PESTICIDES:

A TREATISE ON THE CHRONIC TOXICITY OF PESTICIDE EXPOSURE IN FARMWORKERS.

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PREFACE

Although my initial paper outline was entitled "Pesticides and Cancer", subsequent reading of the current literature and indepth investigation into the subject matter led me to pertinent information concerning the health effects of pesticides in humans. The title was modified to reflect more accurately the information contained in this report. The original outline will be adhered to although the contents will be rearranged so as to provide a more organized progression and to facilitate comprehension of the subject matter for the reader. This manuscript serves as the groundwork for future publication of some the information herein contained.

I would like to thank at this time many of the people who have provided useful insight on the extent of use of pesticides, their role in illness among those exposed to them, regulation, and alternatives to pesticide use. I would like to thank Dr. D. Levins of the HSPH Human Ecology Program, Dr. Toscano of the HSPH Toxicology Department, Mr. D. Williams of MASS-COSH for providing preliminary information on standardized pesticide limits and other useful information, Dr. L. Pepper and his staff of the Occupational Medicine Unit of the Cambridge Hospital, Dr. D. Moeller of HSPH for the opportunity of submitting this report, Dr. Maizlish of the California Health Services division for information on psychiatric disorders and pesticides, Roberto De la Cruz, New England representative of the United Farmworkers Organization, Dr. M. Moses of the Farmworkers Health Group who not only provided the inspiration for this report and much of the information on the subject, but who also has undauntedly been a champion of farmworkers and migrant health, and to L. Martinelli J.D., a fellow colleague and staunch advocate for the health rights of farmworkers. Finally, I wish to thank the faceless population, the migrant and seasonal farmworkers whose tireless efforts and indeed, very lives, contribute tremendously to the well being of this nation.

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"The problem that concerns us here is whether any of the chemicals we are using in our attempts to control nature play a direct or indirect role as causes of cancer."
Rachel Carson, Silent Spring, 1962.

I. INTRODUCTION.

In her book, Silent Spring, Ms. Carson expressed concern about the health effects from pesticide use in this country. More than 26 years later, this same concern is even more real than in Ms. Carson's time. Pesticides are used extensively in many developed and developing countries today. None can escape exposure to their use. Such exposure to pesticides occurs in a variety of occupational settings, in their production, formulation, and use. The general population is exposed by ingestion of pesticide residues on food, home use of pesticides, and by environmental spread by wind drift or ground water contamination. Even the unborn child is exposed either through lactation or in-utero.

Much has been published on pesticides, their acute effects on health, and their inherent toxicity for controlling pests but almost all such publications have considered the perspective of the producer or manufacturer under controlled conditions. Little has been published concerning the effects of pesticides on migrant and seasonal farmworkers, the workers who are the least knowledgeable and the most at risk.[1] Farmworkers are exposed to toxic pesticides from many sources-- the crops they cultivate and harvest, the soil the crops are grown in, drift of toxic sprays that are being applied to adjoining fields or often to the very field in which they are working. Farmworkers live in homes surrounded by fields which are heavily and repeatedly sprayed. Pesticides may be in the irrigation water, in the ground water from which their drinking water is drawn. Since they are more likely to consume produce very soon after harvesting they may get even more

pesticide residues in their food than the general public. Since agriculture is the only industry in which children comprise a significant part of the work force, occupational toxic exposures begin at a very young age.[1,2] Indeed, children of farmworkers which are the most vulnerable may carry the greatest burden of pesticide exposure.

This report is an attempt to compile what information that does exist in relation to delayed health effects on those who, for the sustenance of their families, must bare the brunt of direct, if not indirect, exposure to pesticides. Because so little has been written on the chronic effects of pesticide exposure in this population, portions of subsections may be supplemented with information pertaining to acute as well as chronic health effects. It is left to the reader to assess whether the "economic gain" by a few merits the health impact imposed on all.

A BRIEF HISTORY OF THE TOXICITY OF PESTICIDES.

The history of the health effects of pesticides affords a perspective that may be profitable when interpreted in light of current motivation for pesticide usage. Anciently, chemical compounds were used for their salubrious effects, either directly or indirectly, on man. According to Costa[3], Ebers Payrus, written 1550 B.C. lists preparations to expel fleas from the house. About 1000 B.C. Homer stated that Odysseus burned sulfurs "to purge the hall and the house and the court" (Odyssey XXII 492-494). Pliny the Elder (23-79A.D.) collected in his Natural History anecdotes on the use of pesticides in the previous third to fourth centuries.[4] Dioscorides, a Greek physician (40-90 A.D.) knew of toxic properties of sulfur and of arsenic. About 900 A.D. Chinese were using arsenic sulfides to control garden insects.[3] In 1669, arsenic mixed with honey was used as ant bait; this is the earliest record of insecticide use in the western world.[3] Tobacco was used as a contact insecticide for plant lice. Copper compounds were found to be of fungicidal value in 1807. Bordeaux mixture (hydrated lime and copper sulfate) was first used in France in 1883. Hydrocyanic acid was used as a fumigant in 1877 to kill museum pests in insect collections.[4] Carbon disulfide was used in 1854 as an insect fumigant.[3]

Pesticides were mainly of natural origin or inorganic compounds. Sulfur was recommended for controlling diseases in fruit trees in 1802.[5] Its fumigant properties were discovered in 1850.[4] Inorganic sulfur still remain as one of most important fungicides.

Nicotine and rotenone (1725) have been used in South America. Mercury chloride was used as a fungicide in 1891. It was replaced with organic forms mainly phenly mercury (1915), alkyloxyalkyl mercury (1920), and alkyl mercury (1940). Alkyl mercury was responsible for an outbreak of poisoning in Iraq from 1971 to 1972 due to bread comsumed made from contaminated cereal grains and involved over 5,000 people.[6] The first synthetic organic insecticides that appeared for public use probably were the dinitro compounds and the carbamates in the early 1930's. From 1935-1950's DDT and other chlorinated hydrocarbon insecticides were developed. DDT was first synthesized by Zeidler in 1874 but Dr. Paul Muller found that DDT acted as a contact poison on flies, mosquitoes, and other insects and was subsequently awarded the Nobel prize in 1948.[4] In 1940 the first patent was obtained for DDT and in 1942 was introduced as Gesarol and Neocid.[7] DDT was used in controlling an epidemic of typhus during World War II.[7] DDT was used to control malaria (incidence before used was 50-60/1000 people in 1944 and changed to 0/1000 in 1949) in Italy in 1945.[8]

The first fatal case of DDT poisoning was recorded by Hill and Robinson in 1945.[9] It involved a negro child only 1 year old who drank about an ounce of 5% DDT in crude kerosene. Atropine 1/400gr.(0.16 mg) was given and the stomach washed out about three hours later but death from respiratory failure occurred at 4 hours after ingestion. The lethal dose of DDT was about 150mg per kg. Scientists of that time also pointed out that the kerosene alone may have had the toxic effect. One can not but wonder what effect the so-called "inert" ingredients of today's pesticidal formulations pose to humans. Further toxicity of DDT was discussed in the same journal in March 16, 1946, and concluded that wildlife, mainly fish were the most likely vertebrates to suffer ill effects from DDT. During this period it was reported that symptoms for humans were tiredness, aching, and requirement of serveral weeks to return to "normality". Another report as early as 1948 showed that symptoms of poisoning included "tremors of the hands, decreased body weight, anorexia, muscular weakness, and fine tremors.[10] However, this same report stated that"DDT in its insecticidal form was perfectly safe based on the parameters of body weight and blood pressure" and that "there were no reported cases of poisoning by itself". In almost defiant response, another report gave an account of a healthy adult male eating "DDT pancakes" as a result of losing a bet "without any untowards effects"[11]

In 1950 it was reported that the need to increase food production during the German War of 1939-45 had led to the development of

powerful insecticides.[12] This same article reported 7 deaths and over 100 cases of poisoning due to parathion in the USA and that among other statements, that adequate training and education of workers with provisions of protective clothing, gas proof caps, supplies of atropine in sealed containers to all persons exposed, good supervision, routine medical examination including cholinesterase estimation were essential if fatal accidents were to be prevented. In addition, it stated that the danger of poisoning by organic phosphorus insecticides should be impressed on all medical practitioners, particularly in rural areas and that all practitioners in the country be sent a circular letter describing the eitology, diagnosis, and treatment of poisoning by these compounds. One report on DDT showed that accidental poisoning of contaminated chewing tobacco could be measured in the urine and that the compound had unique pharmacokinetics (dose-response relationship) of excretion with different peaks.[13]

In 1951, a report indicated that a 21 year old male died due to Di-nitro-ortho-cresol (DNOC) poisoning which was introduced as a crop spray in the 1940's.[14] A blood sample at the time of death contained 75ug of DNOC per gram. A recommendation was made for regular blood examination and avoidance of the chemical "for several weeks" if their blood DNOC concentration rises above 20ug per gram.[15] Before Institutional Review Boards (IRB'S), volunteers were given DNOC and a dose-response relationship was confirmed.[16] Another article reported that Aldrin and Dieldrin have a greater chronic toxicity that any of the chlorinated hydrocarbon insecticides.[17] For further information concerning early pesticide poisoning, the reader is referred to Barnes.[18]

In 1962, Rachel Carson's book, Silent Spring, prompted the Federal government to take action against water, air pollution and some pesticides. DDT was banned in 1970 in Sweden. The first ban of any kind in the U.S. was on DDT, Aldrin, and Dieldren in 1967 by a Farmworkers contract with a grape grower and not by the EPA.[1] OSHA and EPA both came into existance in 1970.

CONSUMPTION

> "Today, pesticides are detectable in many food items, in some clothing, in man and animals, and in various parts of our natural surroundings."
>
> Report of the President's Science Advisory Committee. May 15, 1963.

Despite the growing controversy over the use of pesticides, their use has increased since Rachel Carson's 1962 publication of Silent Spring. The average annual increase in pesticides has been about 4-5% on a global basis.[19,20] In 1983, it was estimated to be more than 4 billion pounds of active ingredients annually.[21] The largest single user of pesticides in the U.S. is agriculture.[22,27,33] Pesticides totaled $4.3 billion dollars (25.3%) of expenses of farm production of all manufactured inputs.[23] Actual amount in pounds may help visualize more accurately their relationship to health effects than mere costs. Accordingly, over 2 billion pounds of pesticides are sold annually to U.S. farmers.[24] One report estimates that 225 to 250 million acres (2/3's of American crop lands) are treated annually with Pesticides.[25] Another report states that about 148 million hectares have been treated with 455 million pounds of pesticides.[26] For further information regarding extent of use of pesticides the reader is referred to Lotti.[27]

The public generally believes that pesticides are beneficial from an economic point of view. One study showed that in comparing losses of plots treated with pesticides versus plots untreated showed a net gain of 36%.[28] However, only chemical control was used, not intergrated pest management which may have produced different results. In Nicaragua, a study showed a 90% decrease in expenses not using pesticides, with integrated pest management alone.[29] In addition, extrapolating to different geographical areas with different pests may be difficult and labor intensive crops (fruits and vegetables,etc.) were not completely studied. An earlier report questioned the real beneficial gains from pesticide use where insect damage was reported as ruining 10-20% of the crops.[30] The report indicates that this was true for some fields but not for most and that some fields were not damaged at all. It suggested that repeated spraying applications are "merely insurance sprays and in many cases actually unnecessary". Indeed, pesticides may prove economically beneficial, but the real question is for whom.

