FINAL REPORT *

DETERMINATION OF AIRBORNE RESIDUES FROM FOUR HARVEST AID CHEMICALS (DEF, FOLEX, CACODYLATES, AND PARAQUAT) AT TREATED SAN JOAQUIN VALLEY COTTON FIELD SITES, AS A MEASURE OF POTENTIAL HUMAN EXPOSURE

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Abstract

This project was undertaken to assess airborne concentrations of four cotton harvest aid chemicals in and around sites of use, so that some estimate could be made of potential human exposures to atmospheric residues of these chemicals. For the organophosphorus defoliants DEF and Folex, the principal downwind airborne residue of toxicological concern is butyl mercaptan, a formulation impurity of both defoliants and a byproduct of the oxidation of Folex in the spray mix and in field residues. Further research is needed to find ways to minimize mercaptan formation and the associated airborne mercaptan residues from Folex applications. To assess the potential health effects from worker exposure to DEF, use was made of an animal model (scaleless chicken) placed in a DEF-applied cotten field, and of monitoring workers engaged in applying DEF. While both studies confirmed that normal worker exposure to DEF was below the threshold for onset of delayed neurotoxicity in humans, the margin of safety was considered to be inadequate unless use of protective clothing and other safeguards was enforced.

Airborne levels of paraquat declined rapidly both with distance during spraying and with time following spraying when this desiccant was applied to cotton, reaching inconsequential levels 400 m downwind from a sprayed field and at all downwind sites within an hour after spraying was completed. An unanticipated result of our study was that paraquat levels in the air surrounding a cotton harvester were comparable in concentration to those just downwind from a sprayed field. These residues, generated from paraquat remaining on the cotton plants at harvest, are of sufficient magnitude to argue for the required use of enclosed cab harvesters. Further research is needed on the nature and magnitude of airborne residues of paraquat and other residual chemicals--and human exposures to them--during the harvesting and ginning of cotton.

For DEF, Folex, paraquat, and cacodylates methods were developed for the sampling and analysis of airborne residues at low concentrations to meet the objectives of this project. For cacodylates, the method requirements were only partly met and no analyses of field samples were conducted.

TABLE OF CONTENTS

	Page
Abstract	2
Table of Contents	3
I. INTRODUCTION	4
II. DEF-FOLEX	6
A. Background	6
B. Analytical Method Development	8
C. Field Monitoring of Airborne Levels of DEF, Butyl Mercaptan, and Butyl Disulfide--the Odor Problem	8
D. Use of a Test Animal to Assess Exposure to and Neurotoxic Effects from DEF	19
E. Field Monitoring of Workers for Symptoms of Delayed Neurotoxicity Caused by DEF	20
III. PARAQUAT	25
A. Background	25
B. Analytical Method Development	26
C. Field Monitoring for Airborne Levels	28
IV. CACODYLIC ACID	32
A. Background	32
B. Analytical Procedure	33
C. Method Development Results	34
D. Conclusions	38
E. References	39
V. PROJECT SUMMARY AND CONCLUSIONS	39

APPENDICES (Reprints)

Hermann, B.W. and J.N. Seiber. 1981. Sampling and Determination of S,S,S-Tributyl Phosphorotrithioate, Dibutyl Disulfide, and Butyl Mercaptan in Field Air. Anal. Chem., 53, 1077.

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I. INTRODUCTION

Substantial quantities of "harvest aid" chemicals are applied each year to cotton grown in California. The accompanying table (Table I) shows that DEF (S,S,S-tributylphosphorotrithioate) is generally used in largest quantities, followed by paraquat, Folex (merphos, S,S,S-tributylphosphorotrithioite), and cacodylic acid - sodium cacodylate mixture (Bolls-eye).

Table I. Reported Uses of Four Harvest Aid Chemicals on Cotton in California, 1978 -1981.

	DEF		Folex		Paraquat		Sodium Cacodylate and Cacodylic Acid	
	lbs.	acres*	lbs.	acres	lbs.	acres	lbs.	acres
1978	840	491	18	10	196	1018	79	112
1979	1279	733	421	238	291	1554	198	307
1980	745	434	56	34	228	1075	151	233
1981	888	466	208	114	377	1236	26	35

* Figures are in 1000s

The application of cotton harvest aids is somewhat unique in that use is entirely within a very short time in the late Fall (October-November), and is limited to the major cotton growing areas in the southern San Joaquin Valley and Imperial Valley.

There is increasing concern regarding side-effect exposures to these chemicals among sprayers-applicators, farm workers, and other bystanders or nearby dwellers in and near heavy use areas. For example, each year during the defoliation season complaints are received by local health and agricultural agents describing headache-nausea-respiratory symptoms, mostly in connection with nearby applications of the odoriferous DEF-Folex defoliants.

Recent research findings of delayed neurotoxic responses from chronic exposure to DEF may give substance to the concerns expressed by citizens over long-term hazards resulting from exposure. It appears that both short-term (nausea) and long-term (respiratory/neurotoxicity) exposure/effects need to be considered. In connection with paraquat, no regular complaints of illness are received, although sporadic reports of damage to ornamental plants have been forthcoming. It is also suspected that inhaled paraquat may cause or aggravate chronic respiratory diseases among persons in high exposure work categories.

