Applied Pharmacology 26:352-361.

GELDMACHER, M., V. MALLINCKRODT, and L. LAUTENBACH. 1966. Two fatal poisonings (suicides) with chlorinated phenoxy acetic acids (2,4-D and MCPA). Translated from Archiv. fur Toxikologie 21:261-278.

+ GHASSEMI, M., et al. 1981. Environmental fates and impacts of major forest use pesticides. Report for U.S. EPA, Office of Pesticides and Toxic Substances, Washington, D.C.

+ GHASSEMI, M., S. QUINLIVAN, and M. DELLARCO. 1982. Environmental effects of new herbicides for vegetation control in forestry. Environment International 7:389-401.

GIBSON, J.E. 1973. Teratology studies in mice with 2-sec-butyl-4,6-dinitrophenol (dinoseb). Food and Cosmetics Toxicology 11:31-43.

HALL, J.F. 1979. Letter to the U.S. EPA as a supplemental response to the "Notice of rebuttable presumption against registration and continued registration of pesticide products containing 2,4,5-T." National Forest Products Association, Washington, D.C.

HALL, J.F. 1980. Letter to Edwin L. Johnson of the U.S. EPA transmitting the report "Determination of 2,4-D exposure received by forestry applicators, Spring 1980." National Forest Products Association, Washington, D.C.

HANIFY, J.A., et al. 1981. Aerial spraying of 2,4,5-T and human birth malformations: an epidemiological investigation. Science 212:349-352.

HANSEN, W.H., et al. 1971. Chronic toxicity of 2,4-dichlorophenoxyacetic acid in rats and dogs. Toxicology and Applied Pharmacology 20:122-129.

HARDELL, L. 1981. Epidemiological studies on soft-tissue sarcoma and malignant lymphoma and their relation to phenoxy acid or chlorophenol exposure. Umea University medical dissertations (Sweden). New Series No. 65-ISSN 0346-6612.

HARDELL, L., and A. SANDSTROM. 1979. Case control study: soft tissue sarcomas and exposure to phenoxyacetic acids or chlorophenols. British Journal of Cancer 39:711-717.

HASKELL LABORATORY FOR TOXICOLOGY AND INDUSTRY MEDICINE. 1979a. Toxicological information - fosamine, ammonium salt. Du Pont Company, Wilmington, Delaware.

HASKELL LABORATORY FOR TOXICOLOGY AND INDUSTRY MEDICINE. 1979b. Toxicological information - hexazinone. Du Pont Company, Wilmington, Delaware.

HAWKES, C.L., and L.A. NORRIS. 1977. Chronic oral toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) to rainbow trout. Transactions of the American Fisheries Society 106(6): 641-645.

* HAYES, M.K. 1981. The health effects of herbicide 2,4,5-T. American Council on Science and Health Report. New York.

\+ HEATH, R.G., et al. 1972. Comparative dietary toxicities of pesticides to birds. U.S. Department of the Interior, Fish and Wildlife Service, Bureau of Sport Fisheries and Wildlife. Special Science Report - Wildlife 152. Washington, D.C.

\+ HELLING, C.S., et al. 1973. Chlorodioxins in pesticides, soils, and plants. Journal of Environmental Quality 2(2):171-178.

HIATT, V.G. 1977. Letter to Governor Robert Straub dated February 18, 1977.

\+ HILL, E.F., et al. 1975. Lethal dietary toxicities of environmental pollutants to birds. U.S. Department of the Interior, Fish and Wildlife Service, Bureau of Sport Fisheries and Wildlife. Special Scientific Report - Wildlife 191. Washington, D.C.

HOHENEMSER, C., R.W. KATES, and P. SLOVIC. 1983. The nature of technological hazard. Science 220:378-384.

HOMBERGER, E., et al. 1979. The Seveso accident: Its nature, extent and consequences. Annals of Occupational Hygiene 22:327-370.

HONCHAR, P. 1982. Health hazard evaluation determination report (for maintenance employees of the Long Island Railroad). Rep. 80-039. NIOSH, U.S. Department of Health and Human Services, Washington, D.C.

INNES, J. R. M., et al. 1969. Bioassay of pesticides and industrial chemicals for tumorigenicity in mice: A preliminary note. Journal of the National Cancer Institute 42:1101-1114.

\+ ISENSEE, A.R. 1978. Bioaccumulation of 2,3,7,8 - tetrachlorodibenzopara - dioxin. Ecological Bulletin (Stockholm, Sweden) 27:255-262. Chlorinated phenoxy acids and their dioxins. Edited by C. Ramel.

\+* JRB ASSOCIATES. 1981. Review of literature on herbicides, including phenoxy herbicides and associated dioxins. Vol. I. Analysis of literature. Vol. II. Annotated bibliography. Veterans Administration, Department of Medicine and Surgery, Washington, D.C.

\+ JUNTUNEN, E.T., and L.A. NORRIS. 1972. Field application of herbicides - avoiding danger to fish. Oregon State University, Agricultural Experiment Station, Corvallis, Oregon. Report 354.

\+* KEARNEY, P.C. 1975. The dioxin story: is 2,4,5-T safe? Weeds Today 6(4):16-17.

\+ KEARNEY, P.C., and D.D. KAUFMAN. 1975. Degradation of herbicides. Marcel Decker, Inc., New York.

\+ KEARNEY, P.C., et al. 1973. Tetrachlorodibenzodioxin in the environment: source, fate, and decontamination. Environmental Health Perspectives Experimental Issue 5:273-277. National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina.

\+ KENAGA, E.E. 1969. Tordon herbicides - evaluation of safety to fish and birds. Down to Earth 25:5-9.

+ KENAGA, E.E. 1974. 2,4,5-T and derivatives: toxicity and stability in the aquatic environment. Down to Earth 30(3):19-25.

+ KENAGA, E.E. 1975. The evaluation of the safety of 2,4,5-T to birds in areas treated for vegetation control. Residue Reviews 5:1-19.

+ KENAGA, E.E., and L.A. NORRIS. 1983. Environmental toxicity of TCDD. Pages 277-279 in Human and environmental risks of chlorinated dioxins and related compounds. Edited by R.E. Tucker, A.L. Young, and A.P. Gray. Plenum Publishing Corporation, New York.

KEPHART, L.W. 1945. Proceedings of North Central Weed Control conference 2:68-75.

KHERA, K.S., and W.P. MCKINLEY. 1972. Pre- and postnatal studies on 2,4,5-trichlorophenoxyacetic acid, 2,4-dichlorophenoxyacetic acid and their derivatives in rats. Toxicology and Applied Pharmacology 22:14-28.

KIMBLE, B.J., and M.L. GROSS. 1980. Tetrachlorodibenzo-p-dioxin quantitation in stack-collected coal fly ash. Science 207:59-61.

+* KIMBROUGH, R.D. (ed.). 1980. Halogenated biphenyls, terphenyls, napthalenes, dibenzo-dioxins and related products. Elsevier/North-Holland Biomedical Press, New York.

+ KIMMINS, J.P. 1975. Review of the ecological effects of herbicide usage in forestry. Information Report No. BC-X-139. Canadian Forestry Service, Victoria, British Columbia.

+ KIMMINS, J.P., and P.N. FRAKER. 1973. Bibliography of herbicides in forest ecosystems. Canada Pacific Forest Research Centre. Information Report BC-X-81. Victoria, British Columbia.

KOCHER, C.W., et al. 1978. A search for the presence of 2,3,7,8-tetrachlorodibenzo-p-dioxin in beef fat. Bulletin of Environmental Contamination and Toxicology 19:229-235.

KOCIBA, R.J., et al. 1975. 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD): Results of a 13-week oral toxicity study in rats. Toxicology and Applied Pharmacology 35:553-574.

KOCIBA, R.J., et al. 1978. Results of a two-year chronic toxicity and oncogenicity study of 2,3,7,8-tetrachlorodibenzo-p-dioxin in rats. Toxicology and Applied Pharmacology 46:279-303.

KOCIBA, R.J., et al. 1979a. Long-term toxicologic studies of 2,3,7,8-tetrachlorodibenzo-p-dioxin in laboratory animals. Pages 397-404 in Annals of the New York Academy of Sciences.

KOCIBA, R.J., et al. 1979b. Results of a two-year chronic toxicity and oncogenic study of rats ingesting diets containing 2,4,5-trichlorophenoxyacetic acid (2,4,5-T). Food and Cosmetics Toxicology 17:205-221.

+ KOCIBA, R.J., et al. 1979c. Toxicologic studies of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in rats. Pages 281-287 in Toxicology and Occupational Medicine. Edited by Deichmann. Elsevier/North-Holland, Inc., New York.

KUTZ, F.W. 1978. Human and environmental monitoring for herbicides used in forestry. Pages 83-85 in Symposium on the Use of Herbicides in Forestry, sponsored by the USDA and U.S. EPA, Arlington, Virginia.