Pesticides must be registered with the EPA before they can legally be sold or used in the United States. Fifteen hundred active pesticide ingredients are combined to make 40,000 registered products.[31] The pesticide active ingredients are combined with so-called "inert" ingredients which may be as toxic or even more toxic than the actual pesticide itself.[32] They are neither required to be tested for acute and chronic health effects nor listed by name on the pesticide label. These inert ingredients may make up to 90% or more of a registered pesticide product but due to " trade secret" provisions of the pesticide law

(FIFRA), the identity of these ingredients can not be released to the public by state or federal regulatory agency, not even to a physician on behalf of a poisoned individual.[33]

DEFINITIONS

Pesticide as a word is not used in the U.S. legislative Federal Insecticide Fungicide Rodenticide Act (FIFRA) as such. Instead the word "economic poison" is used which unambiguously defines pesticides as poisons used for economic purposes. Webster's Third International dictionary defines pesticide as any agent used to control pests. The definition of pest is best described by Smith,"The term pest is used broadly to include those living organisms that interfere with man's efforts to manage the planet to his liking. The label may apply to plants, diseases of plants, animals, vertebrates. . . Let us recognize at the outset that a pest is a pest because man says it is one, because it invokes his displeasure."[34] Pesticides may be classified according to the particular use intended such as herbidicides, fungicides insecticides and fumigants.

Chemical carcinogen is used by the International Agency for Research on Cancer (IARC) to mean the induction by chemicals of neoplasms that are not usually observed, earlier induction by chemicals of neoplasms that are commonly observed, and/or induction by chemicals of more neoplasms than are usually found, although fundamentally different mechanisms of action may be involved.[35] Carcinogen is used to define induction of cancer (tumor or neoplasm) of various types or combinations of malignant or benign tumors. IARC assessment of carcinogenic risk will be used, mainly "In the absence of adequate data on humans, it is reasonable for practical purposes, to regard chemicals for which there is sufficient evidence of carcinogenicity in animals as if they presented a carcinogenic risk to humans". Other definitions will be provided according to each section discussed.

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II. DETERMINING EXPOSURE.

> "Knowledge of the full extent of acute and chronic pesticide poisoning among migrant and seasonal farm workers is hampered by the lack of medical training to recognize and treat these problems, the lack of information among farmworkers about their workplace exposures, the reluctance of farmworkers to report poisoning, and the lack of a national reporting system to tabulate such poisonings. Additional research is necessary to understand the full implications of chronic pesticide exposure on farmworker health."
>
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EXTENT OF EXPOSURE

There are many and various ways people are exposed to pesticides as these chemicals are among the few toxic materials deliberately added to our environment. Exposure may commence with the production of pesticides, their manufacture, formulation, and processing, their distribution and application, and through dispersal of pesticides in the environment. Although all phases are important sources of exposure, their dispersal into the environment and their subsequent uptake by humans will be addressed. EPA and other monitoring agencies throughout the world have shown that pesticide contamination is global, including snow caps of the highest mountains and core samples from the arctic ice-packs.[1] Drift is a problem with dispersal of pesticide away from the site of application. About 10-15% of applied pesticides actually reach the target pest, with the remaing 85-90% are dispersed off target to air, soil, and water through run-off, volatilization, off-gassing etc..[2] Important factors in the dispersal of pesticides include physicochemical properties of the pesticide such as polarity, water solubility, octanol-water partition coefficient, bioconcentration, volatility, and environmental relevance such as leaching and mobility in soil.[3] Pesticides can drift as far as 50 miles from the site of application depending on particle size and wind conditions. Significant concentration of almost all pesticides applied aerially or by ground rig sprayers can drift up to a mile or more from the site of application.[1,5] Pesticides concentrate in fog.[4] Pesticides have been found to contaminate indoor air.[5]

Pesticide residues can be very persistent soil contaminants and a source of continuing contamination from run off as well as dust. In Washinton state, DDT has been shown to contaminate the Yakima river basin and wildlife even though the last application of DDT in this area was before the DDT ban in 1972.[6] Equipment used may also serve as a source of continuing contamination. Pesticide residues were found on a cotton gin and rafters in a study in Arizona showing significant concentrations of DEF,Azodrin, and methyl parathion.[7] Communities which abut agricultural land are at risk from pesticide drift. Three major evacuations of community residents due to pesticide drift occurred in California in1987- two from guthion being used in peach orchards and one from methyl bromide off-gassing from a gladiola field.[1]

Pesticide use in agriculture is a major source of involuntary exposure of the general public to carcinogens. Fresh and processed food are contaminated with persistent pesticide residues, most of which can not be washed off or degraded by cooking.[1] This past summer, R. De la Cruz, a farmworker's representative for New England, found 22 foodstores in Boston out of 28 had significant pesticide residues as tested with Enzy Tech, Enzy Tech,Inc., (Lenexa,Kansas). Agricultural pesticide use is the major cause of non-point source of contamination of ground water.[8] A non-point source means there is not a single identifiable place causing the contamination. EPA monitoring data reports many states with ground water contamination (see appendix A). Many pesticides found in ground water have been identified in California (see appendix B). This is very significant considering that nationwide about 50% of the drinking water supply is from groundwater and is 90% or more in rural areas.[1] It should also be noted animals are also treated with pesticides externally through the use of "dips" or internally in their feed. Such exposure in animals leads to contaminated meat, milk, egg, and other animal products.[9,10]

Farmworkers are continually, both directly and indirectly, being exposed. The annual agricultural work force according to the USDA (1986) consists of about two million hired workers and 3 million farm owners and their families (unpaid). Farmworker exposure to pesticides occurs in many ways . These include direct spray or drift from aerial or ground application; contact with pesticide residues on plant leaves and then eating, smoking, urinating or defecating without being able to wash the hands; use of pesticide contaminated hollowed out cucumbers, bell peppers, apples, etc., which have been sprayed with pesticides, as

drinking cups.[11] A survey of 460 agricultural farmworkers in Washington state reported that 43% had been sprayed directly or drifted by pesticides and that 47% worked in a field within two days of its being treated with pesticides.[12] As few farmers actually post signs warning of possible contamination and current law for this is not enforced, this form of contamination is widespread. The primary route of worker exposure to the majority of pesticides is the skin, and not, as commonly believed, the respiratory system with the exception of fumigants which are in the form of gases.[1] Pesticides may persist in the skin for many months.[13] So-called protective clothing does little to reduce exposure even if used adequately. Laundering contaminated fabrics does little to remove pesticides; it may even be a means of contaminating other clothes.[14] Recent work documenting exposure by fluorescent methods shows greater exposure than previously anticipated even with "protective" clothes.[15]

Pesticides are not only ubiquitous in the environment because of their widespread use, they are also found in human adipose tissue, blood, milk, and cord blood from mothers and their infants.[10,16,17,18] In fact, human milk contains higher concentrations of total DDT than does cow's milk.[19] Indeed, although "safe" levels of pesticide exposure have been set using healthy adult males as guidelines, no such levels have been studied for infants and children. A current study is projected to assess such levels by a committee of health, nutrition, and environmental experts but this study consists mainly of a search of the literature.[20]

It is estimated that the extent of actual acute pesticide poisoning worldwide is about 500,000 cases per year. During 1971-73, there were 8,240 cases in the U.S. (30% were organophosphates), and during 1974-1976, there were 9,280 cases (25% organophosphates). [21] These reports are underestimates of actual number of cases because of underreporting. They are underreported by farmworkers because of justifiable fear of employer retaliation and job loss and because of the "abysmal state of knowledge" by physicians in rural communities regarding recognition and management of pesticide related health problems. [22] As initial symptoms are flu-like, many exposed workers are unaware of contamination. In addition, California is the only state where reporting of pesticide incidents by physicians is mandatory. About 5-10% of acute exposure result in chronic effects.[21] Some of these effects include difficulty concentrating, memory loss, depression, and anxiety.

STANDARDS

There are presently three organizations that set pesticide limits for the work place air. Only the Occupational Safety and Health Administration (OSHA) sets limits that are legally binding. The American Conference of Governmental Industrial Hygienists (ACGIH) and the National Institute for Occupational Safety and Health (NIOSH) also set pesticide limits but are not legally binding. The Chemical Substances Threshold Limit Value Committee of ACGIH provides guidelines which are published annually as Threshold Limit Values (TLV's). TLV's by themselves have no legal status but where regulation are based on TLV's (e.g. in states of Illinois, New Jersey, and Pennsylvania) they have the force of law. This committee provide guidelines for occupational exposures, and although no labor representatives currently participate in committee activities, their guidelines are based upon current scientific judgment which should "protect all workers" from harm. TLV's are continually being developed, changed, or eliminated as necessary for confirmed and suspected human carcinogens.[23] The TLV committee designates many more chemicals as carcinogens than are regulated as carcinogens by the OSHA. This disparity is due to the ability of the Committee to make decisions relatively soon after the disclosure of new scientific information, without legal or administrative constraints. It should be noted that this committee is not immune to influence by special interests. NIOSH also sets limits on exposure which are based on the most recent scientific evidence. Hence, if the goal is to enhance worker safety and protect their health, the more up to date NIOSH or ACGIH limits should be followed to prevent occupational disease. See fact sheet below.

PESTICIDE LIMITS

NIOSH[1], ACGIH[2], and OSHA[3] are the three organizations that set pesticide limits he workplace air. Unfortunately, while only the OSHA limits are legally binding, are frequently outdated and not based on the most recent scientific evidence. fore, the more up-to-date NIOSH or ACGIH limits should be followed to prevent ational disease.