As the previous examples illustrate, concerns to date imply that injurious levels of airborne residues exist in several potential "hot spots" in this state. However, no systematic experimental study has been made to ascertain whether or not the implication has a basis in reality. Considering the apparent need for harvest aid chemicals of the type described--a consequence of the way in which cotton is harvested in this state--and the apparent lack of suitable substitutes, it seemed appropriate that such a study be undertaken. This was spurred by the presence of all four of the organic harvest-aid chemicals on the "Current List (as of April 1978) of RPAR Candidates." Should several or all of these chemicals be lost to cotton producers in a short period of time, the effects could vastly alter the current marginally positive economic status of cotton as a major crop in California (California ranks second among the states in lint production). A major concern of EPA officials involved in the RPAR process has to do with the magnitude of airborne residues for potential human exposure.

This project was undertaken to assess airborne levels of the four harvest aid chemicals in and around sites of use, so that some estimate of human exposure resulting from contact with these airborne residues could be made. Much of the work involved development of analytical methods, as no suitable

methods existed previously. In the case of DEF and Folex, systematic measurements of mixer-loader-applicator exposure by both dermal and inhalation routes were made in two separate studies supported by other funds, in addition to the surveillance of airborne residues done in connection with this project. Results of these studies are included in this report. In the case of paraquat, a systematic measurement of mixer-loader-applicator exposure is now underway in our laboratory in a separate study supported by other WRPIAP funds. Only the surveillance of airborne paraquat residues done in connection with this project are reported here. For cacodylate, we pursued the analytical method development with some success, but field-collected air samples were outdated and/or lost by the time the method development was completed. Thus, only the analytical method development is reported here. In short, the project objectives were basically realized for DEF, Folex, and paraquat, but only partly so for cacodylates.

The report is organized by chemical. DEF and Folex results are reported together as these two compounds are closely related chemically and, in fact, Folex is converted to DEF partially in the spray mix and completely following release to the environment. Because much of the information gathered for DEF, Folex, and paraquat has been published, this report will defer to the publications rather than repeat verbatim information presented in them.

II. DEF - FOLEX

A. Background

The organophosphorus compounds DEF (S,S,S-tributylphosphorotrithioate) and Folex (merphos, S,S,S-tributylphosphorotrithioite) are two of the major defoliants used in the U.S. as cotton harvest aids. The use of these

chemicals has elicited complaints of headache, nausea, and respiratory distress from nearby residents during the defoliation season in Arizona and California, due apparently to the odors associated with the defoliation treatment. The odors are considered to arise from the presence in the air of dibutyl disulfide and butyl mercaptan, both of which are formulation impurities and potential environmental conversion products of the parent defoliants.

For the determination of airborne levels of sulfur-containing compounds associated with the use of organophosphorus defoliants, methods were required for sampling and analyzing DEF, dibutyl disulfide, and butyl mercaptan at low levels in agricultural field air. Since merphos forms DEF rather rapidly by oxidation in water and air, there was no need for a separate method for merphos assay.

In addition to the odor problem, there is increasing concern regarding the safe use of DEF and merphos because they produce a delayed neurotoxicity in hens. However, there is presently no documentation of acute or delayed neurotoxicity in humans when these two chemicals are used according to recommendations. In order to gather such information, we obtained mixer-loader-applicator exposure data in two separate field trials. In one trial, carried out with Dr. Barry Wilson, an animal model (scaleless chicken) was employed in the field to see if delayed neurotoxicity would occur in the animals under field use (and exposure) conditions. In the second trial, carried out in collaboration with Drs. Charles Becker and Marcello Lotti at UCSF, field workers were monitored to see if enzymatic and behavorial changes associated with delayed neurotoxicity would occur in humans under field conditions.

B. Analytical Method Development

A method was developed for simultaneously trapping airborne S,S,S-tributylphosphorotrithioate (DEF), di-n-butyl disulfide, and n-butyl mercaptan by accumulative sampling through a two-stage, high-volume sampler. The upstream sampling stage, consisting of XAD-4 resin, quantitatively trapped DEF and dibutyl disulfide; postsampling extraction with ethyl ether, cleanup through a micro-Florisil column for dibutyl disulfide, and element-selective gas-liquid chromatographic (GLC) analysis led to method recoveries of 81% for DEF and 107% for dibutyl disulfide at spiking levels corresponding to ca. 80 ng/m^3. Estimated detection limits were 0.1 for DEF and 1.0 ng/m^3 for dibutyl disulfide. The downstream sampling stage, consisting of mercuric acetate-impregnated silica gel, trapped butyl mercaptan as a mercaptide salt; mercaptan was regenerated through a postsampling workup consisting of treatment with hydrochloric acid and extraction with olefin-free pentane. Analysis of the pentane phase by element-selective GLC led to quantitation of butyl mercaptan at spiking levels corresponding to a detection limit of ca. 1 ng/m^3 with an overall recovery of 65%. The methods were tested for sampling airborne levels of the three chemicals in the vicinity of cotton defoliation treatments. A complete report of this method is in a publication by Hermann and Seiber, 1981, attached to this report.