KUTZ, F.W., R.W. MURPHY, and S.C. STRASSMAN. 1978. Survey of pesticide residues and their metabolites in urine from the general population. Environmental Science Research 12:363-369.

LAMM, S.H. 1979. An epidemiologic assessment of the Alsea II report. Tabershaw Occupational Medical Associates, Rockville, Maryland.

LAMM, S.H. 1980. Spontaneous abortions and forest spraying--A model to test whether the data support the proposed association. American Journal of Epidemiology 112:438-439.

LAVY, T.L. 1979a. Measurement of 2,4,5-T exposure of forest workers. Report to National Forest Products Association. Washington, D.C.

LAVY, T.L. 1979b. Measuring exposure of humans applying pesticides in the field. Arkansas Farm Research. Jan.-Feb., p. 14.

LAVY, T.L. 1980a. Determination of 2,4-D exposure received by forestry applicators. Report to National Forest Products Association, Washington, D.C.

LAVY, T.L. 1980b. Results of field tests to study human exposure to 2,4,5-T application. Weeds Today, Winter:7-8.

LAVY, T.L., J.S. SHEPARD, and D.C. BOUCHARD. 1980a. Field worker exposure and helicopter spray pattern of 2,4,5-T. Bulletin of Environmental Contamination and Toxicology 24:90-96.

LAVY, T.L., J.S. SHEPARD, and J.D. MATTICE. 1980b. Exposure measurements of applicators spraying (2,4,5-trichlorophenoxy) acetic acid in the forest. Journal of Agriculture and Food Chemistry 28:626-630.

LAVY, T.L., et al. 1982a. (2,4-Dichlorophenoxy) acetic acid exposure received by aerial application crews during forest spray operations. Journal of Agriculture and Food Chemistry 30:375-381.

LAVY, T.L., et al. 1982b. Limiting applicator exposure to pesticides. World Agricultural Aviation, March: 33-37.

\+ LENG, M.L. 1977. Comparative metabolism of phenoxy herbicides in animals. Pages 53-76 in Fate of pesticides in large animals. Edited by G.W. Ivie and H.W. Dorough. Academic Press, New York.

LENG, M.L. 1978. Dose levels misinterpreted. Chemical Engineering News, October 23:65,68.

* LENG, M.L., J.C. RAMSEY, and W.H. BRAUN. 1982. Review of studies with 2,4,5-trichlorophenoxyacetic acid in humans including applicators under field conditions. Pesticide residues and exposure. American Chemical Society Symposium Series 182:133-156.

LEWIS, R.J., Sr., and R.L. TATKEN (eds.). 1980. Registry of toxic effects of chemical substances. U.S. Government Printing Office, Washington, D.C.

\+* LOMMEN, C. 1980. Current literature review on 2,4-D. Environmental Management Division, Montana Department of Agriculture, Great Falls.

\+ LOOS, M.A. 1969. Phenoxyalkanoic acids. Pages 1-49 in Degradation of herbicides. Edited by P.C. Kearney and D.D. Kaufman. Marcel Kekker, Inc., New York.

LUSTENHOUWER, J.W.A., K. OLIE, and D. HUTZINGER. 1980. Chlorinated dibenzo-p-dioxins and related compounds in incinerator effluents: a review of measurements and mechanisms of formation. Chemosphere 9:501-522.

\+ LYNN, G.E. 1965. A review of toxicological information on Tordon herbicides. Down to Earth 20(4):6-8.

MAHLE, N.H., H.S. HIGGINS, and M.E. GETZENDANER. 1977. Search for the presence of 2,3,7,8-tetrachlorodibenzo-p-dioxin in bovine milk. Bulletin of Environmental Contamination and Toxicology 18(2):123-130.

MANTEL, N. 1979. An evaluation of the statistical methods used in EPA's "Report of assessment of a field investigation of six-year spontaneous abortion rates in three Oregon areas in relation to forest 2,4,5-T spray practices" (the Alsea II report). Biostatistics Center, George Washington University, Bethesda, Maryland.

MAUGH, T.H. 1978. Chemical carcinogens: How dangerous are low doses? Science 202:37-41.

MAXWELL, R.C. 1982. Meaning of label signal words. Pesticide Report 43:4-5. Washington State University, Cooperative Extension Service, Pullman, Washington.

MAY, G. 1982. Tetrachlorodibenzo-dioxin: a survey of subjects ten years after exposure. 3rd international symposium on chlorinated dioxins and related compounds, Salzburg, Austria. (Abstract 53)

MCCOLLISTER, D.D., and M.L. LENG. 1969. Toxicology of picloram and safety evaluation of tordon herbicides. Down to Earth 25:5-10.

MCCONNELL, E.E., et al. 1978a. The comparative toxicity of chlorinated dibenzo-p-dioxin in mice and guinea pigs. Toxicology and Applied Pharmacology 44(2):335-356.

MCCONNELL, E.E., J.A. MOORE, and D.W. DALGARD. 1978b. Toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin in rhesus monkeys (Macaca mulatta) following a single oral dose. Toxicology and Applied Pharmacology 43:175-187.

MCNULTY, W.P. 1978. Letter to U.S. EPA, July 27, 1978.

MESELSON, M.S., and P.W. O'KEEFE. 1977. Letter to Congressman Jim Weaver, January 26, 1977.

MESELSON, M.S., P.W. O'KEEFE, and R.W. BAUGHMAN. 1978. The evaluation of possible health hazards from TCDD in the environment. Pages 91-94 in Symposium on the use of herbicides in forestry. Sponsored by the USDA and U.S. EPA, Arlington, Virginia.

* MILBY, T.H., et al. 1980. Potential health effects associated with the use of phenoxy herbicides. Report for the National Forest Products Association. Environmental Health Associates, Inc., Berkeley, California.

MILHAM, S. 1982. Workers exposed to phenoxy herbicides and chlorophenols. Unpublished report, Epidemiology section, Washington Department of Social and Health Services, Olympia, Washington.

MILLER, R.A., L.A. NORRIS, and C.L. HAWKES. 1973. Toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in aquatic organisms. Environmental Health Perspectives Experimental Issue 5:177-186. National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina.

* MINNESOTA DEPARTMENT OF HEALTH. 1978. Assessment of human health risk associated with the use of 2,4-D in forestry management. Division of Environmental Health, Minneapolis, Minnesota.

\+ MONTGOMERY, M.L., and L.A. NORRIS. 1970. A preliminary evaluation of the hazards of 2,4,5-T in the forest environment. USDA Forest Service Research Note PNW-116. Pacific Northwest Forest and Range Experiment Station, Portland, Oregon.

MRAK, E. 1969. Report of the Secretary's Commission on pesticides and their relationship to environmental health. I and II. U.S. Department of Health, Education and Welfare, Washington, D.C.

\+* MULLISON, W.R. 1981. Public concerns about the herbicide 2,4-D. Dow Chemical USA, Agricultural Products Department, Midland, Michigan.

MURRAY, F.J., et al. 1979. Three-generation reproduction study of rats given 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in the diet. Toxicology and Applied Pharmacology 50:241-252.

NADER, R., R. BROWNSTEIN, and J. RICHARD. 1981. Who's poisoning America? Corporate polluters and their victims in the chemical age. Sierra Club Books, San Francisco, California.

NASH, R.G., et al. 1982. Agricultural applicators exposure to 2,4-dichlorophenoxyacetic acid. Pesticide residues and exposure. American Chemical Society Symposium Series 182:119-132.

+* NATIONAL ACADEMY OF SCIENCES. 1974. The effects of herbicides in South Vietnam. Part A. Summary and conclusions. Committee on the effects of herbicides in Vietnam. Washington, D.C.

NATIONAL FOREST PRODUCTS ASSOCIATION. 1981. Forest Chemicals Workbook. 3rd edition. Washington, D.C.

NATIONAL RESEARCH COUNCIL. 1977. Drinking water and health. Safe Drinking Water Committee. National Academy of Sciences, Washington, D.C.

+* NATIONAL RESEARCH COUNCIL OF CANADA. 1974. Picloram: The effects of its use as a herbicide on environmental quality. NRCC 13684. Associate committee on scientific criteria for environmental quality. Ottawa, Canada.

+* NATIONAL RESEARCH COUNCIL OF CANADA. 1978. Phenoxy herbicides - their effects on environmental quality, with accompanying scientific criteria for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). NRCC 16075. Ottawa, Canada.

+* NATIONAL RESEARCH COUNCIL OF CANADA. 1981. Polychlorinated dibenzo-p-dioxins: criteria for their effects on man and his environment. NRCC 18574. Ottawa, Canada.

+* NAU, C.A., and Associates. 1979. Review summaries on 2,4,5-T/TCDD. Report submitted to the U.S. EPA. School of Medicine, Texas Tech University, Lubbock, Texas.