ICIDE	NIOSH Limits (ppm) 8-hour TWA[4]	Ceiling[5]	ACGIH Limits (ppm) 8-hour TWA	Ceiling	OSHA Limits (ppm) 8-hour TWA	Ceiling
on Disulfide	1.0	10	10	-	20	30[A]
on Tetrachloride	2.0	2.0	5.0	20	10	25[B]
ropicrin	-	-	0.1	0.3	0.1	-
lene Dibromide	0.13	0.13	-	-	20	30[C]
lene Dichloride	5.0	15	10	15	50	100[D]
thion	15 mg/m^3	-	10 mg/m^3	-	15 mg/m^3	-
yl Bromide	-	-	5.0	15	20	-
phine (Phostoxin)	-	-	0.3	1.0	0.3	-

n be exceeded up to 100 ppm once every 8 hours for only 30 minutes.
n be exceeded up to 200 ppm once every 4 hours for only 5 minutes.
n be exceeded up to 50 ppm once every 8 hours for only 5 minutes.
n be exceeded up to 200 ppm once every 3 hours for only 5 minutes.

- National Institute for Occupational Safety and Health
- American Conference of Governmental Industrial Hygienists
- Occupational Safety and Health Administration
- TWA (Time Weighted Average) - the maximum amount of the air contaminant a worker can be exposed to, averaged over an 8-hour day
- g - the maximum air contaminant concentration which should never be exceeded, not even for a minute, except where noted.

ct sheet prepared by the Health and Safety staff of the Food and Beverage Trades ent, AFL-CIO, 815 16th Street, N.W., Washington, D.C. 20006, (202) 347-2640.

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III. CHRONIC TOXICITY OF PESTICIDES AND ORGAN SPECIFICITY.

> " Pesticides may gain entrance to the body through the intestine subsequent to ingestion;through the lungs as a result of inhalation of air borne laden dusts, vapors and aerosols; by penetration through intact skin; and (rarely) by absorption directly into the blood stream through the broken skin."
>
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Despite limited information on the health effects of pesticide exposure, the information that does exist is very helpful in gaining a perspective on the public health impact of pesticide use. The discussion of all the health effects on humans from pesticides is beyond the scope of this report. Focus will be placed on chronic toxicity, specifically cancer. No attempt is made to evaluate the validity of studies cited, rather, the purpose will be to present published findings of pesticide associated neoplasms in relation to farmworkers or agriculture related populations.

An association has been made relating acute pesticide exposure to chronic effects. As previously mentioned some of these effects include difficulty concentrating, memory loss, depression, and anxiety (pg.11). Field studies have linked chronic exposure to pesticides with various types of cancer. A study of six types of cancer mortality in Iowa from 1971 to 1978, found that farmers had "significantly elevated" mortality rates compared to non-farmers.[2] Males exposed in a pesticide manufacturing plant showed significant increased risk for all cancer when compared to the U.S. general population.[3] A comparison between acute and chronic toxicities and toxicological interactions involving pesticides has been made.[4] Certain categories of chronic toxicity , even though involving a long latent period, may be induced in some instances after only one single exposure. If only one area of chronic toxicity is considered such as chemical carcinogenesis, the target sites would be hematopoietic, respiratory, digestive, endocrine, urinary and reproductive systems in addition to the specific area of nervous dysfunction associated with acute toxicity.[4] Although many studies have been published correlating tumors in laboratory animals with pesticides, only pesticide associated cancer in humans will be addressed. The following is a brief presentation of published findings on pesticides and

cancer according to organ specific sites. It is important to state that organ specific findings may be associated with indirect or secondary contact as well as direct or primary exposure depending the specific exposure pathway involved.

PULMONARY SYSTEM

A mortality study by Mabuchi et al found a significant increase of risk for lung cancer in males (n=1,393). In addition, they found a dose response relationship by the SMR for lung cancer which increased with increasing duration of exposure to arsenicals.[5] A mortality study by Barthel showed a statistically significant increased risk for lung cancer (n=1,658).[6] Blair et al found that for those with 20 or more years latency, a statistically significant increased risk was found for lung cancer (n=3,827).[7] A mortality study by MacMahon et al showed a statistically significant increased risk for lung cancer (n=1,082).[8] A case control study found that lung cancer cases were more likely to have been exposed to herbicides.[9] Nonsignificant elevated ratios were found for all cancers and cancer of the lung by Wong et al.[10] In addition, non-significant increased ratios were found in California farmers[11], in pesticide sprayers in England and Wales[12], and in Finnish pesticide sprayers.[13]

HEPATIC AND PANCREATIC SYSTEMS

Alavanja et al found significant increased risk for pancreatic cancer among workers in the grain industry.[14] Gallager et al in a proportionate mortality study found statistically significant increased risk for pancreatic cancer.[15] Saftlas et al found significant increased risk for cancer of the pancreas in Wisconsin farmers.[16] Stubbs et al found non-significant increased risk for liver and gallbladder in white farmers.[11] Alavanga et al also found statistically significant increased risk for liver cancer in a mortality study of Swedish grain millers.[17] A case control study by Austin et al of 86 persons aged 18 to 84 of five medical centers (Alabama, Duke, Miami, Pennsylvania, and Harvard) with primary liver cancer found non-significant elevated risk for pesticide exposure, employment in agriculture and occupation as a farmworker.[18] In another case control study by Stemhagen et al found statistically significant increased risk of liver cancer associated with agriculture, agriculture production, and occupation as a farm laborer.[19] A case report

of 14 patients diagnosed with angiosarcoma fo the liver at the same hospital in Egypt from 1980 to 1984 found that 10 had a history of 11 to 20 years (mean=14) of chronic recurrent exposure to agricultural pesticides as sprayers of a variety of organophosphates, organochlorines, and arsenates.[20] Perrelli et al discusses etiologic and pathogenetic aspects of occupational toxic hepatopathies in association with pesticides. [21] Pesticides are implicated in extra hepatic bile duct cancer.[22]

HEMATOLOGIC AND LYMPHATIC SYSTEMS

Alavanja et al reported a significant increased risk of lymphoma in a mortality study of grain workers.[14] Bond et al found statistically significant increased risk for lymphopoietic cancer among employees in production of 2,4-dichlorophenoxyacetic acid.[23] Burmeister et al found statistically significant increased risk of multiple myeloma and lymphoma among Iowa farmers.[24] Fasal et al found non-significant elevated ratios in farmers both males and females for leukemia, and in females for Hodgkin disease and multiple myeloma.[25] Gallagher found significant increased risk for leukemia and aplastic anemia in British columbia farmers.[15] Non-significant elevated ratios were found in Finnish pesticide sprayers for multiple myeloma.[13] Saftlas et al found significant increased risk in Wisconsin farmers for multiple myeloma, leukemia, Hodgkin disease, and other lymphoma.[16] In Swedish agricultural workers, a significant increased risk was found for multiple myeloma.[26] A case control study in Nebraska of 1,084 males who died of leukemia from 1957-74 showed statistically significant increased risk for leukemia with the risk being higher for those born after 1900 and even higher for those from high insecticide use counties.[27] A further analysis of this study showed farmers from high pesticide use counties had higher risk of acute lymphatic, acute myeloid and chronic myeloid cancer.[28] A case control study in Iowa farmers showed significant excess mortality for high herbicide use counties for those born after 1900 and elevated risk for leukemia.[29] A case control study of other Iowa farmers found significant excess mortality from multiple myeloma and non-Hodgkin lymphoma.[30] Another case control study of Iowa and Minnesota white males found excess mortality for farmers from small cell lymphocytic lymphoma, especially in those reporting use of high volume pesticides 20 or more years prior.[31] A significant association between pesticides and multiple myeloma was found for high insecticide use counties in Wisconsin for those born after 1905.[32]

A population based case control study in Iowa and Minnesota showed a significant increased risk of leukemia associated with exposure to insecticides, herbicides, and for non-Hodgkin lymphoma associated with methly bromide, insecticides, herbicides and pentachlorophenol.[33] A case control of 111 Swedish survivors of clinically and and cytologically proven chronic lymphatic leukemia showed that the highest risk was associated with exposure to DDT.[34] In a case-control study from SEER (Surveillance Epidemilogical End Results) cancer registry data involving counties in Washington, Utah, Detroit and Alabama, 698 cases of multiple myeloma revealed significant risk for subjects who reported past exposure to pesticides.[35] A case control study in Utah farmers showed significant increased risk of non-Hodgkin lymphoma.[36] A case control study in 13 counties in western Washington state found significant increased risk for non-Hodgkin lymphoma for farmers, forestry herbicide applicators, and for those with 15 years or more of occupational exposure to phenoxy herbicides 15 years prior to their diagnosis of cancer.[37] A case control study of 123 children in Los Angeles aged 10 or less found a significant increased risk of acute lymphocytic leukemia for children when either parent used household pesticides, garden pesticides and if the father used household pesticides.[38] There is a case report of two firemen involved in a clean up of a tank-truck spill of 1,3-di- chloropropane (a restricted use fumigant) both of whom developed malignant lymphoma 6 years later.[39]

GASTROINTESTINAL SYSTEM

Increased risk of stomach cancer has been found in farmers in Iowa[24], British Columbia [15], Wisconsin[16], and Sweden.[26] Farmworkers were also at increased risk for stomach cancer in California.[11] A case report of 9 children with colorectal cancer which is very rare in children found that 8 were from rural areas and had exposure to insecticides.[40] See section on hepatic and pancreatic cancer for further information.