C. Field Monitoring of Airborne Levels of DEF, Butyl Mercaptan, and Butyl Disulfide--The Odor Problem.

The illness and nuisance reports associated with DEF/merphos and their use are consistent with the drift of noxious odors as vapors away from the site. The magnitude of the vapor pressures of DEF, merphos, butyl disulfide, and butyl mercaptan, and the presence of the latter as formulation impurities

which readily volatilize after spraying also point toward vapor phase transport as important to the etiology of the problem. Thus, the field study primarily involved monitoring atmospheric residues from commercial air applications. Three commercial air applications were followed, two with DEF and one with merphos. All sites were owned and operated by Southlake Farms, Incorporated, in Kings County, California. Useful information was obtained for two of these applications, one each with DEF and merphos. In conjunction with the air sampling, foliage samples were taken to measure the defoliant dissipation in the field. Mylar sheets were also placed in the field and sampled over time to measure loss due to evaportion.

Samples collected 50 m northwest of the field during spraying gave 1189, 2.21 and 14.5 ng/m^3 for DEF, dibutyl disulfide, and butyl mercaptan, respectively, while corresponding values for the 24 h posttreatment samples were 450, 0.52, and 3.5 ng/m^3 (Table II). Residues of DEF (24 ng/m^3) were detected at 72 h posttreatment at the same sampling site. No noticeable interferences were visible at these concentration levels. A GLC peak corresponding to DEF in the pretreatment sample represents ca. 10 ng/m^3 of DEF from spraying of the defoliant at other locations in the general vicinity of the study field. There was no clear pattern of airborne residue concentrations of the three chemicals collected at eight sampling sites in the proximate vicinity of the study field for up to 4 days posttreatment. This may be due in part to variations in wind speed and direction during the 4-day period. Maximum residues were as follows: DEF, 1243 ng/m^3, 350 m southwest of field, during treatment; dibutyl disulfide, 2.5 ng/m^3, 350 m north of field, 24 h posttreatment; and butyl mercaptan, 167 ng/m^3, 100 m north of field, 24 h posttreatment. The majority of the samples contained much lower air residues than these maximum values.

Analyses conducted similarly at a second cotton field treated with merphos gave somewhat comparable results, except that the maximum levels of DEF (6080 ng/m^3, 10 m north of field, during treatment) and butyl mercaptan (1576 ng/m^3, 10 m south of field, 2 h posttreatment) were greater than those recorded near the DEF-treated field.

Complete results of air levels associated with these two treatments are in Tables II and III, taken from Chapter 5 of the Ph.D. thesis of Dr. Bruce Hermann (Chapter 5 is attached as an appendix to this report). One clear result of the study was that mercaptan air levels at the merphos application were higher than at the DEF application site, above 1.5 μg/m^3 2 hours after spraying. The mercaptan levels did drop off rapidly, and by the third day were at or below our ability to detect the chemical ($<$0.05 ng/m^3). A mercaptan air level of 1.5 μg/m^3 (0.4 ppb) is above the odor-threshold level, but less than the threshold for nausea reported at 0.5 ppm.

An analysis of the tank mix (Table IV) shows that a possible reason for the higher mercaptan level at the merphos application site is that the mercaptan level in the merphos tank mix is over 10 times that of the DEF formulation. Additionally, most of the merphos had already been converted to DEF in the tank mix before spraying occurred.

The question arose as to the source of the mercaptan in the merphos tank mix. Analysis of another merphos formulation (the commercial defoliant before being mixed with the water and other spray adjuvants) showed levels of mercaptan well below 0.1% prior to mixing. Therefore, we either sprayed a merphos formulation that had an unusually high mercaptan content, or mercaptan was being generated in the tank.

In addition to demonstrating the rapid conversion of merphos to DEF in the vapor form, we showed that merphos in a commercial formulation mixed with

Table II. Air Residues (ng/m^3) collected at DEF Application Site.

Station	Compound	SAMPLING PERIOD Day 0 2:00	Day 0 4:00	Day 1 8:00	Day 1 2:00	Day 2 8:00	Day 2 2:00	Day 3 8:00	Day 3 2:00	Day 4 8:00	Day 4 2:00
10mNW[l]	Def	1019	711	—[a]	483	368	96	59	—	tr[b]	545
	BuSSBu	tr	tr	0[c]	0	0	0	0	tr	0	0
	BuSH	tr	tr	0	0	0	0	0	tr	—	0
50mNW[h]	Def	1189	575	4	450	167	13	44	24	0.1	—
	BuSSBu	2.21	2.25	0.703	0.524	0.45	0	0	0	tr	—
	BuSH	14.5	14.9	4.8	3.5	3.0	0	0	0	tr	—
100mN[l]	Def	19	387	59	75	341	tr	--	76	—	21
	BuSSBu	tr	tr	0	0.63	0	0	—	tr	tr	0
	BuSH	tr	tr	0	167	0	0	—	—	0	—
350mN[h]	Def	—	—	70	10	160	8	12	—	—	30
	BuSSBu	—	—	0.14	2.53	0	0	tr	—	—	tr
	BuSH	—	—	1	27	0	0	tr	—	—	tr
250mE	Def	1187	264	77	41	21	tr	165	135	36	8
	BuSSBu	tr	1.46	0	0	0	0	0	0	0	0
	BuSH	tr	20	0	0	0	0	0	0	0	0
50mS[h]	Def	115	--	—	—	—	—	—	—	—	—
	BuSSBu	0.19	--	--	—	—	--	--	--	—	—
	BuSH	1.8	—	—	—	—	--	--	--	--	—
5mSW[l]	Def	—	—	—	337	20	--	260	67	19	118
	BuSSBu	—	—	--	tr	0	0	0.79	0	0	0.14
	BuSH	—	—	—	tr	0	0	—	0	0	72
350mSW[h]	Def	1243	174	—	2*	37	0.3	37	30	12	—
	BuSSBu	0.43	tr	--	0	tr	tr	tr	0	0	0.11
	BuSH	4.2	tr	0	0	tr	tr	tr	0	0	1.2