NEAL, R.A., et al. 1982. The toxicokinetics of 2,3,7,8-tetrachlorodibenzo-p-dioxin in mammalian systems. Drug Metabolism Review 13:355-385.

+* NEW SOUTH WALES STATE POLLUTION CONTROL COMMISSION. 1981. Environmental impact of the chlorophenoxy herbicides 2,4,5-T and 2,4-D.

* NEW ZEALAND DEPARTMENT OF HEALTH. 1977. 2,4,5-T and human birth defects.

* NEW ZEALAND DEPARTMENT OF HEALTH. 1979. An evaluation of the "Preliminary report of assessment of a field investigation of six-year spontaneous abortion rates in three Oregon areas in relation to forest 2,4,5-T spray practices." Division of Public Health report. Wellington, New Zealand.

NEWTON, M. 1975. Constructive use of herbicides in forest management. Journal of Forestry 73:329-336.

+ NEWTON, M., and F.N. DOST. 1981. Environmental effects of vegetation management practices on DNR forest lands. State of Washington, Department of Natural Resources, Olympia, Washington.

+* NEWTON, M., and F.B. KNIGHT. 1981. Handbook of weed and insect control chemicals for forest resource managers. Timber Press, Beaverton, Oregon.

+* NEWTON, M., and J.A. NORGREN. 1977. Silvicultural chemicals and protection of water quality. U.S. EPA Report, 910/ 9-77-036. Washington, D.C.

NEWTON, M., and L.A. NORRIS. 1968. Herbicide residues in blacktail deer from forests treated with 2,4,5-T and atrazine. Proceedings of the Western Society of Weed Science 1968:32-34.

+* NEWTON, M., and L.A. NORRIS. 1976. Evaluating short- and long-term effects of herbicides on non-target forest and range biota. Down to Earth 32(3):18-26.

+* NEWTON, M., and L.A. NORRIS. 1981. Potential exposure of humans to 2,4,5-T and TCDD in the Oregon Coast Range. Fundamental and Applied Toxicology 1:339-346.

NEWTON, M., and S.P. SNYDER. 1978. Exposure of forest herbivores to 2,3,7,8 - tetrachlorodibenzo - p - dioxin (TCDD) in areas sprayed with 2,4,5-T. Bulletin of Environmental Contamination and Toxicology 20:743-750.

+ NORRIS, L.A. 1967. Chemical brush control and herbicide residues in the forest environment. Pages 103-123 in Herbicides and vegetation management in forests, ranges and noncrop lands. Symposium Proceedings, Oregon State University, Corvallis.

+ NORRIS, L.A. 1970. Degradation of herbicides in the forest floor. Pages 397-411 in Tree growth and forest soils. Edited by C.T. Youngberg and C.B. Davey. Oregon State University, Corvallis.

+ NORRIS, L.A. 1971a. The behavior of chemicals in the forest. Pages 90-106 in Pesticides, pest control and safety on forest range lands. Proceedings, short course for pesticide applicators. Oregon State University, Corvallis.

+ NORRIS, L.A. 1971b. Chemical brush control: assessing the hazard. Journal of Forestry 69:715-720.

NORRIS, L.A. 1974. The behavior and fate of organic arsenical herbicides in the forest: final report on cooperative studies. USDA Forest Service. Pacific Northwest Forest and Range Experiment Station, Corvallis, Oregon.

+ NORRIS, L.A. 1977. The behavior of 2,4,5-T and TCDD in the environment. Society of American Foresters, Proceedings:252-255.

NORRIS, L.A. 1980a. Herbicide residues in air, Alsea Basin - 1977. USDA Forest Service. Pacific Northwest Forest and Range Experiment Station, Corvallis, Oregon.

NORRIS, L.A. 1980b. TCDD in fish from Oregon forest streams. Unpublished office report. USDA Forest Service. Pacific Northwest Forest and Range Experiment Station, Corvallis, Oregon. (Also presented in direct testimony, FIFRA docket Nos. 415 et al. The Dow Chemical Company et al. vs. U.S. EPA, Washington, D.C.)

NORRIS, L.A. 1980c. TCDD persistence in low light intensities. Unpublished office report. USDA Forest Service. Pacific Northwest Forest and Range Experiment Station, Corvallis, Oregon. (Also presented in direct testimony, FIFRA docket Nos. 415 et al. The Dow Chemical Company et al. vs. U.S. EPA, Washington, D.C.)

+ NORRIS, L.A. 1981. The movement, persistence, and fate of the phenoxy herbicides and TCDD in the forest. Residue Reviews 80:66-135.

NORRIS, L.A., and R.A. MILLER. 1974. The toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in guppies (Poecilia reticulatus Peters). Bulletin of Environmental Contamination and Toxicology 12(1):76-80.

NORRIS, L.A., M.L. MONTGOMERY, and E.R. JOHNSON. 1977. The persistence of 2,4,5-T in a Pacific Northwest forest. Weed Science 25:417-422.

+ NORRIS, L.A., and D.G. MOORE. 1970. The entry and fate of forest chemicals in streams. Pages 138-158 in Forest land uses and stream environment. Symposium Proceedings, Oregon State University, Corvallis.

NORRIS, L.A., and J. PIEROVICH. 1978. Thermal conversion of 2,4,5-T to TCDD: analysis of the problem, exhibit 6. In Vegetation management with herbicides. Final environmental statement. USDA Forest Service, Pacific Northwest Region, Portland, Oregon.

NUNN, D.M. 1983. Decision concerning proposed use of 2,4-D and 2,4,5-T by Nova Scotia Forest Industries, Ltd. Trial Division, Supreme Court of Nova Scotia, Canada. S. SN. No. 02555.

OTT, M.G., B.B. HOLDER, and R.D. OLSON. 1980. A mortality analysis of employees engaged in the manufacture of 2,4,5-Trichlorophenoxyacetic acid. Journal of Occupational Medicine 22:47-50.

+ PALMER, J.S. 1972. Toxicity of 45 organic herbicides to cattle, sheep and chickens. USDA, Agricultural Research Service, Production Research Report 137. Washington, D.C.

PALMER, J.S., D.E. CLARK, and L.M. HUNT. 1964. Toxicological effects of silvex on yearling cattle. Journal of the American Veterinary Medical Association 144:750-755.

PALMER, J.S., and R.D. RADELEFF. 1964. The toxicologic effects of certain fungicides and herbicides on sheep and cattle. Annals of the New York Academy of Science 111:729-736.

+ PALMER, J.S., and R.D. RADELEFF. 1969. The toxicity of some organic herbicides to cattle, sheep and chickens. USDA, Agricultural Research Service, Production Research Report 106. Washington, D.C.

PAYNTER, O.E., et al. 1960. Toxicology of dalapon sodium (2,2-dichloropropionic acid, sodium salt). Journal of Agricultural and Food Chemistry 8:47-51.

PETERS, J.W., and R.M. COOK. 1973. Effects of atrazine on reproduction in rats. Bulletin of Environmental Contamination and Toxicology. 9:301-304.

+ PIONKE, H.B., and G. CHESTERS. 1973. Pesticide - sediment - water interactions. Journal of Environmental Quality 2:29-45.

POCCHIARI, F., et al. 1983. Environmental impact of the accidental release of tetrachlorodibenzo-p-dioxin (TCDD) at Seveso (Italy). Pages 5-35 in Accidental exposure to dioxins. Human health aspects. Edited by F. Coulston and F. Pocchiari. Academic Press, New York.

* PRESIDENT'S SCIENCE ADVISORY COMMITTEE. 1971. Report on 2,4,5-T. Panel on Herbicides. U.S. Government Printing Office, Washington, D.C.

* QUEENSLAND CABINET. 1981. Report on 2,4-D and 2,4,5-T. Land Administration Commission, Queensland, Australia.

+* RAMEL, C. (ed.) 1978. Chlorinated phenoxy acids and their dioxins. Ecology Bulletin/NFR 27:302. Swedish Natural Science Research Council, NFR, Stockholm, Sweden.

RAMSEY, J.C., T.L. LAVY, and W.H. BRAUN. 1979. Exposure of forest workers to 2,4,5-T: calculated dose levels. Report submitted to the U.S. EPA as a supplemental response to the "Notice of rebuttable presumption against registration and continued registration of pesticide products containing 2,4,5-T." Dow Chemical USA, Midland, Michigan.

RAMSEY, J.C., et al. 1980. Dose levels of 2,4-D in forest workers. Determination of 2,4-D exposure received by forestry applicators. Project Completion Report to National Forest Products Association, Washington, D.C.

REGGIANI, G. 1977. Medical problems raised by the TCDD contamination in Seveso, Italy. 5th international conference on occupational health in the chemical industry (Medichem), San Francisco, California.