DERMATOLOGIC SYSTEM

Increased risk of skin cancer was found in Iowa farmers[24], in white and nonwhite farmers in North Carolina[41], and in Swedish agricultural workers.[26] Non-significant increased risk of skin cancer was found with occupational pesticide exposure[4], in pesticide applicators[8], in Wisconsin farmers[16], and in California agricultural workers.[11] A

prevalence study of premalignant skin lesions in 228 workers in 28 paraquat production plants showed 69 workers with hyperpigmented macules and 17 hyperkeratosis.[42] Human exposure to 2,3,7,8-tetrachloro dibenzo-p-dioxin (TCBD) and chlorinated analogs commonly result in pathological changes in the skin and its appendages.[43] In southwest Georgia, 6 cases of melanoma were shown to be higher than in the general population and that these melanomas occurred more in males on covered body sites and that cases were exposed more often to pesticides in non occupational settings than controls.[44]

NEUROLOGICAL SYSTEM

Excess mortality from brain cancer was found in California farmworkers[11], and in Italian farmers.[45] Nonsignificant elevated ratios were found in Florida pest control operators[7], in herbicides sprayers in England and Wales[12], in pesticide manufacturing workers[10], and in farmers in Iowa[24],North Carolina[41], and Wisconsin.[16] A case control study of 84 children with primary brain cancer in Maryland found that cases were more likely to have been exposed to insecticides in the home.[46] Reports of 5 cases of neuroblastoma diagnosed in Ohio at the same pediatric hospital showed that all 5 children had prenatal and/or extensive environmental exposure to chlordane.[47]

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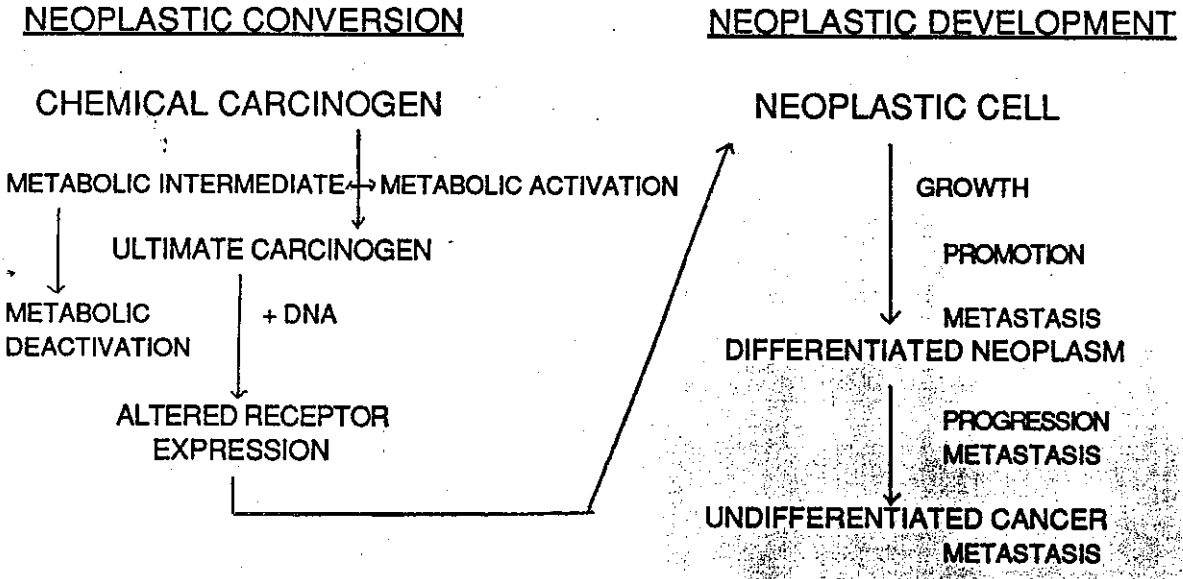
IV. EVALUATING CARCINOGENICITY.

> "...the deliberate aim of carcinogenic test systems should be the acquisition of data that permit evaluation of the carcinogenic risk for humans. Therefore, the key issue regarding chronic bioassays is the degree to which data obtained in such systems actually reflect a human carcinogenic risk..."
>
> Williams and Weisburger, Chemical Carcinogens, In: Toxicology: The basic science of Poisons. 1986

Chemical carcinogens are a type of toxic agents which produce an adverse effect in animals or humans, namely, cancer. Such agents share relationships with other toxic agents and drugs. They may have dose-response relationships, undergo biotransformation, and the effects of chemical carcinogens vary with species, strain and sex of the animal being experimented on. They interact with other environmental agents which may either enhance or diminish their effects. Chemical carcinogens are different from other toxic substances and drugs in that they have the ability to damage DNA (genotoxic) directly or may be indirectly associated with DNA interaction (epigenetic). DNA is a critical target for carcinogens. Hence, their overall effect may be persistant and cumulative, the pathways by which they interact with DNA may be distinct, and individual large doses may not be as effective as repeated doses particularly when given during critical periods of replication or growth.[1] By definition, carcinogens are capable of producing neoplasms which is evidenced by four responces; 1) presence of tumors not seen in controls,2) an increased incidence of tumors in controls, 3) earlier development of tumors than in controls, or 4) an increase multiplicity of tumors.[1]

No distinction is made between benign or malignant neoplasms. Hence, any agent eliciting any one or a combination of responses is considered a carcinogen. Although many agents could be so classified, our concern here is mainly with pesticides in our environment. Our knowledge of how carcinogens result in neoplasms or cancer is not complete, but it is believed to occur through a complex set of reactions which usually take a certain period of time between exposure and the manifestation of the neoplasm. This process of reactions is generally considered in two events; neoplastic conversion and neoplastic development. See Fiqure 1 below. Binding of electrophiles to macromolecules with the cell may result in toxic reactions.

Figure 1.



ADAPTED AND MODIFIED FROM WILLIAMS.[1]

Any agent that contributes to the conversion or the development of a neoplasm and hence effecting any of the aforemention responses is considered a carcinogen. In general, cocarcinogens enhance conversion while promotors enhances development of neoplasms.

Many classes and types of agents have been found to be carcinogenic. Some were discovered in the routine bioassays for the detection of adverse effects in chronic toxicity studies. Many of these studies involved animals and/or unicellular organisms. Other agents were discovered after they were suspected of being involved in cancer development in humans. Finally some agents were identified as a result of their structural similarity to known carcinogens such as dimethlyhydrazine. Several biological models have been used and are still currently being used to evaluate carcinogenicity.

BIOLOGICAL MODELS

Several types of chemicals were discovered to be carcinogens in laboratory animals after being suspected of causing cancer in humans.[2] Animals have been used extensively in evaluating carcinogenic compounds. In the early 1960's the enormous loss of turkey poults with liver necrosis led to investigations of contaminated feeds and the discovery of aflatoxins.[3] Present bioassays systems primarily use rats,

mice and occasionaly hamsters.[4] The EPA currently uses various number and multiple species of animals in registering the pesticides and their toxicity. See table 1 below.

Table 1.

EPA TOXICOLOGY DATA REQUIREMENTS

TEST	SPECIES
ACUTE	
ORAL/DERMAL/INHALATION	RAT,RABBIT
PRIMARY EYE/DERMAL IRRITATION	RABBIT
DERMAL SENSITIZATION	GUINEA PIG
SUBCHRONIC	
90 DAY FEEDING	RAT AND DOG
90 DAY DERMAL/INHALATION	RAT
90DAY NEUROTOXICITY	HEN
CHRONIC	
ONCOGENICITY	RAT AND MOUSE
CHRONIC FEEDING	RAT AND DOG
TERATOGENICITY	RAT AND RABBIT
REPRODUCTION,2-GENERATION	RAT
MUTAGENICITY	
GENE MUTATION	
CHROMOSOME ABERRATION	
DNA DAMAGE AND REPAIR	
SPECIAL	
METABOLISM	RAT
DERMAL PENETRATION	RAT

FROM CARDONA.[5]

The purpose of testing is to provide a data base that can be used to evaluate the hazard and assess the risk associated with the use of a chemical. Although separate categories exist for registration, it is unclear whether all categories must be satisfied in order for a chemical to be registered. It must be noted that testing is done under controlled conditions with a known amount of chemical. The no observable effect level (NOEL) is used in the most sensitive species and on chronic studies. Then information obtained is extrapolated to humans using a safety factor of 100. However, NOEL is a subthreshold dosage level and the safety factor approach would not be applicable to pesticides that are carcinogenic and mutagenic and have no threshold dose. Subsequently, risk estimation is used but this also is not without imperfections as important statistical issues have yet to be resolved. In addition, an appropriate risk model, one which fits most accurately the experimental

data, and takes into account the probable mechanism of actions of the test substance is needed.

UNICELLULAR MODELS

The analysis of carcinogenicity of pesticides is complicated due to not only the diversity of compounds, but also by their mutiple combinations both among each other and with inert ingredients. Many unicellular systems have been devised to test mutagenicity and, hence, carcinogenicity. The use of salmonella typhimurium is well known.[6] The Ames test uses a mutant strain of salmonella bacteria that is unable to grow in the absence of histidine because of a mutation in one of the genes for histidine biosynthesis. The bacteria that is incubated with a potential carcinogen in rat liver abstract to be tested with medium containing no histidine. If the compound is mutagenic it will cause a large number of cells to mutate which will reverse the original mutation for some bacteria and hence they will grow. The number of colonies formed is proportional to the number of histidine revertant mutations and thus a measure of potency of the mutagen. Background mutation is assessed via control cultures.[7] About 80% of compounds that are mutagens turn out to be carcinogens using this test. The use of E. Coli is also used frequently for the detection of mutagenicity.[8] These methods allow for improved efficiency in screening for carcinogens in that it is less time consuming and less expensive. In addition, the number of animals needed for experiments would be reduced. However, they are not without problems as many epigenetic compounds may not be discovered using these methods. Hence, not only do we need more cell systems to test carcinogenic compounds, we need systems to quantify the extent of mutagenic compounds. Such is a report by Miertus.[9] Human cells can also be used in assessing carcinogenicity. [10] These bioassays may prove the best cellular model in use for evaluating carcinogens. Finally, such cell systems would not only help in determining carcinogenicity, but also help further elucidate the actual process of neoplastic conversion and development.[11]

HUMAN MODELS

Human cancers were first found to be related to exposure to specific chemicals in the workplace. Examples include the aromatic amines and bladder cancer. The association between exposure to soot and

coal tars and cancer was identified by the English physician Percival Pott in the late 18th century. Before IRB's, reported incidents involving pesticides were largely acute and fatal poisoning.[12] Few,if any, reports prior to IRB's were concerned with pesticides and carcinogenicity. However, Fitzhugh in 1947 described chronic oral toxicity due to DDT.[13] Dose-dependent carcinogenic effects have been observed with human exposures to cocarcinogens.[14] Notwithstanding, even if studies were to be performed on humans, it would be difficult because humans are genetically heterogenous. Humans have wide variations in environment, diet, and lifestyle. Finally, they are all exposed so no controls would be available. Hence, the human as a model at present can not be used for various reasons in evaluating carcinogenicity. However, given that exposure is present, it seems reasonable if not imperative that cases of chronic exposure be fully and adequately assessed in order to determined the actual chronic effects of pesticide exposure.