[l] LoVol Sampler

[h] HiVol Sampler

* Sample went to dryness during concentration

[a] Sample not taken or lost during extraction

[b] trace (>0.05ng/m^3, <0.1ng/m^3). Identifiable peak (2 x baseline noise) seen, but not quantitable.

[c] no peak seen (<0.05ng/m^3)

Table III. Air Residues (ng/m^3) Collected at Merphos Application Site.

		Sampling Period									
		Day 0		Day 1		Day 2		Day 3		Day 4	
STATION	Compound	2:00	4:00	8:00	2:00	8:00	2:00	8:00	2:00	8:00	2:00
10m[1]	Def	669	258	87	—	421	—	—	—	123	23
	BuSSBu	0	0	0	—	0	—	—	—	0	0
	BuSH	tr	tr	0	—	tr	—	—	—	0	0
50m[h]	Def	457	34	22	—	54	157	190	46	86	26
	BuSSBu	0	0	—	—	.42	0	0	0	0	0
	BuSH	10.1	12.2	1.6	—	1.5	—	3.6	0	0	0
10m[l]	Def	6030	—	—	—	—	—	—	—	—	—
	BuSSBu	tr	—	—	—	—	—	—	—	—	—
	BuSH	—	—	—	—	—	—	—	—	—	—
5m[l]	Def	—	—	29	—	208	—	130	18	135	730
	BuSSBu	—	—	tr	—	tr	—	0	0	0	0
	BuSH	—	—	—	—	—	—	—	—	—	—
10m[h]	Def	1321	1047	67	—	—	47	63	—	171	20
	BuSSBu	0	2.7	.45	—	—	0	0	—	0	0
	BuSH	27.5	1576	0.8	—	—	1.0	1.0	—	.8	0
0.5m[h]	Def	182	4	12	—	16	40	2	8	56	9
	BuSSBu	0	0	0	—	0	0	0	0	0	0
	BuSH	1.6	1.5	tr	tr	1.4	2.0	0	0	0	0
0.5m[h]	Def	201	4	3	—	—	33	2	39	41	—
	BuSSBu	0	0	0	—	—	0	0	0	0	—
	BuSH	0	0	0	0	1.2	—	0	0	0	0
Field (u)[l]	Def	—	—	—	602	—	253	—	160	301	131
	BuSSBu	—	—	—	—	—	tr	—	0	0	0
	BuSH	—	—	—	32	—	—	0	tr	0	0
Field (L)[l]	Def	—	—	—	411	—	110	—	151	5497	123
	BuSSBu	—	—	—	tr	—	0	—	0	tr	0
	BuSH	—	—	—	36.1	—	0	—	0	tr	0

Table IV. Defoliant Formulation Analysis

Component	Devil's Den DEF 6 (Treatment #1)	Merphos (Treatment #3)
Folex	--	4.15 mg/ml (28.0%)
DEF	23.0 mg/ml (94.4%)	10.3 mg/ml (69.6%)
BuSSBu	1.35 mg/ml (5.54%)	0.16 mg/ml 1.08%)
BuSH	0.024 mg/ml (0.10%)	0.109 mg/ml (1.32%)

water (simulated tank mix) has a half life of eleven hours in the light and that an important aspect of this photooxidative reaction is that two of the products of side reactions are butyl mercaptan and butyl disulfide. In fact, in the photooxidation reactions that we ran in the laboratory in air and in a simulated tank mix, the level of mercaptan increased from 0.08% to over 4% when the reaction went to completion. In the dark control merphos tank mix, only 8% of the merphos was converted to DEF at the end of the experiment, suggesting that much of the merphos in the tank mix was converted to DEF when exposed to light and air during sampling and storage, reflected in the oxidation shown in Table IV. Levels of DEF and mercaptan were probably lower at the time of sampling than when the material was actually sprayed.

The highest mercaptan levels in field air appeared the evening after the merphos application and were reaching their highest levels after the termination of the 4:00 p.m. sampling period on the day of spraying. The instantaneous levels actually reached may have been much greater than those of the time averaged values. These emissions gave us a strong headache while collecting the air and foliage samples at the 4:00 p.m. sampling. This headache was eased after leaving the application site.