* REGGIANI, G. 1978. The estimation of the TCDD toxic potential in the light of the Seveso accident. 20th congress of the European Society for Toxicology, West Berlin, Germany.

REGGIANI, G. 1980. Acute human exposure to TCDD in Seveso, Italy. Journal of Toxicology and Environmental Health 6:27-43.

+* REGGIANI, G. 1981. Toxicology of 2,3,7,8 - tetrachlorodibenzo - p - dioxin (TCDD): Short review of its formation, occurrence, toxicology, and kinetics, discussing human health effects, safety measures, and disposal. Regulatory Toxicology and Pharmacology 1:211-243.

RIIHIMAKI, V., et al. 1978. Symptomatology, morbidity and mortality experience of chlorinated phenoxy acid herbicide (2,4-D and 2,4,5-T) sprayers in Finland: a clinical and epidemiological study. Institute of Occupational Health, Helsinki, Finland.

RIIHIMAKI, V., S. ASP, and S. HERNBERG. 1982. Mortality of

2,4-dichlorophenoxyacetic acid and 2,4,5-trichlorophenoxyacetic acid herbicide applicators in Finland. 3rd international symposium on chlorinated dioxins and related compounds, Salzburg, Austria. (Abstract 54)

ROAN, C.C. 1980. An investigation of the possible effects of pesticide exposures on reproductive mortality and morbidity. Part 1. Preliminary report: Comparisons between populations of agricultural pilots and their siblings who are not occupationally exposed to pesticides. Report submitted to the National Agricultural Aviation Association. Hopes Consulting, Inc., Aberdeen, Maryland.

ROLL, R. 1971. Untersuchungen uber die teratogene. Wirkung von 2,4,5-T bie Mausen. Food and Cosmetics Toxicology 9:671-676.

ROSE, J.Q., et al. 1976. The fate of 2,3,7,8 - tetrachlorodibenzo - p - dioxin following single and repeated oral doses to the rat. Toxicology and Applied Pharmacology 36:209-226.

+ ROWE, V.K., and T.A. HUMAS. 1954. Summary of toxicological information on 2,4-D and 2,4,5-T type herbicides and an evaluation of the hazards to livestock associated with their use. American Journal of Veterinary Research 15:622-629.

* ROYAL COMMISSION OF INQUIRY INTO THE USE OF PESTICIDES AND HERBICIDES. 1975. Final report to the Commissioners. Vol. 1. Province of British Columbia, Canada.

+* ROYAL SWEDISH ACADEMY OF SCIENCES. 1977. Chlorinated phenoxy acids and their dioxins. Mode of action, health risks, and environmental effects. Conclusions and recommendations. Stockholm, Sweden.

SAUERHOFF, M.W., et al. 1977. Fate of silvex following oral administration to humans. Journal of Toxicology and Environmental Health 3:941-952.

+ SCHWETZ, B.A. 1977. Toxicology of phenoxy acid herbicides. Society of American Foresters, Proceedings: 256-260.

+ SCHWETZ, B.A., et al. 1973. Toxicology of chlorinated dibenzo-p-dioxins. Environmental Health Perspectives Experimental Issue 5:87-99. National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina.

SELL, C.R., J.C. MAITLEN, and W.A. ALLER. 1982. Perspiration as an important physiological pathway for the elimination of 2,4-dichlorophenoxyacetic acid from the human body. Paper delivered at the American Chemical Society meeting, Las Vegas, Nevada.

SHADOFF, L.A., R.A. HUMMEL, and L. LAMPARSKI. 1977. A search for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in an environment exposed annually to 2,4,5-trichlorophenoxy-acetic acid ester (2,4,5-T) herbicides. Bulletin of Environmental Contamination and Toxicology 18(4):478-485.

+* SHEARER, R., and M. HALTER. 1980. Literature reviews of four selected herbicides: 2,4-D, dichlobenil, diquat and endothall. Water Quality Planning Division, Municipality of Metropolitan Seattle, Washington.

SHEPARD, B.M. 1982. A review of ongoing epidemiologic research in the United States on the phenoxy herbicides and chlorinated dioxin contaminants. 3rd international symposium on chlorinated dioxins and related compounds, Salzburg, Austria. (Abstract 49)

SINGER, J. 1980. Pesticide safety: guidelines for personnel protection. USDA Forest Service, Methods Application Group, Davis, California.

SMITH, A.H. 1979. Seasonal analysis of Oregon data on spontaneous abortions and 2,4,5-T spraying. Paper presented at ANZERCH, Annual Conference, Dunedin, New Zealand.

SMITH, A.H., et al. 1981. Preliminary report of reproductive out-

comes among pesticide applicators using 2,4,5-T. New Zealand Medical Journal 680:177-179.

SMITH, A.H., et al. 1982a. Congenital defects and miscarriages among New Zealand 2,4,5-T sprayers. Archives of Environmental Health 37(4):197-200.

SMITH, A.H., et al. 1982b. The New Zealand soft tissue sarcoma case-control study: interview findings concerning phenoxyacetic acid exposure. 3rd international symposium on chlorinated dioxins and related compounds, Salzburg, Austria.

SMITH, F.A., et al. 1978. Three-generation reproductive study in rats ingesting 2,4,5-trichlorophenoxyacetic acid in the diet. Toxicology and Applied Pharmacology 45:293.

SPARSCHU, G.L., et al. 1971. Study of the effects of high levels of 2,4,5-trichlorophenoxyacetic acid on fetal development in the rat. Food and Cosmetics Toxicology 9:527-530.

STEHL, R.H., and L.L. LAMPARSKI. 1977. Combustion of several 2,4,5-trichlorophenoxy compounds: formation of 2,3,7,8 - tetrachlorodibenzo - p - dioxin. Science 197:1008-1009.

* STEVENS, K.M. 1981. Agent Orange toxicity: a quantitative perspective. Human Toxicology 1:31-39.

STREISINGER, G. 1978. Assessment of hazards posed by TCDD. Pages 101-103 in Symposium on the use of herbicides in forestry. Sponsored by the USDA and U.S. EPA. Arlington, Virginia.

SUN, M. 1983. Missouri's costly dioxin lesson. Science 219:367-369.

SUSKIND, R.R. 1982. Long-term health effects of exposure to 2,4,5-T and/or its contaminants. 3rd international symposium on chlorinated dioxins and related compounds, Salzburg, Austria. (Abstract 52)

THOMAS, H.F. 1980. 2,4,5-T use and congenital malformation rates in Hungary. Lancet 2:214-215.

TOWNSEND, J.C., et al. 1982. Survey of reproductive events of wives of employees exposed to chlorinated dioxins. American Journal of Epidemiology 115(5):695-713.

TUCHMANN-DUPLESSIS, H. 1977. Problemes embryologiques poses par l'accident de Seveso. Le Concours Medical 44:6889-6897.

TUCHMANN-DUPLESSIS, H. 1983. Concluding discussion. Page 282 in Accidental exposure to dioxins. Human health aspects. Edited by F. Coulston and F. Pocchiari. Academic Press, New York.

+* TURNER, D.J. 1977. The safety of the herbicides 2,4-D and 2,4,5-T. British Forestry Commission Bulletin 57.

+* UNITED KINGDOM ADVISORY COMMITTEE ON PESTICIDES. 1979. Review of the safety for use in the U.K. of the herbicide 2,4,5-T. Ministry of Agriculture, Fisheries and Food, London, England.

+* UNITED KINGDOM ADVISORY COMMITTEE ON PESTICIDES. 1980. Further review of the safety for use in the U.K. of the herbicide 2,4,5-T. Ministry of Agriculture, Fisheries and Food, London, England.

+* UNITED NATIONS, FOOD AND AGRICULTURE ORGANIZATION. 1980. 2,4,5-T Monograph. Data and recommendations of the joint meeting of the F.A.O. panel of experts on pesticide residues in food and the environment and the W.H.O. expert group on pesticide residues. Document PB 398. Department of Primary Industry, Canberra, Australia.

UPTON, A.C. 1982. The biological effects of low-level ionizing radiation. Scientific American 246 (2):41-49.

+* U.S. DEPARTMENT OF AGRICULTURE. 1978. Vegetation management with herbicides. Final environmental statement. USDA Forest Service, Pacific Northwest Region, Portland, Oregon.

+ U.S. DEPARTMENT OF AGRICULTURE. 1979. The biologic and economic assessment of 2,4,5-T. Technical Bulletin 1671. USDA, Washington, D.C.

+* U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE. 1969. Report of the Secretary's commission on pesticides and their relationship to environmental health. Washington, D.C.

+* U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE. 1973. Proceedings of conference on dibenzodioxins and dibenzofurans. Environmental Health Perspectives.

+* U.S. ENVIRONMENTAL PROTECTION AGENCY. 1971. Report of the Advisory Committee on 2,4,5-T to the Administrator of the Environmental Protection Agency.