CHEMICAL STRUCTURE AS A MODEL

There are over 400,000 new organic compounds synthesized throughout the world per year. About 1000 are introduced for economic use yearly.[15] Only about 2% of more than 65,000 chemicals in commerce have been adequately tested for effects on human health and on the environment.[16] Structure-activity studies have provided considerable information on which predictions about a chemical's carcinogenicity are based.[17] For example, dimethlyhydramine was identified as a result of its structural similarity to known carcinogens. Structure must be evaluated against the backdrop of species differences in biotransformation, which can render a weak carcinogenic agent in one species into a powerful carcinogen in another.[18] Chemically induced neoplasms reflect an association that is specific and related to structure of the chemical. Studies of polycyclic aromatic hydrocarbons show that structures that are closely related chemically, even stereoisomers, may show quite divergent carcinogenic properties under identical exposure conditions.[19] Structural criteria cannot predict entirely new structual types of carcinogens.[15] For example, in the 1950's information on polynuclear compounds, aromatic amines, azo dyes, and aliphatic alkylating agents did not suggest that nitrosamines were carcinogenic. Notwithstanding, when structural critera of a chemical compound and its functional criteria (biometabolism, pharmacokinetics, etc.,) are analyzed, useful information is provided in

assessing a chemical's carcinogenicity and indeed are essential.[15,20] The unifying concept is that most chemical carcinogens act as electrophiles and interact covalently with nucleophilic sites in nucleic acids, proteins, and other macromolecules in bringing about neoplasms.[21]

EXTRAPOLATION

Extrapolating data from all the aforemention methods in evaluating carcinogenicity is at best problematic. Although induction of cancer in animals determines a chemical as a carcinogen, evaluation of the basis for carcinogenicity cannot be based exclusively on chronic testing alone because chemical carcinogens exhibit varied modes of action which are not necessarily reflected by chronic bioassays. Such tests do not provide for differences between genotoxic and epigentic effects. Unicellular methods are useful but also show no characteristics of metabolic changes in mammals which may lead to electrophilic intermediates and thus carcinogenic activity. It is impossible to conduct studies in humans and hence laboratory animals are used as surrogates. Structure of a chemical may be useful but again must be correlated with functional criteria. Many have proposed various risk estimates concerning carcinogen extrapolation to humans.[18,22,23,24,25,26,27,28] Williams sugest what he calls a "Decision Point Approach to Carcinogenic Testing" which is based on established toxicologic methods applied in a systemic manner.[18] See table 2 below.

Models should reflect inherent characteristics important to human extrapolation. The following are just a few of the criteria that must not be overlooked in assessing both carcinogenicity and risk analysis. Much of the testing done on bioassays use healthy specimens. In reality, many people exposed include vulnerable populations such as the elderly, infants and children, and pregnant women. No consideration is given to the possibility that not only are these populations vulnerable but many of them may have ongoing illnesses which may interact with such chemical stressors, resulting in synergy and potentiation of health effects. Many of the fieldworkers exposed to pesticides are undernourished, not only here in the U.S. but also in third world countries where pesticides are used in high volume. Malnourishment may compound health effects in pesticide exposures. Hepatic enzyme induction is critical to the detoxification of pesticides in mammals. Diets poor in quality protein impairs microsomal enzyme induction and

Table 2

DECISION POINT APPROACH TO CARCINOGENIC TESTING

STAGE A:
STRUCTURE OF CHEMICAL
STAGE B:
SHORT TERM TESTS IN VITRO
1 MAMMALIAN CELL DNA REPAIR
2 BACTERIAL MUTAGENESIS
3 MAMMALIAN MUTAGENESIS
4 CHROMOSOME TESTS
5 CELL TRANSFORMATION
DECISION POINT 1: EVALUATION OF ALL TESTS CONDUCTED IN A AND B.
STAGE C:
TESTS FOR PROMOTERS
1 IN VITRO
2 IN VIVO
DECISION POINT 2: EVALUATION OF ALL RESULTS FROM STAGES A TO C.
STAGE D:
LIMITED IN VIVO BIOASSAYS
1 ALTERED FOCI INDUCTION IN RODENT LIVER
2 SKIN NEOPLASM INDUCTION IN MICE
3 PULMONARY NEOPLASM INDUCTION IN MICE
4 REAST CANCER INDUCTION IN FEMALE SPRAGUE-DAWLY RATS
DECISION POINT 3: EVALUATION OF ALL RESULTS FROM A TO D.
STAGE E:
LONG TERM BIOASSAYS
DECISION POINT 4: FINAL EVALUATION OF ALL RESULTS AND APPLICATIONS TO HEALTH RISK ANALYSIS (INCLUDING STAGES A,B,C,D AND E).

FROM WILLIAMS.[18]

thus potentiate metabolic responces to DDT and Lindane.[29] Hypo-vitaminosis C impairs the induction of hepatic microsomal enzymes. This may lead to increased suceptibility to toxicity and/or carcinogenicity of pesticide exposure. Dieldren partially offsets the effects of thiamine deficiency but does not prevent the enzymatic effect to riboflavin and pyridine deficiency.[30] Another issue of importance is dosage. Normally in experimental studies a controlled measure of exposure is used. In reality, pesticides are widespread in our environment.[26,30,32] Hence, the public in general and the farmworkers in particular, experience not only multiple doses, but concentrated doses because humans are at the top of most food chains.[33,34,35,36] There are species differences in biotransformation as mentioned earlier. One author states "species and strain unique mechanisms and pharmacokinetic information must be available to the risk assessors before their estimates can be any better

than guesstimates".[37] Other issues include modes of administration, single chemical versus combinations of chemical exposure,and pure pesticide exposure versus inert ingredients. Nothwithstanding these considerations, pesticides are believed to act as promoters, as well as in other various ways, in bringing about neoplasms.[38]

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V. REGULATION OF PESTICIDES

> "The realities of agricultural practices and the lack of farmworker protection standards coupled with the inherent weaknesses in FIFRA assure that significant gains in health and safety of farmworkers cannot occur with the law as currently written and enforced."
>
> M.Moses, Hearings on Ammendments to the Federal Insecticide Funigicide Rodenticide Act (FIFRA),1987.[5]

The regulation of pesticides exist at both the federal and state level in the United States. However, legislative provisions between these two levels do not necessarily overlap. Legislation on occupational health in the application of pesticides is the perogative of the states. The first Federal legislation on pesticides was in 1910 by enactment of the Insecticide Act. This Act was concerned primarily with the protection of consumers against substandard or fraudulent products and was not a measure to protect the public health. It remained in force for 3 years but was recognized as being inadequte during World War II when the flood of new products based in part on war time research began to reach the market. [1] It was subsequently superseded by the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) in 1947. This Act, for the first time, introduced some measure of control of pesticides in the U.S.. This Act has been amended since its enactment on several occasions. In 1959 its provisions were extended to cover nematocides, plant regulators, defoliants and dessiccants. The enforcement of this Act was delegated to the Pesticides Regulation Division of the Agricutural Research Services of the USDA.

Another goverment agency, the Federal Aviation Administration is reponsible for the control of agricultural aircraft operations which includes the spraying of pesticides from aircraft. This was through Part 137 of the Federal Aviation Regulations which was adopted in 1965. The transportation of poisons including pesticides is the responsibility of the Department of Transportation.

FIFRA was enacted to protect the public from the effects of toxic pesticides. Protection supposedly comes from a process of registration-a determination of safe uses of the pesticide and the restrictions that must be placed on each type of use. Hence, each pesticide should be "safe" when it is used according to product label instructions but FIFRA has never sucessfully provided this protection. In 1972, Congress added more stringent health and safety requirements

and transferred pesticide regulations to the newly created Environmental Protection Agency(EPA). Congress also required older pesticides to be reregistered after testing for new effects and environmental risks. The EPA, however, has been slow in carrying out its responsibilities. The Federal Pesticide Act of 1978 was passed to expedite the reregistration process. A National Academy of Science report in 1984 showed that out of 3350 pesticides and their inert ingredients, complete health hazard assessment was possible for only 10% and less than the "minimum" information was available for 64% of these chemicals. The EPA had identified some 600 active pesticide ingredients regarded as commercially important (about 1500 active ingredients are offically registered). Currently only 2 of the 600 have been reregistered.[2] Congress has attempted several reforms of FIFRA. The latest amendments to FIFRA , S 1516, was introduced in the 100th Congress by Senator Patrick Leahy (D-VT), chairman of the Senate Agriculture Committee. The National Coalition Against The Misuse of Pesticides (NCAMP) in Washngton D.C. supports this but qualifies it as a temporary, emergency measure.[3] NCAMP is supporting HR 3174 introduced by representative Jim Oborston (D-MN) which establishes a higher standard of prevention of groundwater contamination. This last September the Senate passed the measure cosponsored by Sen. P. Leahy (d-VT). This bill sets a nine-year deadline for companies to test old pesticides against modern health standards and for EPA to decide whether they should stay on the market. See clipping below. According to a NCAMP board member, real reform may not be possible as long as the issue is brought before the Agriculture committee as it represents the proverbial fox guarding the chicken house.[4]

Despite current amendments to FIFRA, many problems still exist. The issue of definitions in the Law is of concern. The word pesticide is not used as such, rather the term "economic poison" is used. Misbranding is a vital part of the Act but the term as such, is not defined in it. For more complete information on pesticide law and labeling, the reader is referred to publications by the US Dept. of HHS and WHO. [1,5] M.Moses has eloquently testified about the inadequacies of FIFRA in regards to real dangers posed to agricultural workders.[6] Despite such inadequacies, the EPA has moved to lower its risk assessments for many environmental carcinogens and these proposed precedent setting changes in science policy could have a great impact on human health.[7,8] Currently, farmworkers are boycotting grapes not only as a means of bringing their plight to America's conscience, but also in an attempt to obtain protection that current legislation fails to provide.[9] See appendix C.

Senate approves pesticide controls

Los Angeles Times

WASHINGTON – Landmark legislation to speed up the retesting of 600 active ingredients used in nearly 50,000 commercial pesticides easily cleared its last congressional hurdle yesterday and headed for President Reagan's expected signature.

In a matter of seconds and without discussion, the Senate approved by voice vote the first significant change in pesticide control laws since 1978.

The bill sets a nine-year deadline for companies to test old pesticides against modern health standards and for the Environmental Protection Agency to decide whether they should stay on the market.

"This is a major breakthrough," said Sen. Patrick J. Leahy (D-Vt.), a cosponsor of the same measure approved last week by the House. "Instead of taking more than 30 years for EPA to find out which pesticides are dangerous, they can do it in nine."

Industry and environmental groups reluctantly backed the bill after sponsors removed controversial provisions that had been holding up action for years. The compromise measure avoids issues such as ground-water contamination, a key concern of environmentalists, and demands by the chemical industry that Congress prevent states from passing pesticide regulations tougher than those issued by EPA.