Another clear result of our study was that the primary loss of DEF and merphos from treated surfaces is by evaporation, about half of which occurs 2-6 days after treatment. This is in addition to evaporative losses from the spray droplets and drift of small droplets themselves which constitute the source of atmospheric entry during spraying. For example, leaf samples showed a rapid drop during the first 2 days after DEF treatment followed by a slow loss during days 2-4, with another rapid drop at day 8 (Figure 1). Overall, the half-life was approximately 4-6 days. In contrast, the mylar sheets showed a steady decline during the entire sampling period, but the estimated half-life was comparable to that for leaves. This decline was caused solely by evaporative losses, since Dr. Hermann had shown DEF to be unaffected by any photodegradative or hydrolytic processes. The more rapid loss of DEF in the plant tissues during the first 2 days could be due to metabolic breakdown of the chemical. This is to be expected since DEF causes physiological changes (defoliation) in the plant, showing that it has indeed penetrated the leaf tissue. The slow loss rate during days 2-4 reflect that DEF is not on the leaf surface where it would be subject to rapid evaporative loss, but is rather inside the leaf for the most part. The large drop in the day 8 residues is due to sampling discrimination. The leaves of the cotton plants begin to drop off on day 4, so that by day 8 the leaves remaining on the plant are those which did not receive an effective defoliant dose.

When the vapor pressure of DEF is considered together with the conditions and method of application, the atmosphere is indicated to be a major loss route from the field, especially during, and for several days following, application. The defoliants are sprayed onto the fields during warm weather, so that much of the chemical is vaporized before hitting the leaves. This vaporization was demonstrated by examining the DEF (volatile) to paraquat (nonvolatile) ratio of a sample taken from a defoliant tank mix containing

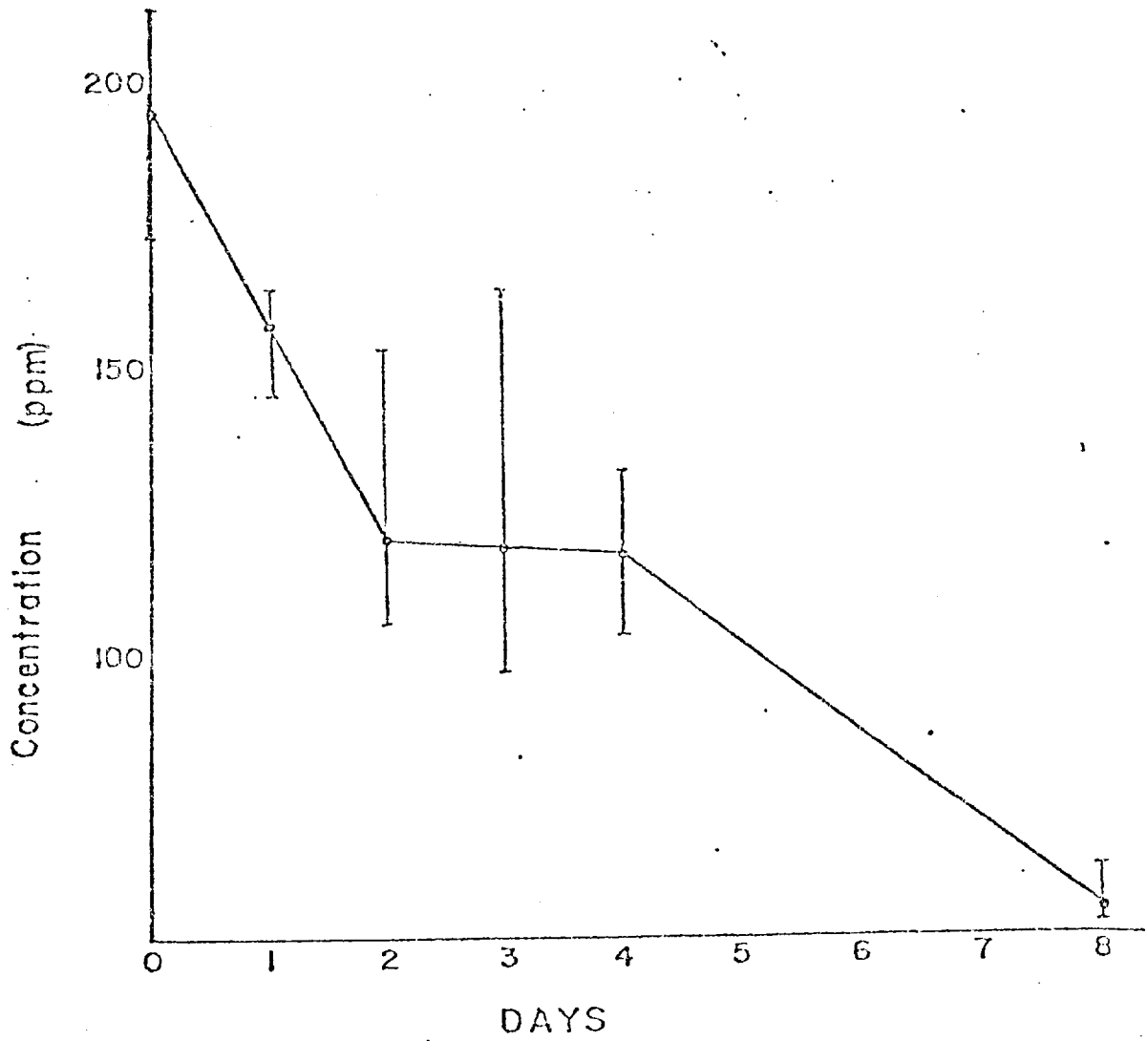


Figure 1. Def^{R} loss from cotton foliage (Treatment #1, n = 3).