+* U.S. ENVIRONMENTAL PROTECTION AGENCY. 1977. Dioxin: Position Document. Dioxin Working Group.

U.S. ENVIRONMENTAL PROTECTION AGENCY. 1978a. 2,4,5-T pesticide being reviewed by EPA. Environmental News, April 12, 1978.

+* U.S. ENVIRONMENTAL PROTECTION AGENCY. 1978b. 2,4,5-T: Position Document 1. Federal Register 43(78):17118-17157.

+* U.S. ENVIRONMENTAL PROTECTION AGENCY. 1979a. Final determination concerning the rebuttable presumptions against registration for certain uses of pesticide products containing 2,4,5-T and Silvex and notice of intent to hold a hearing. Federal Register 44(241): 72316-72341.

+* U.S. ENVIRONMENTAL PROTECTION AGENCY. 1979b. Preliminary determination concerning the rebuttable presumption against registration of certain uses of pesticide products containing 2,4,5-trichlorophenoxyacetic acid (2,4,5-T); Hearing; Availability of position document. Federal Register 44(138): 41531-41543.

U.S. ENVIRONMENTAL PROTECTION AGENCY. 1979c. Report of assessment of a field investigation of six-year spontaneous abortion rates in three Oregon areas in relation to forest 2,4,5-T spray practices. Epidemiologic Studies Program, Human Effects Monitoring Branch, Benefits and Fielc Studies Division, OPP, OTS, EPA. Washington, D.C.

+* U.S. ENVIRONMENTAL PROTECTION AGENCY. 1979d. Review of notices of intent to hold FIFRA section 6(b)(2) hearing on 2,4,5-T and silvex. Report submitted to Deputy Assistant Administrator of the EPA by Scientific Advisory Panel.

+* U.S. ENVIRONMENTAL PROTECTION AGENCY. 1979e. Suspensions and notices of intent to cancel 2,4,5-T and silvex. Federal Register 44(52): 15874-15920.

U.S. ENVIRONMENTAL PROTECTION AGENCY. 1980a. Dioxin not detected in mother's milk. EPA Environmental News. R-10.

* U.S. ENVIRONMENTAL PROTECTION AGENCY. 1980b. EPA asks for more information on herbicide 2,4-D. EPA Environmental News. R-75.

U.S. ENVIRONMENTAL PROTECTION AGENCY. 1981. Canada to phase out some 2,4-D products. Office of Pesticides and Toxic Substances. Weekly report from OPP V(4).

U.S. ENVIRONMENTAL PROTECTION AGENCY. 1982a. Picloram. Office of Pesticides and Toxic Substances.

U.S. ENVIRONMENTAL PROTECTION AGENCY. 1982b. 2,4-D Fact Sheets. Office of Pesticides and Toxic Substances.

U.S. ENVIRONMENTAL PROTECTION AGENCY. 1983. 2,4,5-T and silvex products; intent to cancel registrations of pesticide products containing 2,4,5-T and silvex; revocation of notices of intent to hold a hearing to determine whether certain uses of 2,4,5-T or silvex should be cancelled. Federal Register 48(202):48434-48436.

VAN HOUDT, J.J., L.G. FRANSMAN, and J.J. STRIK. 1982. Epidemiological case control study in personnel exposed to 2,4,5-T. Results of a survey conducted by the State Occupational Health Service, the Netherlands.

VELSICOL CHEMICAL COMPANY. 1981. Untitled, toxicological summary for dicamba and dicamba-related materials. Chicago, Illinois.

VETTORAZZI, G. 1979. International regulatory aspects for pesticide chemicals. Vol. I. Toxicity profiles. CRC Press, Inc., Boca Raton, Florida.

VOS, J.G., and J.A. MOORE. 1974. Suppression of cellular immunity in rats and mice by maternal treatment with 2,3,7,8-tetrachlorodibenzo-p - dioxin. International Archives of Allergy and Applied Immunology 47:777-794.

VOS, J.G., J.A. MOORE, and J.G. ZINKL. 1973. Effect of 2,3,7,8-tetrachlorodibenzo-p-dioxin on the immune system of laboratory animals. Health Perspectives Experimental Issue 5:149-162. National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina.

+* WAGNER, S.L. 1981. Clinical toxicology of agricultural chemicals. Environmental Health Sciences Center, Oregon State University, Corvallis.

WAGNER, S.L., et al. 1979. A scientific critique of the EPA Alsea II study and report. Environmental Health Sciences Center, Oregon State University, Corvallis.

+ WALSTAD, J.D. 1976. Weed control for better southern pine management. Southern Forestry Research Center, Weyerhaeuser Company, Hot Springs, Arkansas.

WEED SCIENCE SOCIETY OF AMERICA. 1983. Herbicide Handbook. 5th edition. Champaign, Illinois.

* WHEATLEY, G.A. 1973. Pesticides in the atmosphere. Pages 365-408 in Environmental pollution by pesticides. Edited by G.A. Edwards. Plenum, New York.

WILLIAMS, M. 1983. Reproduction not affected by pesticide exposure NAWG study shows. Agricultural Aviation 10(11): 46,48-50.

WINDHOLZ, M. (ed.). 1976. The Merck Index. 9th edition. Merck and Company, Inc., Rahway, New Jersey.

WOODS, J.S. 1979. Review of the preliminary report of assessment of a field investigation of six-year spontaneous abortion rates in three Oregon areas in relation to forest 2,4,5-T spray practices (Alsea II study). Battelle Human Affairs Research Centers, Seattle, Washington.

WOOLSON, E.A., et al. 1973. Dioxin residues in lakeland sand and bald eagle samples. Advances in Chemistry Series 120:112.

* WORLD HEALTH ORGANIZATION. 1978. Long-term hazards of polychlorinated dibenzodioxins and polychlorinated dibenzofurans. World Health Organization International Agency for Research on Cancer, Lyons, France. No. 78/001.

+ YOUNG, A.L., et al. 1976. Fate of 2,3,7,8 - tetrachlorodibenzo - p - dioxin (TCDD) in the environment: summary and decontamination recommendations. USAFATR-76-18. Department of Chemistry and Biological Sciences, USAF Academy, Colorado Springs, Colorado.

+* YOUNG, A.L., et al. 1978. The toxicology, environmental fate, and human risk of herbicide Orange and its associated dioxin. USAF Occupational and Environmental Health Laboratory Technical Report TR-78-92. Brooks Air Force Base, Texas.

YOUNG, J.F., and T.J. HALEY. 1977. Pharmacokinetic study of a patient intoxicated with 2,4-dichlorophenoxyacetic acid and 2-methoxy-3,6-

dichlorobenzoic acid. Clinical Toxicology 11(5):489-500.

ZACK, J.A., and R.R. SUSKIND. 1980. The mortality experience of workers exposed to tetrachlorodibenzodioxin in a trichlorophenol process accident. Journal of Occupational Medicine 22(1):11-14.

APPENDICES

APPENDIX 1

PROCEDURES FOR CALCULATING HYPOTHETICAL AMOUNTS OF VARIOUS SUBSTANCES CONTAINING HERBICIDES THAT COULD BE INGESTED WITHOUT EXCEEDING CERTAIN TOXICOLOGICAL POINTS OF REFERENCE

A simple formula can be used to determine the hypothetical amounts of various substances, ranging from commercial herbicide concentrates to contaminated animal meat, that could be ingested without exceeding certain toxicological points of reference, such as the acute oral LD_{50} (lethal dose of a chemical which induces 50% mortality in a test population within a short period of time following ingestion) and the chronic or subchronic oral NOEL (the highest dose which causes no observable effect in test animals following long term intake of a chemical, or intake during a critical stage of development). Oral intake is used in this analysis, since chemicals are usually more potent via this route of exposure than by dermal absorption. The formula and an explanation of its components are given below, followed by a series of example situations.

Formula

$$X = \frac{W \times T}{C}$$

where:

X = hypothetical amount that can be ingested without exceeding the LD_{50} (single dose) or NOEL (daily dose);

W = body weight of animal involved;

T = toxicological points of reference [e.g., LD_{50} or NOEL] expressed in milligrams of chemical per kilogram of body weight (i.e., mg/kg);

C = concentration of herbicide active ingredient (ai) in the substance internalized.