Boston Globe Thur Sept 29 1988 A-21

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VI. BIOLOGICAL MONITORING PROGRAMS

The clinical evaluation of the toxic effects of pesticides usually follows high exposure. [1,2] The most prominent effects of most pesticides are on the nervous system. Major clinical effects on other organs are less common in acute pesticide poisoning. A comprehensive review of all reported human cases of pesticide poisoning is available.[2] Epidemiological studies are necessary in monitoring occupational exposures and in the evaluation of low environmental exposures to pesticides. The best model for studing the effects of pesticide exposure in humans are humans. Little if any information exists for evaluating chronic effects of pesticides. What information that does exist is concerned more with biological monitoring in acute cases and their effects. The Health and Nutrition Examination Survey (HANES II) was a 4 year endeavor to collect and evaluate medical and nutritional information from a random sample of the general population residing in 64 locations throughtout the U.S.. The National Human Monitoring Program participated in this survey. Specimens of human blood serum and urine were surveyed under cooperative agreement with the National Center for Health Statistics of the Public Health Service and forwarded to EPA laboratories for pesticide related residue determination. Appendix D indicates urinary metabolite residue levels which may result from exposure to selected pesticides. Some protocols for the detection of pesticide poisoning have been put forth.[3]

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VII. CONCLUSIONS

> "... by the time the medical and scientific community is aware of or has been alerted to the potential risk of exposure, a sizeable number of persons would have been unwittingly exposed, and they could become cancer victims."
>
> Council on Scientific Affairs, The American Medical Association, 1988.[1]

Cancer is not the only adverse effect of these poisons. Pesticides can also produce other types of delayed toxicity such as reproductive effects, fetal damage, delayed neurologic manifestations, possible immunologic disorders and other adverse health effects.[2] These types of studies should also be implemented as requirements for the registration of pesticides. Indeed, not using pesticides at all will avoid many of the legal and technologic questions implied by their use. Since this may not be likely, their selective use in minimal,required amounts and in least environmentally sensitive areas, and the prevention of unnecessary exposure are imperative if the health effects of these "economical poisons" are to be averted.

No mention was made of the subclinical effects of pesticides. Significant changes of neurotransmitters within the brain on exposure to such chemicals has been established.[3,4] Neurobehavioral effects on humans from pesticides have been documented and include an influenza type illness characterized by weakness, anorexia, and malaise. Neuro psychiatric effects include schizoid and depressive reactions, impaired memory and concentration, combativeness, and hallucinations or psychoses.[5,6] Pesticides also affect learning as intellectual functioning, academic skills, abstraction, flexibility of thought and motor skills are impaired. It is no small wonder that this particular and neglected segment of our society continues to perform undersuch adverse conditions. Indeed, this may be associated with the educational performance experienced by this population.

The overall long term impact of the use of pesticides results in erradication of primary pests and their replacement with secondary, perhaps resistant pests that then become the major problem. Examples include onion worm, old worm and white fly.[7] In considering alternatives to these poisons, the equilibrium or "natural balance" between plants and their natural enemies must not be forgotten.[8] Polycultures are needed to provide mixed vegetation. Integrated pest management may provide

many as yet untapped benefits. Nontoxic pheromones can be used to detect the presence of pests and to suppress pest populations through mating disruption and mass trapping.[9] Botanical molluscicides may have potential for controlling pests.[10] With application of mammaliam physiology and molecular modeling, "designer pesticides" made may yield chemicals with high potency, low use rate, and high mammalian safety and crop selectivity.[11]These innovative approaches to chemical design however, are dependent on more research on the physiology, biochemistry, and molecular biology of insects, fungi, and plants.

Although our understanding is limited, what information that does exist could and should serve for assessing the overall impact of pesticide use in this country. Appendix E lists suspected carcenogenic pesticides. With this knowledge also comes responsibility for action. Re-entry intervals should be firmly adhered to by the agricultural community. Appendix F lists Residue Incidents involving Field Workers and Appendix G lists Re-entery Intervals. In addition, the exportation of poisonous chemicals to third world countries should only be done for specific health reasons after careful deliberations on overall net benefit analysis.[12,13,14]

The focus of this report has been on the association of pesticides and cancer in humans, specifically those who are on "the frontlines" of exposure, the farm laborers. An effort was made to present a perspective on pesticide use, its history, its current use, extent of exposure, organ specific illnesses associated with pesticide use, methods for evaluating carcinogenicity, regulation of pesticides and monitoring programs. Because of time and space constraints, a brief overview of each of these areas has been attempted. It is hoped that this report will stimulate further research in these areas so that the public as a whole, and farmworkers in particular, may learn how best to ameliorate, if not prevent, the health effects of pesticide exposure.

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Appendix A

Pesticides Found in Ground Water

EPA Monitoring Data

Pesticide	States Found	Levels Found (ppm)
Alachlor (Lasso)	Iowa, Maryland, Nebraska, Pennsylvania,	.04
Aldicarb (Temik)	Arizona, California, Florida, Maine Missouri, North Carolina, New Jersey, York, Oregon, Rhode Island, Texas, Virginia, Washington, Wisconsin	1-50
Arsenic	Texas *	---
Atrazine	Iowa, Hawaii *, Maryland Nebraska, Pennsylvania, Wisconsin	.3-3
Bromacil	Florida	300
Carbofuran	Maryland, New York, Wisconsin	1-50
Dibromochloropropane	Arizona, California, Hawaii, Maryland, South Carolina	.02-20
DCPA	New York	50-700
1,2-Dichloropropane	California, Maryland, New York, Washington	1-50
Dinoseb (DNBP)	New York	1-5
Dyfonate (Fonofos)	Iowa	0.1
Ethylene dibromide	Arizona, California, Connecticut Florida, Georgia, Hawaii*, South Carolina, Washington	.05-20
Metolachlor (Dual)	Iowa, Pennsylvania	--
Metribuzin (Sencor)	Iowa	0.9-4.35
Oxamyl	New York, Rhode Island	5-65
Simazine (Princep)	California, Pennsylvani	1-3
Trichloropropane	California, Hawaii	0.2-2

Appendix B

Pesticides Found in Ground Water - California

Aldrin
Aldicarb (Temik)
Atrazine (Princep)
Betnazon (Basagran)
Benzaldehyde
Carbaryl (Sevin)
Carbofuran (Furadan)
Chlordane
Chlorpyrifos (Lorsban, Dursban)
Chloropham
2,4-D
Dacthal
DBCP (Dibromochloropropane)
DDD
DDE
DDT
DEF
Diazinon (Spectracide)
Dibrom (Naled)
Dichlone
1,2-Dichloropropane
1,3-Dichloropropene (cis)
1,3-Dichloropropene (trans)
Dicofol (Kelthane)
Dieldrin
Difolatan (Captafol)
Dimethoate
Dinoseb (DNBP)
Diphenamid
Disulfoton (Di-Syston)
DNOC (Dinitro-o-cresol)
EDB (Ethylene dibromide)
Endosulfan (Thiodan)
Endrin
Ethion
Ethylene thiourea
HCB (Hexachlorobenzene)
Heptachlor
Lindane (BHC, gamma-HCH)
Malathion
Methylene chloride
Methyl parathion
Ordram (Molinate)
Paraoxon
Parathion
PCNB (Pentachloronitrobenzene)
PCP (Pentachlorophenol)
Phorate (Thimet)
Phthalates
Propargite (Omite, Comite)
Simazine
2,4,5-T
TCP (Tetrachlorophenol)
Toxaphene
2,4,5-TP (Trichlorophenol)
Trifluralin (Treflan)

Source: California Legislature Assembly Office of Research: The Leaching Fields, A Nonpoint Threat to Groundwater. Joint Publications Office, Sacramento, California 95814, March, 1985; and Cohen, S.Z., Creeger, S.M., Carsel, R.F., et al.: Potential Pesticide Contamination of Groundwater from Agricultural Uses. In Krieger, R.F. and Seiber, J.N.: Treatment and Disposal of Pesticide Wastes, ACS Symposium Series # 259, American Chemical Society, Washington, D.C., 1984.

Appendix C

Fact Sheet on Five Pesticides the United Farm Workers Union Wants Banned in Grape Production

CAPTAN: A fungicide first marketed in 1949. Its largest use in California is on grapes (41% of reported use in 1986). Other major uses are in almonds, prunes, strawberries and peaches.

Captan is a carcinogen in the mouse and the rat, and a teratogen (causes birth defects) in the hamster and the mouse. It is structurally similar to thalidomide. Captan is mutagenic and damages chromosomes and DNA. There are data gaps (inadequate or no studies on file) in four of the ten required toxicity tests (chronic effects, teratogenicity, DNA damage).

Captan is a frequent cause of skins rashes (contact dermatitis) in grape workers, and can cause an allergic skin reaction as well. It is not otherwise acutely toxic and does not cause acute systemic poisoning or death from occupational exposure. The risk of chronic effects such as cancer and birth defects in farmworkers is of great concern with this pesticide.

Captan is among the pesticides the National Academy of Sciences listed as posing a cancer risk to consumers. It is the pesticide most frequently found in testing of residues on grapes. The California Department of Food and Agriculture removed Captan from its multiresidue screening panel in 1987 for reasons which have not been explained.

DINOSEB: A herbicide and insecticide first marketed in 1945. It was emergency suspended by the Environmental Protection Agency in October, 1986 (the UFW had called for its ban in July, 1985). Dinoseb is banned in California and is currently registered for selected uses only in Washington, Oregon, and Idaho. Grapes were the major food crop use in California (17% of reported use in 1986).

Dinoseb was banned because of its teratogenicity (birth defect producing) properties. It also causes tumors in laboratory animals as well as sterility and other effects on reproduction.

Dinoseb is highly toxic and has caused deaths in farmworkers from absorption through the skin -- most recently in Texas in 1984.

Dinoseb is not used when it could leave residue on grapes and is therefore not a hazard to the consumer. However it is a ground water contaminant and therefore a potential drinking water contaminant.

METHYL BROMIDE: A fumigant, nematicide, insecticide first marketed in 1932. It is injected into the soil to kill nematodes (microscopic worms) before planting of new vineyards. Grape production accounted for 10.5% of reported use in 1986. Other major uses are strawberries (31%), and structural fumigation (22%).

There are no studies in EPA or CDFA files for five of ten required categories (cancer in rat and mouse, chronic effects in rat, mouse and dog),

and no adequate studies in four others (teratogenicity in the rat and rabbit, reproduction in the rat, mutagenicity and chromosome damage). A study from Holland reports it to be a mouse carcinogen. There is one adequate study on record which shows damage to DNA.

Methyl bromide has caused more occupational deaths in California than any other pesticide. It is highly poisonous and workers who survive acute poisoning often suffer permanent damage to the nervous system. Recent studies show that low level exposures over time may cause neuropsychological and neurobehavioral effects in workers. It affects the lungs and can cause toxic hepatitis. There have also been deaths reported in home owners who re-entered their home too soon after fumigation.

Methyl bromide is used in post harvest fumigation, but is not known to be used for grapes, so does not pose a residue risk to consumers. However the evacuation of 1200 people in Fremont, California was required last year when off gassing occurred from application in a field near a residential area.