these two chemicals and comparing that ratio with ratios in air samples taken during application of the mixture (Table V). Since paraquat is nonvolatile, its residues could only be the result of particulate drift, while the DEF residues were also contributed to by vaporized material. The net result was higher DEF/paraquat ratios in all of the air samples than existed in spray mixture. The material that hits the target is still subject to vaporization, being exposed on the leaf surface for at least several hours prior to absorption into the plant tissue. The differences in vapor pressures of DEF and merphos would not be expected to give rise to significantly different loss rates of these two chemicals to the atmosphere, especially considering merphos' rapid oxidation to DEF in the tank mix and after spraying to the environment. In addition, soil and plant material blown into the air, especially during the harvest process, would provide other major loss routes to the atmosphere. Therefore, atmospheric residues for DEF and merphos applications can be a concern when seeking to ensure the welfare of nearby residents.

Table V. DEF and Paraquat Collected by Same Samplers (Devil's Den)

Time of Sampling	DEF	Paraquat	Ratio
10m NW			
During spray	3,700 ng	56 ng	66
2-4 hr post-spray	2,600	<10	>260
50m NW			
During spray	179,900	750	240
2-4 hr post-spray	87,000	<10	>8,700

DEF/Paraquat ratio in spray mix was 18.

However, the field results suggest that these defoliants are a small, if not a negligible, threat to the health of residents in the area. The airborne levels, even during application, were well below toxic threshold levels. The highest DEF level obained (1.3 $\mu g/m^3$) is, for example, much lower than the TLV value for parathion (0.1 mg/m^3). With the exception of an improper application, a prolonged period of atmospheric inversion during the defoliation season represents the most likely environmental circumstance which could markedly alter ambient exposure. During the defoliation season (October - November) the dominant atmosphere is calm. These calm conditions cause the heavy fogs and inversions that blanket the San Joaquin Valley during the October - November defoliation season. These inversions foster a high atmospheric concentration of chemicals with the formation of slow moving drift clouds, and do not promote efficient dispersal of compounds volatilized from the application site.

The risk to the comfort of people in the area is a more serious problem. These defoliants, along with other organophosphorus compounds, give offensive odors. In the case of DEF and merphos, this odor is mostly from butyl mercaptan. One company (Mobay) has mitigated this problem by lowering the mercaptan content in the DEF formulation, and our results show that additional mercaptan is not formed to any great extent from DEF in the tank mix or following application in the field. Another company (Mobil) has done the same with merphos; however, this formulation still produces significant quantities of mercaptan impurity as a side product during its oxidation to DEF, both in the tank mix and under field conditions. Thus, unless the oxidation, or at least this side reaction, can be prevented applications of merphos will continue to be accompanied by the odor of mercaptan.

The applicators can help to alleviate the nuisance of defoliant smells by limiting sprays to the morning or early afternoon hours. The time when this area benefits from a breeze is during the afternoon hours. This breeze would help to disperse the mercaptan odor before it can build up to nuisance levels. When sprays are done in the evening or in the night under quiet atmospheric conditions, the vapors concentrate within a few feet of the ground and slowly move out into the surrounding area.

Being of low acute toxicity has not kept DEF and merphos from being surrounded by controversy. Public pressure has caused increasingly strict government regulations on their use and caused some farmers to switch to other defoliants such as sodium chlorate or the cacodylates.

One reason for the controversy stems from the high profile of the compounds. They are consistently among the most heavily used agricultural chemicals both in terms of pounds applied and acreage. Their use is limited to a concentrated area and a few weeks during the year, so that any discomfort caused by their application is intensified. The adverse weather conditions under which they are applied and the accompanying malodorous formulation components have been previously described.

A second factor is the influx of people into the San Joaquin Valley. This area, like most of California, is being subdivided and urbanized, increasing the potential for human exposure. A large proportion of these people are unfamiliar with the use of agricultural chemicals, and become alarmed when crop dusters take to the sky, or the air takes on an unfamiliar and disagreeable odor.

D. Use of a Test Animal to Assess Exposure to and Neurotoxic Effects from DEF

One approach to assessing the hazard of a chemical in the human workplace environment is to place a sensitive test animal in that environment alongside humans engaged in their normal work activities. This approach was used to find out whether the delayed neurotoxicity produced by DEF in the laboratory would occur under real exposure conditions in the field. Scaleless chickens were put into cotton fields, exposing them to DEF during its application by ground rig, and observing them for signs of ataxia and other injury. A complete report of this study is in Wilson et al. (1980) and in Wilson et al. (1982), reprints of which are appended to this report.

The applicator intercepted significant residues of DEF on all outside surfaces of his coveralls. Values outside the coveralls were as high as 250-260 $\mu g/cm^2$ (on the sleeves), with most coverall values in the 20-100 $\mu g/cm^2$ for sleeves, shoulders, chest, thighs, and legs for the 7 hour duration of the field test. Exposure values inside the garment ranged from 1 to 7 $\mu g/cm^2$. DEF levels measured in the air and on the surfaces of fallout collectors during the 7 hr exposure level suggested that the major route of human exposure was dermal rather than by inhalation.