Depending upon the substance internalized, the general parameters in the above formula have the following specific dimensions:

Substance	X	W	T		C
			LD_{50} or NOEL		
1. Commercial herbicide product					
a. liquid formulations (e.g., emulsifiable concentrate, soluble concentrate, flowable powder concentrate)	mL product	kg	mg/kg	mg/kg/day	mg ai/mL product
b. dry formulations (e.g., wettable powders, soluble powders, granulars)	g product	kg	mg/kg	mg/kg/day	mg ai/g product

2. Aqueous spray mixture	mL spray	kg	mg/kg	mg/kg/day	mg ai/mL spray
3. Environmental samples					
a. stream water	L water	kg	mg/kg	mg/kg/day	ppm (mg ai/L)
b. ambient air	m^3 air	kg	mg/kg	mg/kg/day	mg ai/m^3 air
c. animal meat	kg meat	kg	mg/kg	mg/kg/day	ppm (mg ai/kg)

SITUATION 1 - COMMERCIAL HERBICIDE PRODUCT - LIQUID FORMULATION

Given: An emulsifiable concentrate of a commercial herbicide product containing 45% ai (i.e., 450 mg ai/mL product);

The herbicide has an acute oral LD_{50} of 500 mg/kg and a chronic or subchronic oral NOEL of 10 mg/kg/day;

A person weighing 132 lb (60 kg).

Question 1: How much of the above product contains the equivalent of the LD_{50}?

Solution:

$$X = \frac{60 \text{ kg} \times 500 \text{ mg/kg}}{450 \text{ mg ai/mL product}}$$

$$X = 66.7 \text{ mL product}$$

$$\approx 4.5 \text{ tbsp product}$$

Question 2: How much of the above product can be ingested daily without exceeding the NOEL?

Solution:

$$X = \frac{60 \text{ kg} \times 10 \text{ mg/kg/day}}{450 \text{ mg ai/mL product}}$$

$$X = 1.33 \text{ mL product/day}$$

$$\approx 0.27 \text{ tsp product/day}$$

(Note--With the application of a 100-fold safety factor, the amount would be 0.0133 mL product/day, or 0.2 drops/day.)

SITUATION 2 - COMMERCIAL HERBICIDE PRODUCT - DRY FORMULATION

Given: A wettable powder formulation of a commercial herbicide product containing 80% ai (i.e., 800 mg ai/g product);

The herbicide has an acute oral LD_{50} of 500 mg/kg and a chronic or subchronic oral NOEL of 10 mg/kg/day;

A person weighing 132 lb (60 kg).

Question 1: How much of the above product contains the equivalent of the LD_{50}?

Solution:

$$X = \frac{60 \text{ kg} \times 500 \text{ mg/kg}}{800 \text{ mg ai/g product}}$$

$$X = 37.5 \text{ g product}$$

$$\approx 1.3 \text{ oz product}$$

Question 2: How much of the above product can be ingested daily without exceeding the NOEL?

Solution:

$$X = \frac{60 \text{ kg} \times 10 \text{ mg/kg/day}}{800 \text{ mg ai/g product}}$$

$$X = 0.75 \text{ g product/day}$$

(Note--With the application of a 100-fold safety factor, the amount would be 0.0075 g product/day.)

SITUATION 3 - AQUEOUS SPRAY MIXTURE

Given: An aqueous spray mixture of an herbicide containing 2 lb ai/10 gal spray (24 mg ai/mL spray);

The herbicide has an acute oral LD_{50} of 500 mg/kg and a chronic or subchronic oral NOEL of 10 mg/kg/day;

A person weighing 132 lb (60 kg).

Question 1: How much of the above spray mixture contains the equivalent of the LD_{50}?

Solution:

$$X = \frac{60 \text{ kg} \times 500 \text{ mg/kg}}{24 \text{ mg ai/mL spray mixture}}$$

$$X = 1{,}250 \text{ mL spray mixture}$$

$$\approx 1.3 \text{ qt spray mixture}$$

Question 2: How much of the above spray mixture can be ingested daily without exceeding the NOEL?

Solution:

$$X = \frac{60 \text{ kg} \times 10 \text{ mg/kg/day}}{24 \text{ mg ai/mL spray mixture}}$$

$$X = 25 \text{ mL spray mixture/day}$$

$$\approx 1.7 \text{ tbsp spray mixture/day}$$

(Note--With the application of a 100-fold safety factor, the amount would be 0.25 mL spray mixture/day, or 4 drops spray mixture/day.)

SITUATION 4 - STREAM WATER CONTAINING HERBICIDE

Given: A stream containing 0.1 ppm of herbicide (i.e., 0.1 mg ai/L stream water). (Note - This amount represents an actual "worst case" situation. See Appendix 2 for details);

The herbicide has an acute oral LD_{50} of 500 mg/kg and a chronic or subchronic oral NOEL of 10 mg/kg/day;

A person weighing 132 lb (60 kg).

Question 1: How much stream water contains the equivalent of the LD_{50}?

Solution:

$$X = \frac{60 \text{ kg} \times 500 \text{ mg/kg}}{0.1 \text{ mg ai/L stream water}}$$

$$X = 300{,}000 \text{ L stream water}$$

$$\approx 79{,}200 \text{ gal stream water}$$

Question 2: How much of the stream water can be ingested daily without exceeding the NOEL?

Solution:

$$X = \frac{60 \text{ kg} \times 10 \text{ mg/kg/day}}{0.1 \text{ mg ai/L stream water}}$$

$$X = 6{,}000 \text{ L stream water/day}$$

$$\approx 1{,}584 \text{ gal stream water/day}$$

(Note--With the application of a 100-fold safety factor, the amount would be 60 L stream water/day, or 15.8 gal stream water/day.)

SITUATION 5 - AMBIENT AIR CONTAINING HERBICIDE

Given: Ambient air near a sprayed area containing 1.0 ug ai/m^3 (0.001 mg ai/m^3) of an herbicide. (Note - This amount represents an "upper limit" as estimated by Newton and Norris 1981);

The herbicide has an acute oral LD_{50} of 500 mg/kg and a chronic or subchronic oral NOEL of 10 mg/kg/day;

A person weighing 132 lb (60 kg).

Question 1: How much air contains the equivalent of the LD_{50}?

Solution:

$$X = \frac{60 \text{ kg} \times 500 \text{ mg/kg}}{0.001 \text{ mg ai/m}^3}$$

$$X = 30 \times 10^6 \text{ m}^3 \text{ air}$$

$$\approx 39.3 \times 10^6 \text{ yd}^3 \text{ air}$$

Question 2: How much air can be inhaled daily without exceeding the NOEL?

Solution:

$$X = \frac{60 \text{ kg} \times 10 \text{ mg/kg/day}}{0.001 \text{ mg ai/m}^3}$$

$$X = 600{,}000 \text{ m}^3 \text{ air/day}$$

$$\approx 786{,}000 \text{ yd}^3 \text{ air/day}$$

(Note--With the application of a 100-fold safety factor, the amount would be 6,000 m^3/day, or 7,860 yd^3/day.)

SITUATION 6 - ANIMAL MEAT CONTAINING HERBICIDE

Given: Animal meat containing 0.1 ppm (i.e., 0.1 mg ai/kg meat) of herbicide (Note - This amount exceeds the maximum concentration reported by Newton and Norris 1981);

The herbicide has an acute oral LD_{50} of 500 mg/kg and a chronic or subchronic oral NOEL of 10 mg/kg/day;

A person weighing 132 lb (60 kg).

Question 1: How much meat contains the equivalent of the LD_{50} level?

Solution:

$$X = \frac{60 \text{ kg} \times 500 \text{ mg/kg}}{0.1 \text{ mg ai/kg meat}}$$

$$X = 300{,}000 \text{ kg meat}$$

$$\approx 661{,}380 \text{ lb meat}$$

Question 2: How much meat can be ingested daily without exceeding the NOEL?

Solution:

$$X = \frac{60 \text{ kg} \times 10 \text{ mg/kg/day}}{0.1 \text{ mg ai/kg meat}}$$

$$X = 6{,}000 \text{ kg meat/day}$$

$$\approx 13{,}228 \text{ lb meat/day}$$

(Note--With the application of a 100-fold safety factor, the amount would be 60 kg meat/day, or 132 lb meat/day.)

APPENDIX 2

HERBICIDE CONCENTRATIONS IN STREAM WATER

I. HYPOTHETICAL MAXIMUM CONCENTRATION

a. Assumptions:

Application rate of 2 kg herbicide/ha (≈ 2 lb/A)

Direct application to a shallow stream 10 cm (≈ 4 in.) deep, with complete mixing of the chemical throughout that depth.