Methyl bromide is in the same family of chemicals as the two nematicides it has replaced -- DBCP, banned in 1979, and EDB, banned in 1984. Both DBCP and EDB cause sterility in human males and both are animal carcinogens. They are also both widespread ground water contaminants and DBCP has been found in hundreds of drinking water wells in the San Joaquin Valley. Methyl bromide is a gas and has been found in the upper atmosphere. It has been postulated that it may react with ozone causing depletion, much as the chlorofluorocarbon gases do.

There is no information available on the environmental fate of methyl bromide in spite of the use of more than 10 million pounds a year in California, with approximately 80% of this use being in agriculture.

PARATHION: An insecticide first marketed in 1947. It is a "nerve gas" type of pesticide. Grapes accounted for 2% of total usage in 1986, with major uses being in almonds (38%), peaches/nectarines (16%), and plums (14%).

Parathion is a carcinogen in the rat and also causes retinal degeneration and other eye damage as well as damage to the nervous system in both rats and mice. There are data gaps (no studies or no acceptable studies on file) for eight of 11 required toxicity tests (cancer in rat and mouse, chronic effects in rat and mouse, mutagenicity, chromosome and DNA damage and neurotoxicity).

Parathion is highly poisonous and is responsible for more occupational deaths throughout the world than any other pesticide. Parathion and Phosdrin (see below) together are responsible for more than two-thirds of acute poisoning of workers in agriculture reported to the state of California. Parathion breaks down on leaf surfaces to a much more toxic chemical called paraoxon which is readily absorbed through the skin and has caused many episodes of poisoning of crews of farmworkers harvesting crops. There is also evidence of permanent long term effects on the nervous system after recovery from acute poisoning.

Parathion is taken up and bound by the cuticle (skin) of fruits and vegetables and cannot be washed off and therefore can pose a residue hazard to the consumer.

PHOSDRIN: An insecticide first marketed in 1953. It is a "nerve gas" type pesticide. In 1986 use on grapes was 2.5% of total usage, with major uses being in lettuce (30%) and artichokes (11%).

It is not known if Phosdrin is a carcinogen since there are no cancer studies on file in either rat or mouse. There are data gaps (no studies or no acceptable studies on file) for nine of 11 required toxicology tests (carcinogenicity; chronic effects in rat, mouse, dog; reproduction in the rat; teratogenicity in the rabbit; mutagenicity, chromosome and DNA damage).

Phosdrin is highly poisonous, is readily absorbed through the skin and has caused worker deaths. Phosdrin and parathion are responsible for more than two-thirds of acute systemic poisoning of farmworkers reported in California.

Phosdrin breaks down more rapidly than parathion, but can be present on food at the time of sale and therefore could pose a residue hazard to the consumer.

Reported Use of the Five Pesticides in California - 1986

From California Department of Food and Agriculture Pesticide Use Reports

Pesticide	Total Pounds Reported	Pounds Reported in Grape Production
Captan *	483,471	200,050 (41%)
Dinoseb **	622,748	108,071 (17%)
Methyl bromide	10,031,345	1,057,855 (10.5%)
Parathion	814,091	13,847 (2%)
Phosdrin	273,874	7,029 (2.5%)

* Captan is not a restricted use pesticide and therefore all usage is not reported; actual use is higher than this figure. Only commercial applicators are required to report use.

** Dinoseb was banned in California in October, 1986.

Parathion is taken up and bound by the cuticle (skin) of fruits and vegetables and cannot be washed off and therefore can pose a residue hazard to the consumer.

PHOSDRIN: An insecticide first marketed in 1953. It is a "nerve gas" type pesticide. In 1986 use on grapes was 2.5% of total usage, with major uses being in lettuce (30%) and artichokes (11%).

It is not known if Phosdrin is a carcinogen since there are no cancer studies on file in either rat or mouse. There are data gaps (no studies or no acceptable studies on file) for nine of 11 required toxicology tests (carcinogenicity; chronic effects in rat, mouse, dog; reproduction in the rat; teratogenicity in the rabbit; mutagenicity, chromosome and DNA damage).

Phosdrin is highly poisonous, is readily absorbed through the skin and has caused worker deaths. Phosdrin and parathion are responsible for more than two-thirds of acute systemic poisoning of farmworkers reported in California.

Phosdrin breaks down more rapidly than parathion, but can be present on food at the time of sale and therefore could pose a residue hazard to the consumer.

Reported Use of the Five Pesticides in California - 1986
From California Department of Food and Agriculture
Pesticide Use Reports

Pesticide	Total Pounds Reported	Pounds Reported in Grape Production
Captan *	483,471	200,050 (41%)
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* Captan is not a restricted use pesticide and therefore all usage is not reported; actual use is higher than this figure. Only commercial applicators are required to report use.

** Dinoseb was banned in California in October, 1986.

Appendix D

Frequency and Mean Levels of Selected Pesticide Residues in Human Urine, Preliminary Data[1]

Pesticide	Chemical Detected	Percent of Samples Positive	Arithmetic Mean (ppb)
Carbaryl & Naphthalene	alpha-Naphthol	2.3	<10
Propoxur	Isopropoxyphenol	5.0	<40
Carbofuran	Carbofuran phenol and 3-Ketocarbofuran	4.4 4.5	<40 <30
Pentachlorophenol, Lindane and Hexachlorobenzene	Pentachlorophenol	81.0	7.4
Methyl and Ethyl Parathion	para-Nitrophenol	3.2	<10
2,4-D	2,4-D	0.5	< 5
2,4,5-T	2,4,5-T	ND*	-
Silvex	Silvex	ND	-
Chloropyrifos	3,5,6-Trichloro-2-pyridinol	6.5	< 5
2,4,5-Trichlorophenol used as a disinfectant; or a metabolite of certain organochlorine insecticides	2,4,5-Trichlorophenol	3.1	< 5
Dicamba	Dicamba	1.3	< 5
Malathion	alpha-Monocarboxylic Acid and Dicarboxylic Acid	1.6	< 30
Any organophosphorus insecticide containing these phosphate or thiophosphate molecules	DMP	11.7	< 20
	DEP	7.5	< 20
	DMTP	6.5	< 20
	DETP	7.0	< 20
	DMDTP	0.4	< 20
	DEDTP	0.1	< 20

1 Preliminary data based on the analysis of 4480-4580 samples collected from the general population via the Health and Nutrition Examination Survey II (HANES II) National

Appendix E

Oncogenic and Suspect Pesticides -- Based on EPA Data
with Classification Code *
(as of April 1988)

Pesticide	Classification *	Pesticide	Classification *
Acephate (Orthene)	C	Dimethoate	NA
Acetochlor	B2	Dinoseb	C
Aciflurofen (Tackle/Blazer)	B2	2,4-DP Acid	NA
Alachlor	B2	Ethalfluralin	NA
Allette	C	Ethylene dibromide	B2
Amdro	B2	Ethylene thiourea (ETU)	B2
Amitraz	C	Fenarimol	D/E
Amitrole	B2	Fluridone	E
Apollo (Clofentezine)	C	Folpet	B2
Assert	D	Fomesafen	C
Assure	C	Formaldehyde vapor	NA
Asulam	C	Furmecyclox	B2
Atrazine	C	Galben	NA
Barban (Carbyne)	NA	Gardona	C
Baygon (Propoxur)	B2	Glyphosate (Roundup)	C
Baytan (Triadimenol)	C	Guthion	D
Benomyl	C	Haloxyfop-methyl (Verdict)	C
Biphenox (Mowdown)	NA	Harvade	C
Biphenthrin	C	HCB (cont. with PCNB)	B2
Bromacil	NA	Heptachlor	B2
Bromoxynil	C	Hoelon	NA
Cadmium	B1	Imidan (Phosmet)	C
Captafol	B2	Isoxaben	C
Captan	B2	Kerb (Pronamide)	C
CDEC	NA	Lactofen	B2
Chloramben	NA	Larvadex (Cyromazine)	NA
Chlordane	B2	Lindane	B/C
Chlordimeform	B2	Linuron	C
Chlorobenzilate	NA	Maleic hydrazide	NA
Chlorothalonil	B2	Mancozeb	NA
4-chloro-o-toluidine	NA	Maneb	NA
CPA	NA	MBC	MA
Cypermethrin	C	Metalaxyl	E
2,4-D	C	Methane arsenic acid	NA
Dalapon	NA	Methidathion	C
Daminozide (Alar)	B2	Metolachlor pending	(C)
DBCP	B2	Methoxychlor	NA
DDT, DDE, DDD	B2	Metronidazole	NA
DDVP	B2	Mirex	NA
Diallate	NA	Monuron	NA
Diclofop-methyl (Hoelon)	NA	Nemacur	NA
Dicofol	C/B2	Nitrofen (TOK)	NA
p-Dichlorobenzene	C/B2	Norflurazon	NA
Dieldrin	B2	OPP	NA

Pesticide	Classification *	Pesticide	Classification *
Oryzalin (Surflan)	C	Rotenone	pending
Oxadiazon (Ronstar)	B2	Savey	C/B2
Paraquat	C	Sutan	NA
Parathion	C	Telone II	B2
PCNB	D	Terbuthylazine	NA
Permethrin	NA	Terbutryn	C
PHMB	NA	Tetrachloroethylene	NA
Picloram	NA	Toxaphene	NA
Primicarb	NA	1,1,2-Trichloroethane	NA
Prochloraz	C	Trichlorfon	NA
Profluralin	NA	Tridiphane	NA
Propazine	C	Trifluralin	C
Propioconazol (Tilt)	C	UDMH (Daminozide metab.)	B2
Pydrin	NA	Vel	NA
Rabon	NA	Vinylidene chloride	NA
Resmethrin	NA	Zineb	NA
Ronilan	E		

* Classification Code

A – Human Carcinogen
B – Probable Human Carcinogen
B1 – Sufficient evidence of carcinogenicity from animal studies with limited evidence from epidemiologic studies
B2 – Sufficient evidence of carcinogenicity from animal studies, with inadequate or no epidemiologic data
C – Possible Human Carcinogen limited evidence of carcinogenicity in the absence of human data

D – Not classifiable as to human carcinogenicity — inadequate or no human and animal data for carcinogenicity
E – Evidence of non-carcinogenicity for humans — no evidence of carcinogenicity in at least two animal species in adequate studies — based on available evidence and does not mean is not a carcinogen under any circumstances
NA – Not available or not provided

Teratogenic Pesticides -- Based on EPA Data
(as of June, 1988)