Chickens were exposed by placing them on the spray rig near the applicator, where a dermal exposure of 47.8 $\mu g/cm^2$ was achieved, in the rows of cotton where they received direct sprays of DEF, and at several sites to one side of the spray area (Table VI). In addition, some birds were exposed to direct sprays repeatedly. There was a log-linear relationship between dermal dose and cholinestease inhibition, indicating that not only were the birds exposed but that they actually absorbed the toxicant. However, upon observing the birds for 30 days after the trial ended, none exhibited ataxia or other behavioral signs of delayed neurotoxicity. This series of

Table VI. DEF Exposures and Scaleless Chicken Cholinesterase Levels[a]

Group	Site	DEF $\mu g/cm^2$	DEF $\mu g/m^3$	CHE nmole/min/ml
OFF	400 m, off site	0.0017	0.11	413
ON	50 m, open road	0.04	6.2	300
ADJ	10 m, in cotton	0.0092	--	360
ROW	In sprayed cotton	4.4	--	251
ROW	In sprayed cotton	17.7	--	190
[RIG	On spray rig	47.8	13.8	299]

$$\text{Estimated exposure } \frac{\text{dermal}}{\text{inhalation}} \cong 100$$

[a] Wilson et al. 1980

experiments showed that field exposure of groundrig applicators under normal conditions of use was probably of insufficient magnitude to produce symptoms of delayed neurotoxicity.

E. Field Monitoring of Workers for Symptoms of Delayed Neurotoxicity Caused by DEF

The results of Section D experiments suggested that exposures to DEF in the field were too little to lead, under normal use conditions, to intoxication, at least for ground rig applicators. To further assess this for workers engaged in both ground and aerial treatment of cotton, a study was conducted in which an estimate of exposure was made by analyzing cloth patches fixed to the clothing of mixer-loaders, flaggers, and pilots and measurements were made of blood enzyme levels and peripheral nerve function. Complete results will be presented by Lotti et al. (Journal of Occupational Medicine, 1983); a copy of that manuscript will be furnished as soon as journal reprints are available.

Exposure measurements to DEF and merphos in a group of 7 workers suggested that the major route of exposure to DEF was through the skin. The

information on work category, and measured exposure levels for exposed body parts (head, neck, and hands) and air, are in Tables VII and VIII. From Table VII data, the total exposure to DEF can be calculated for each worker on the days monitored. The results, normalized to a 7 hour work day, are in Table IX. Head and neck exposures for the flaggers and mixer-loaders (subjects 2-5) were considerably greater than for the pilots. For all workers, significant exposures occurred through the hands, probably because all of them helped to clean and adjust leaking spray nozzles on the aircraft and to collect spent defoliant cans without wearing protective gloves. Also, for all workers the air (inhalation) exposure was insignificant in comparison to the dermal exposure. A very rough estimate of season-long exposure can be made for workers in each category by multiplying Table IX data by the estimated number of 7 hour days each subject worked with DEF or Merphos over the defoliation season (Table VII). For example, subject 4 received the rough estimate of 2.8 grams on his head and neck, 0.4 grams on his hands, and 0.003 grams by inhalation over the season, assuming that his exposure on all days of working with defoliant was the same as on the two days this subject was monitored. Also, Table IX data allow one to calculate the single 7 hr workday dose for each individual in mg/kg, using subject weights in Table VIII. Again for subject 4, the calculated dose on the day he was monitored was approximately 0.7 mg/kg, neglecting a correction for skin absorption of DEF (~10% of total dose). By way of comparison, the median acute dose of DEF administered s.c. to scaleless hens which produced ataxia after 12 days was 800 mg/kg, while the no observed effect level (NOEL) for ataxia in normal hens is reported to be 0.1 mg/kg of body weight per day for chronic exposure.

Table VII. The Study Group of Workers Exposed to DEF and Merphos

Subject No.	Age (yr)	Previous Occupational Exposure to OPs (yr)	1981 DEF/Merphos Exposure[a] (hr/day)	Job Description[b]
1	38	7	67/27	Pilot
2	19	0	294/27	Mixer/loader-flagger
3	18	0	286/28	Mixer/loader-flagger
4	46	>10	374/34	Ground rig operator and mixer/loader
5	41	2	25/29	Mixer/loader-flagger
6	35	6	108/9	Ground rig operator
7	30	10	108/9	Mixer/loader in ground operation

[a] Estimated total hours of exposure calculated according to the records kept by the company's office versus the length of exposure period.

[b] Subjects 1, 2, and 3 were fellow employees as were subjects 6 and 7.