(Note - Current forest practice rules in Oregon and many other states are designed to prevent the direct application of herbicides to waterways and areas of open water by requiring buffer strips and other precautions.)

b. Maximum concentration that would be expected under the conditions described above:

$2\ kg/ha = 2\ kg/10{,}000\ m^2$

$= 2\ kg/10^4\ m^2$

$= 2\ kg/10^8\ cm^2 \times 10\ cm\ depth = 2\ kg/10^9\ cm^3$

$= 2\ kg/10^9\ g$

$= 2\ kg/10^6\ kg$

$= 2\ ppm$

2. ACTUAL DETERMINATIONS FROM WATER MONITORING

a. Concentrations of phenoxy herbicides such as 2,4,5-T greater than 0.01 ppm are seldom encountered in streams following conventional application in forest management (Norris 1977, 1981). Historically, concentrations as high as 0.1 ppm have been detected, but these occurred before the advent of strict regulations governing application procedures. Most water samples collected nowadays do not contain detectable (> 1 ppb) amounts. Any minute amounts which are present rapidly dissipate due to dilution, adsorption, and breakdown.

b. Recommended maximum concentrations of certain herbicides permitted in streams of various size and use can be found in an EPA publication (Table 3, Newton and Norgren 1977), or in a recent handbook (Table 5-4, Newton and Knight 1981). For example, the drinking water standards for 2,4-D established by the U.S. Public Health Service allow a lifetime consumption of water containing up to 100 ppb of 2,4-D. In general, the amounts of herbicide actually detected in forest streams have been well below recommended concentration maxima for drinking and irrigation purposes.

APPENDIX 3

PROCEDURES FOR CALCULATING HYPOTHETICAL AMOUNTS OF VARIOUS SUBSTANCES CONTAINING TCDD THAT COULD BE INGESTED WITHOUT EXCEEDING CERTAIN TOXICOLOGICAL POINTS OF REFERENCE

As in Appendix 1, a simple formula can be used to determine the hypothetical amounts of various substances containing TCDD (as a result of 2,4,5-T use) that could be ingested without exceeding certain toxicological points of reference. The formula is identical to that presented in Appendix 1, except that the dimensions for many of the parameters are different, due to the minute quantities of TCDD involved.

The specific dimensions for each of these parameters are given below:

Substance	X	W	T	C
			LD_{50} or NOEL	
1. Commercial formulation of 2,4,5-T (e.g., liquid emulsifiable concentrate, water-soluble amine concentrate)	mL product	kg	µg/kg µg/kg/day	µg TCDD/mL product
2. Aqueous spray mixture made from 2,4,5-T	L spray	kg	µg/kg µg/kg/day	µg TCDD/L spray
3. Environmental samples				
a. stream water	L water	kg	µg/kg µg/kg/day	µg TCDD/L water
b. ambient air	m^3 air	kg	µg/kg µg/kg/day	µg TCDD/m^3 air
c. animal meat	kg meat	kg	µg/kg µg/kg/day	µg TCDD/kg meat

SITUATION 1 - COMMERCIAL HERBICIDE PRODUCT CONTAINING TCDD

Given: An emulsifiable concentrate of 2,4,5-T herbicide (e.g., Esteron® 245) containing 45% acid equivalent (ae) of 2,4,5-T (0.45 g 2,4,5-T/mL product) which in turn contains 0.01 ppm TCDD (i.e., 0.0045 µg TCDD/mL product);

TCDD has an acute oral LD_{50} of 0.6 µg/kg and a chronic or subchronic oral NOEL of 0.001 µg/kg/day;

A person weighing 132 lb (60 kg).

Question 1: How much of the above product contains the equivalent of the LD_{50} for TCDD?

Solution:

$$X = \frac{60\ kg \times 0.6\ \mu g/kg}{0.0045\ \mu g\ TCDD/mL\ product}$$

$$X = 8{,}000\ mL\ product$$

$$\approx 2.1\ gal\ product$$

Question 2: How much of the above product can be ingested daily without exceeding the NOEL for TCDD?

Solution:

$$X = \frac{60 \text{ kg} \times 0.001 \text{ µg/kg/day}}{0.0045 \text{ µg TCDD/mL product}}$$

$$X = 13.3 \text{ mL product/day}$$

$$\approx 2.7 \text{ tsp product/day}$$

(Note--With the application of a 100-fold safety factor, the amount would be 0.133 mL product/day, or 2.1 drops product/day.)

SITUATION 2 - AQUEOUS SPRAY MIXTURE CONTAINING TCDD

Given: A commercial product of 2,4,5-T herbicide containing 0.01 ppm TCDD which is diluted with water to form a spray mixture containing 2 lb ae 2,4,5-T/10 gal spray mixture (24 g ae 2,4,5-T/L spray mixture), and which therefore contains 0.24 µg TCDD/L spray mixture;

TCDD has an acute oral LD_{50} of 0.6 µg/kg and a chronic or subchronic oral NOEL of 0.001 µg/kg/day;

A person weighing 132 lb (60 kg).

Question 1: How much of the above spray mixture contains the equivalent of the LD_{50} for TCDD?

Solution:

$$X = \frac{60 \text{ kg} \times 0.6 \text{µg/kg}}{0.24 \text{ µg TCDD/L spray mixture}}$$

$$X = 150 \text{ L spray mixture}$$

$$\approx 39.6 \text{ gal spray mixture}$$

Question 2: How much of the above spray mixture can be ingested daily without exceeding the NOEL for TCDD?

Solution:

$$X = \frac{60 \text{ kg} \times 0.001 \text{ µg/kg/day}}{0.24 \text{ µg TCDD/L spray mixture}}$$

$$X = 0.25 \text{ L spray mixture/day}$$

$$\approx 1 \text{ cup spray mixture/day}$$

(Note--With the application of a 100-fold safety factor, the amount would be 2.5 mL spray mixture/day, or 0.5 tsp spray mixture/day.)

SITUATION 3 - STREAM WATER CONTAINING TCDD

Given: A commercial herbicide product of 2,4,5-T containing 0.01 ppm TCDD which is applied to a stream resulting in a 2,4,5-T concentration in the stream water of 0.1 ppm (0.1×10^{-6} g ae 2,4,5-T/mL stream water). (Note - This amount represents an actual "worst case" situation. See Appendix 2 for details.) Therefore, the maximum amount of TCDD present would be 1.0×10^{-9} µg TCDD/mL stream water, or 1.0×10^{-6} µg TCDD/L stream water;

TCDD has an acute oral LD_{50} of 0.6 µg/kg and a chronic or subchronic oral NOEL of 0.001 µg/kg/day;

A person weighing 132 lb (60 kg).

Question 1: How much stream water contains the equivalent of the LD_{50} for TCDD?

Solution:

$$X = \frac{60 \text{ kg} \times 0.6 \mu\text{g/kg}}{1.0 \times 10^{-6} \mu\text{g TCDD/L stream water}}$$

$$X = 36 \times 10^{6} \text{ L spray mixture}$$

$$\approx 9.5 \times 10^{6} \text{ gal stream water}$$

Question 2: How much stream water can be ingested daily without exceeding the NOEL for TCDD?

Solution:

$$X = \frac{60 \text{ kg} \times 0.001 \mu\text{g/kg/day}}{1.0 \times 10^{-6} \mu\text{g TCDD/L stream water}}$$

$$X = 0.06 \times 10^{6} \text{ L stream water/day}$$

$$= 60{,}000 \text{ L stream water/day}$$

$$\approx 15{,}840 \text{ gal stream water/day}$$

(Note--With the application of a 100-fold safety factor, the amount would be 600 L stream water/day, or 158.4 gal stream water/day.)

SITUATION 4 - AMBIENT AIR CONTAINING TCDD

Given: A commercial herbicide product of 2,4,5-T containing 0.01 ppm TCDD which is applied to an area resulting in an ambient air concentration in a nearby unsprayed area of 1.0 µg ae 2,4,5-T/m^3 of air. (Note - This amount represents an "upper limit" as estimated by Newton and Norris 1981). Therefore, the maximum amount of TCDD present would be 0.01×10^{-6} µg/m^3;

TCDD has an acute oral LD_{50} of 0.6 µg/kg and a chronic or subchronic oral NOEL of 0.001 µg/kg/day;

A person weighing 132 lb (60 kg).

Question 1: How much air contains the equivalent of the LD_{50} for TCDD?

Solution:

$$X = \frac{60\ kg \times 0.6\mu g/kg}{0.01 \times 10^{-6}\ \mu g\ TCDD/m^3\ air}$$

$$X = 3{,}600 \times 10^6\ m^3\ air$$

$$\approx 4{,}716 \times 10^6\ yd^3\ air$$

Question 2: How much air can be inhaled daily without exceeding the NOEL for TCDD?

Solution:

$$X = \frac{60\ kg \times 0.001\ \mu g/kg/day}{0.01 \times 10^{-6}\ \mu g\ TCDD/m^3\ air}$$

$$X = 6 \times 10^6\ m^3\ air/day$$

$$\approx 7.9 \times 10^6\ yd^3\ air/day$$

(Note--With the application of a 100-fold safety factor, the amount would be 60,000 m^3 air/day, or 78,600 yd^3 air/day.)

SITUATION 5 - ANIMAL MEAT CONTAINING TCDD

Given: Animal meat comprised of 20% fat (i.e., 0.2 g fat/g meat) which contains a TCDD concentration of 60 ppt ("worst case" situation) in the fat. Therefore, this amounts to:

$$12 \times 10^{-12}\ g\ TCDD/g\ meat$$
$$= 12 \times 10^{-6}\ ug\ TCDD/g\ meat$$
$$= 12 \times 10^{-3}\ ug\ TCDD/kg\ meat;$$

TCDD has an acute oral LD_{50} of 0.6 ug/kg and a chronic or subchronic oral NOEL of 0.001 ug/kg/day;

A person weighing 132 lb (60 kg).