Pesticide	Use	Pesticide	Use
Acrolein (Aqualin)	H	Fenarimol (Rubigam)	F
Altosid (Methoprene)	IGR	Fenoxaprop ethyl	H
Amiben (Chloramben)	H	Fluazifop-butyl (Fusilade)	H
Avermectin		Folpet	F
Bacquacil		Hexachlorobenzene	F
Baycor (Bitertanol)	F	Imidan (Phosmet)	I
Bayleton (Triadimefon)	F	Kinoprene	IGR
Benazolin - ethyl	H	Larvadex (Cyromazine)	I
Benomyl	F	Mancozeb	F
Bentazon (Basagran)	H	Methyl parathion	I
Bladex (Cyanazine)	H	Mirex	I
Bromoxynil	H	Nemacur (Fenamiphos)	N
Cacodylic acid	H	Nitrofen (TOK)	H
Captafol	F	Omite (Propargite)	A
Captan	F	OPP	D,F
Carbaryl (Sevin)	I	OPP - sodium salt	D,F
Chlordimeform	I,A	Paclobutrazol	PGR
Chlorpropham	H,PGR	PCNB	F
Copper sulfate	F	Picloram	H
Cyclohexiimide (Acti-dione)	F	Potassium maleic hydrazide	PGR
2,4-D acid	H	Sodium arsenate	I
Dichlobenil	H	Sodium arsenite	F,H,I
Dichlorophene	F,B	Sodium omadine	
DMF		2,4,5-T	H
2,4-DP Acid (Dichlorprop)	H	Terrazole	F, NI
Dinocap (Karathane)	F,A	Tributyltin oxide	F
Dinoseb	H	Trichlorfon	I
Diquat	H	Trifluralin	H
Endosulfan	I	Triphenyltin fluoride	F
Endothall	H	Triphenyltin acetate	F,H,M
Ethion	I	Triphenyltin hydroxide	F
2-Ethyl 1,3-hexanediol		Vinyzene	
Ethylene dichloride	Fum	Warfarin	R

* A = acaracide
B = bactericide
D = disinfectant
F = fungicide
Fum = fumigant
H = herbicide
I = insecticide
IGR = insect growth regulator
M = molluscicide
N = nematicide
NI = nitrification inhibitor
PGR = plant growth regulator
R = rodenticide
Rep = repellant
S = solvent
WP = wood preservative

Appendix F

Reported Crop Residue Incidents (Re-entry Poisonings)
Involving Field Workrs
California - 1949 to 1987

Year	County	Number Ill	Crop	Pesticide(s) Implicated
1949	Yuba	20-25	Pears	Parathion
1951	Kern	16	Grapes	Parathion
1952	Riverside	11	Oranges	Parathion
1953	Riverside	7	Oranges	Parathion
1953	Riverside	-	Citrus	Parathion
1953	San Bernardino	-	Citrus	Parathion
1959	Various	275	Citrus	Parathion
1961	Tulare	10	Lemons	Parathion
1963	Stanislaus	94	Peaches	Parathion
1966	Tulare	9	Oranges	Parathion
1966	Tulare	6	Oranges	Parathion
1966	Tulare	3	Oranges	Parathion
1966	Los Angeles	11	Oranges	Parathion/Malathion
1966	Tulare	9	Oranges	Parathion/Ethion
1967	Stanislaus	24	Peaches	Guthion/Ethion
1967	Merced	3	Peaches	Guthion
1968	Tulare	19	Oranges	Parathion
1970	Tulare	3	Lemons	Dioxathion/Naled
1970	Tulare	2	Oranges	Parthion/Ethion
1970	Tulare	8-11	Oranges	Guthion/Ethion
1970	Kern	35	Oranges	Parathion
1970	Tulare	11	Oranges	Parathion/Malathion
1971	Fresno	8	Olives	Parathion
1972	Fresno	3	Oranges	Parathion
1972	Tulare	9	Oranges	Parathion
1972	Lettuce	31	Lettuce	Parathion
1973	Fresno	27	Grapes	Phosalone/Dialifor
1974	Fresno	2	Grapes	Phosalone/Guthion
1975	Tulare	16	Oranges	Parathion
1976	Madera	118	Grapes	Phosalone/Dialifor
1977	Fresno	25	Oranges	Parathion
1978	Tulare	7	Grapes	Ethion
1980	Merced	6	Peaches	Guthion
1980	Monterey	22	Cauliflower	Phosdrin/Phosphamidon
1981	Monterey	41	Lettuce	Phosdrin
1982	Tulare	17	Oranges	Parathion
1982	Monterey	35	Caulflower	Phosdrin/Metasystox-R
1983	Monterey	23	Cauliflower	Metasystox-R/Dimethoate
1986	Tulare	121	Oranges	Omite-CR
1987	Fresno	35	Peaches	Guthion
1987	Madera	24	Grapes	Phosalone
1987	Madera	30	Grapes	Phosalone
1987	Fresno	24	Grapes	Phosalone

Appendix G

Re-entry Intervals (REI) * in Days - 1988
California Department of Food and Agriculture (CDFA)
and the Environmental Protection Agency (EPA)

Pesticide	CALIFORNIA Apples	Citrus	Corn	Grapes	Peaches	Other	EPA All Crops
All Category I (a)	1	1	1	1	1	1	1
Acephate (Orthene	–	–	–	–	–	–	1
Aldicarb (Temik	1	1	1	1	1	1	1
Aliette *	–	–	–	–	–	–	7 a
Amitraz (Baam)	–	–	–	–	–	–	1
Anilazine (Dyrene)	2 b	2 b	2 b	2 b	2 b	2	1
Azinphosmethyl	14 c	30	–	21	14 c	14 d	1
Benomyl	–	–	–	–	–	–	1
Captafol **	–	–	–	–	–	e	1
Captan	e	e	–	e	e	e	4
Carbofuran	–	–	14	–	–	–	2
Chlordimeform **	–	–	–	–	–	–	5
Chlorobenzilate	–	1	–	–	–	–	1
Chlorothalonil	–	–	e	–	e	e	1
Chlorpyrifos	–	2	–	–	–	–	4,1 f
Cyhexatin **	–	–	–	–	–	–	18 g
Daminozide (Alar)	–	–	–	–	–	–	1
Diazinon	–	5	–	5	5	–	–
1,2-Dichloropropene	–	–	–	–	–	–	3
Dicroptophos (Bidrin)	2 b	2 b	2 b	2 b	2 b	2	2
Dimecron	2	14	2 b	2 b	2 b	–	
Dimethoate	–	2	–	2	–	–	4 g
Dioxathion	–	30	–	30	30	–	1
Diquat dibromide	–	–	–	–	–	–	1
Disulfoton	2 b	2 b	2	2 b	2 b	2	1
Endosulfan	2	2	2	2	2	2	2
EPN **	14	14	14	14	14	14	2
Ethion	2	30	2	14	14	2	1
Fenamiphos (Nemacur)	1	1	1	1	1	1	2
Fenbutatin oxide	–	–	–	–	–	–	1
Fenitrothion	–	–	–	–	–	–	1
Fensulfothion	1	1	1	1	1	1	1
Folpet **	e	e	–	e	e	e	4
Fonofos (Dyfonate)	1	1	1	1	1	1	1
Formethanate HCl	1	1	1	1	1	1	1
Linuron	–	–	–	–	–	–	1
Malathion	–	1	–	1	1	–	–
Mancozeb	–	–	–	–	–	–	1
Methamidophos	2 b	2 b	2 b	2 b	2 b	2 b	1
Methidathion	2 h	30,40 i	2 b	2 b	2 h	2	1
Methiocarb	–	–	–	–	7	–	1
Methomyl (Lannate)	2	2	2	2	2	–	2
Methyl bromide	–	–	–	–	–	–	2
Methyl parathion	14	14 j	14 j	14 k	21	14 j	1
Methyl parathion encap	2	2	2	2	2	2	–
Mevinphos (Phosdrin)	2	4	2	4	4	2	–
Monocroptophos	2 b	2 1	2 b	2 b	2 b	2	1

Pesticide	CALIFORNIA Apples	Citrus	Corn	Grapes	Peaches	Other	EPA All Crops
Naled (Dibrom)	-	1	-	1	1	-	1
Oxamyl (Vydate)	2	2	-	-	2	-	2
Oxydemeton methyl	2	2	2	2	2	2	2
Parathion - ethyl	14	30 **m** 45 **n** 60 **o** 90 **p**	14 **q**	21	21	14 **q**	2
Phorate (Thimet)	2 **b**	2 **b**	7	2 **b**	2 **b**	2	1
Phosalone (Zolone)	**r**	7 **s**	-	**t**	7 **r**	1	1
Phosmet (Imidan)	-	-	-	5 **b**	5 **b**	-	1
Propargite (Omite)	-	14	-	14 **u**	-	-	7 **v**
Propargite (Omite CR)	-	42 **w**	-	-	-	-	-
Sulfur	-	1	-	1,3 **x**	1	1	-
Thiram	-	-	-	-	-	-	1
Trichlorfon	-	-	-	-	-	-	1

* A re-entry interval (REI) is the time after a pesticide has been sprayed before workers are permitted to enter the field. When a longer interval is not on the label, workers can enter "when sprays have dried and dusts have settled." In California (but not EPA) all Toxicity Category I pesticides have a 1 day REI.

** Registration has been cancelled for these pesticides.

a On hops
b CDFA is proposing to delete this REI.
c If less than one lb/acre applied on apples, peaches or nectarines, REI is 7 days.
d On stone fruit, except almonds.
e CDFA proposed and then withdrew a 14 day REI for this pesticide.
f REI 4 days on citrus and grapes, 1 day for all other crops.
g On citrus and apples.
h Dormant use only.
i For concentrated sprays authorized by Special Local Need REI is 40 days.
j For application less than one lb/acre REI is 2 days.
k In Monterey County on grapes REI is 6 days.
l CDFA is proposing to increase this REI to 7 days.
m For applications less than 2 lbs/100 gallons, less than 8 lb/acre, and a total of not more then 10 lbs/acre in the previous 12 months.
n For applications greater than 2 lbs/100 gallons, greater than 8 lb/acre, and a total of more than 10 lbs/acre in the previous 12 months.
o For all applications greater than 2 lbs/100 gallons.
p Applies to Fresno, Kern, Madera and Tulare counties from May 15 to September 15, before and after which REI is reduced to 30, 45, or 60 days as applicable.
q For 1/2 to 1 lb/acre REI is 7 days; for less than 1/2 lb/acre REI is 2 days.
r Proposed by CDFA
s For applications less than 3 lbs/acre REI is 2 days.
t Phosalone is no longer registered for use on grapes in California.
u CDFA is proposing to change this REI to 14 days.
v For strawberries the REI is 3 days.
w The manufacturer has withdrawn this product from the California market.
x In Riverside county during March and April, and in San Joaquin, Stanislaus, Merced, Madera, Fresno, Kings, Tulare and Kern counties from May 15 through harvest, the REI is 3 days.