Question 1: How much meat contains the equivalent of the LD_{50} for TCDD?

Solution:

$$X = \frac{60\ kg \times 0.6ug/kg}{12 \times 10^{-3}\ ug\ TCDD/kg\ meat}$$

$$X = 3{,}000\ kg\ meat$$

$$\approx 6{,}614\ lb\ meat$$

Question 2: How much meat can be ingested daily without exceeding the NOEL for TCDD?

Solution:

$$X = \frac{60 \text{ kg} \times 0.001 \text{ ug/kg/day}}{12 \times 10^{-3} \text{ ug TCDD/kg meat}}$$

$$X = 5 \text{ kg meat/day}$$

$$\approx 11 \text{ lb meat/day}$$

(Note--With the application of a 100-fold safety factor, the amount would be 50 g meat/day, or 1.75 oz meat/day.)

APPENDIX 4

REFERENCES USED IN ESTABLISHING THE NO OBSERVABLE EFFECT LEVEL OF VARIOUS HERBICIDES.

Herbicide	Test Animals	References
2,4,5-T	rats	Emerson et al. 1971, Sparschu et al. 1971, Khera and McKinley 1972, Schwetz 1977, Smith et al. 1978, Kociba et al. 1979b
	mice	Roll 1971
	dogs	Drill and Hiratzka 1953
	rhesus monkeys	Dougherty et al. 1975
	rabbits	Emerson et al. 1971
	sheep	Binns and Balls 1971
2,4,5-TP	cattle	Palmer et al. 1964
	sheep	Palmer and Radeleff 1969
2,4-D	rats	Hansen et al. 1971
	swine	Erne 1966
	cattle	Palmer and Radeleff 1964, Palmer 1972
	dogs	Hansen et al. 1971
2,4-DP	rats	Weed Science Society of America 1983
Amitrole	mice	Lewis and Tatken 1980
Asulam	unknown	NOEL value based on personal communication with Rhone-Poulenc, manufacturer of Asulox®
Atrazine	mice	Mrak 1969, Innes et al. 1969
	rats	Peters and Cook 1973
Dalapon-Na	rats	Paynter et al. 1960, Emerson et al. 1971
	dogs	Paynter et al. 1960
Dicamba	rats and rabbits	Velsicol 1981, Newton and Dost 1981

Herbicide	Test Animals	References
Dinoseb	mice	Gibson 1973
	dogs and rats	Weed Science Society of America 1983
Fosamine	rats	Haskell Laboratory 1979a, Weed Science Society of America 1983
Glyphosate	rats, dogs, and rabbits	Federal Register, Dec. 5, 1978, Vol. 43 (234):57000-57006; and Aug. 5, 1980, Vol. 45 (152):51768-51769.
Hexazinone	rats, mice, and hamsters	Haskell Laboratory 1979b; Federal Register, Nov. 21, 1980, Vol. 45 (227):77030.
MSMA	unknown	NOEL estimate based on approximately 1/100 of the LD_{50} value for rats
Picloram	rats	National Research Council of Canada ca. 1974
	dogs	Lynn 1965, McCollister and Leng 1969
Simazine	unknown	NOEL estimate based on data for atrazine
Triclopyr	rats and rabbits	Weed Science Society of America 1983, and personal communication with L. E. Warren of Dow Chemical USA

APPENDIX 5

COMMERCIAL HERBICIDE PRODUCT SPECIFICATIONS

The mention of trade names should not be construed as an endorsement of these products by Oregon State University. They are simply used to provide realistic examples for calculations.

Herbicide		Manufacturer	Active Ingredient (ai)	
Common name	Trade name		%	lb/gal
2,4,5-T	Esteron® 245	Dow Chemical	45.0	4
2,4,5-TP	Kuron®	Dow Chemical	45.8	4
2,4-D	Esteron® 99® Concentrate	Dow Chemical	44.9	4
2,4-DP	Weedone® 2,4-DP	Union Carbide	44.7	4
Amitrole	Amitrol T®	Union Carbide	21.6	2
Asulam	Asulox®	Rhone-Poulenc	34.0	3.34
Atrazine	Aatrex® 4L	Ciba-Geigy	40.8	4
Dalapon	Dowpon® M	Dow Chemical	74.0	
Dicamba	Banvel® 4-W.S.	Velsicol	40.6	
Dinoseb	Red-Top Contact Weedkiller	Wilbur-Ellis	30	3
Fosamine	Krenite®	DuPont	41.5	4
Glyphosate	Roundup®	Monsanto	30.7	3
Hexazinone	Velpar® L Weedkiller	DuPont	25	2
MSMA	Trans-Vert®	Union Carbide	51.19	6.66
Picloram	Tordon® K	Dow Chemical	20.8	2
Simazine	Princep® 80W	Ciba-Geigy	80	
Triclopyr	Garlon® 4	Dow Chemical	44.3	4

APPENDIX 6

METRIC-ENGLISH EQUIVALENTS AND ABBREVIATIONS

Length

cm = centimeter
= 0.3937 inch (in.)

m = meter
= 100 cm
= 1.0936 yards (yd)

Area

m^2 = square meter
= 1.196 square yards (yd^2)

ha = hectare
= 10,000 m^2
= 2.4711 acres (A)

Mass

kg = kilogram
= 2.2046 pounds (lb)

g = gram
= 10^{-3} kg
= 0.035 ounce (oz)

mg = milligram
= 10^{-3} g

µg = microgram
= 10^{-6} g

ng = nanogram
= 10^{-9} g

Volume

L = liter
= 4.23 cups
= 2.11 pints (pt)
= 1.06 quarts (qt)
= 0.264 gallon (gal)

mL = milliliter
= 10^{-3} L
= 16 drops
= 0.2 teaspoon (tsp)
= 0.067 tablespoon (tbsp)
= 0.00423 cup

m^3 = cubic meter
= 1.31 cubic yards (yd^3)

Concentration

ppm = part per million = 10^{-6}

ppb = part per billion = 10^{-9}

ppt = part per trillion = 10^{-12}

APPENDIX 7

SOME SOURCES OF OTHER POINTS OF VIEW AND ADDITIONAL ISSUES CONCERNED WITH HERBICIDES

EPSTEIN, S. S. 1978. The politics of cancer. Sierra Club Books, San Francisco, California.

GREEN, K., and K. COHN. 1982. Forests, herbicides and people. A case study of phenoxy herbicides in western Oregon. Council on Economic Priorities, New York.

HAY, A. 1982. The chemical scythe. Lessons of 2,4,5-T and dioxin. Plenum Publishing Corporation, New York.

NADER, R., R. BROWNSTEIN, and J. RICHARD. 1981. Who's poisoning America? Corporate polluters and their victims in the chemical age. Sierra Club Books, San Francisco, California.

SHEARER, R., and M. HALTER. 1980. Literature reviews of four selected herbicides: 2,4-D, dichlobenil, diquat and endothall. Water Quality Planning Division, Municipality of Metropolitan Seattle, Washington.

VAN STRUM, C. 1983. A bitter fog: Herbicides and human rights. Sierra Club Books, San Francisco, California.

WARNOCK, J. W., and J. Lewis. 1978. The other face of 2,4-D. A citizens report. South Okanagan Environmental Coalition. Penticton, British Columbia, Canada.

WHITESIDE, T. 1979. The pendulum and the toxic cloud. The course of dioxin contamination. Yale University Press, New Haven, Connecticut.

WALSTAD, JOHN D., AND FRANK N. DOST. THE HEALTH RISKS OF HERBICIDES IN FORESTRY: A REVIEW OF THE SCIENTIFIC RECORD. Forest Research Laboratory, Oregon State University, Corvallis. Special Publication 10. 60 p.

This report focuses on the phenoxy herbicides 2,4,5-T and 2,4-D, and the contaminant TCDD (dioxin). Several other herbicides used in forestry are also evaluated. Toxicologic methods of determining a safe dose and the regulatory control process enforced by government agencies are explained.

In order to estimate the health risks of various levels of occupational and environmental contact with herbicides, data from studies of herbicide toxicity in laboratory animals have been extrapolated to humans. Calculations based on body weight are presented which indicate that, once the herbicides are diluted and applied according to regulations and label directions, it is highly unlikely that humans or other animals could ingest or absorb enough sprayed material to approach levels that might cause harm. An extensive list of scientific reviews supports this view.

KEYWORDS: 2,4-D, 2,4,5-T, TCDD, dioxin, herbicides, phenoxies, toxicology, risk assessment, forest vegetation management, regulatory control.

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