Table VIII. Monitoring Environmental Exposure to DEF and Merphos during Cotton Defoliation

Subject	Day of Exposure	Length of Monitoring (hr)	H + N ($\mu g/cm^2$)[a] A	H + N ($\mu g/cm^2$)[a] P	Hands (mg)	Air ($\mu g/m^3$)	Weight (kg)	Height (cm)	H + N (cm^2)[ab]
1	1	2.90	0.31	0.05	3.17	5.79	104.33	187.96	1,588.83
	27	4.53	0.58	0.12	1.66	7.12			
2	1	3.00	1.35	34.29	4.49	39.79	68.04	177.80	1,272.58
	27	4.35	1.03	98.03	4.25	50.98			
3	1	3.05	0.81	5.35	24.06	39.73	79.38	182.88	1,386.77
	27	4.37	2.97	46.82	5.17	31.12			
4	9	7.45	54.16	0.18	7.46	6.06	88.45	177.80	1,422.69
5	19	1.83	3.82	1.44	1.65	20.36	68.04	175.26	1,259.37
	20	2.17	8.35	108.47	13.27	53.76			
6	9	6.63	0.32	0.29	0.87	3.94	95.26	182.88	1,500.77
7	9	6.78	0.24	0.13	1.54	5.50	115.67	185.42	1,646.24

[a] Head (H) and neck (N); A = anterior, P = posterior. Amounts ($\mu g/cm^2$) on patches.

[b] Total body area (cm^2) = [weight (kg)$^{0.425}$ × height (cm)$^{0.725}$] × 71.84; Area H + N = 0.069 × (total body area); A/(H + N) = 0.73, P/(H + N) = 0.27.

Using the approach of DuBois and Dubois[35], total skin surface areas were computed for each worker. From Berkow[36] the relative area of the head plus neck was estimated to be 6.9% of the total surface area. Moreover, from Peoples et al.[37] the anterior and posterior head and neck surface areas were estimated to be about 73% and 27%, respectively, of the total head and neck. Cloth patches placed on the upper chest near the face and on the collar at the back of the neck were used to determine exposure of the anterior and posterior head and neck to DEF and merphos.

Table IX. Worker Exposures to DEF Per 7 Hour Workday for Each Workday Monitored

Subject	Job Description	Day of Exposure	Total DEF (mg) Head and Neck[a]	Hands	Air
1	Pilot	1	0.92	7.65	0.05
		27	1.13	2.56	0.06
2	Mixer/Loader-Flagger	1	30.44	10.46	0.35
		27	55.79	6.84	0.45
3	Mixer/Loader-Flagger	1	6.48	55.22	0.34
		27	32.92	8.28	0.27
4	Ground-rig Operator and Mixer/Loader	9	52.89	7.01	0.06
5	Mixer/Loader-Flagger	19	15.30	6.31	0.19
		20	143.84	42.81	0.48

[a] Anterior and posterior treated as separate exposures (Table VIII).

Significantly, exposures in the test group of human subjects did not result in any detectable subclinical effect on the peripheral nervous system, as assessed by electromyography and nerve conduction studies carried out at UCSF Medical Center by Drs. Lottie, Becker, and colleagues. However, these same workers showed that neurotoxic esterase (NTE)--the putative molecular target in neural tissue for the initiation of delayed neuropathy--was measureably inhibited. Both the intensity and the length of exposure seemed to be important in determining the inhibition of NTE in lymphocytes, which was about 50% of the preexposure values when measured 3-4 weeks after the beginning of the exposure. This level of NTE inhibition did not have any associated detectable electrophysiologic effects.

In sum, workers involved in applying DEF to cotton were measureably exposed to the chemical--an exposure which occurred at least over a 30 day

period of the defoliation season and approximated in some cases the chronic NOEL for DEF in hens. This exposure did lead to a significant depression in NTE activity by the end of the season, but was not of sufficient magnitude to measureably affect the nervous system. We conclude from this study of humans, and from the study with scaleless chickens, that normal field exposure of applicators, mixer-loaders, and flaggers to DEF and/or merphos will not produce delayed neurotoxicity in these individuals because normal exposure is below the threshold level for this disease in humans. However, our results do show that the desireable 100 fold safety factor could be approached and, perhaps, violated for some workers on occasion. This argues for the use of proper safety apparel (coveralls and rubber gloves), and alerting workers to the inherent dangers in undue exposure when handling these organophosphorus defoliants. With regard to persons working or residing downwind from defoliation treatments, we see no condition under which delayed neurotoxicity could develop from the relatively minor exposures to airborne drift to which they might be exposed by inhalation or dermally.

III. PARAQUAT

A. Background

Paraquat, a non-volatile bipyridinium herbicide with a variety of agricultural uses, is extensively employed as a harvest aid for cotton defoliation. Concern over these uses arises from three sources: small amounts of particulate drift from paraquat spraying may injur sensitive plant species downwind from the source; inhaling large amounts of paraquat aerosol may produce immediate, acute toxic effects, principally in the lung of humans; and prolonged exposure at lower levels may cause or aggravate asthma and emphysema-like symptoms in exposed individuals.

We developed an analytical method for determining low levels of paraquat in air which combined accumulative high volume sampling of airborne particulates by filtration with nitrogen-selective GLC of a reduced paraquat derivative. The method was used to assess the concentration of paraquat downwind from commercial applications to cotton and paraquat residues in the dust generated during mechanical harvesting of a treated cotton field. An effort was made to identify maximum inhalation exposure conditions in the spraying and harvesting operations, and to recommend practices which could minimize occupational exposure to airborne paraquat in these operations. The method development and aplications are reported in detail in the paper by Seiber and Woodrow (1981), a reprint of which is attached as an Appendix to this report.

B. Analytical Method Development

We developed a procedure for determining low concentrations of paraquat downwind from treatment sites by combining accumulative filtration for sampling with N-selective gas chromatograhic analysis of reduced paraquat derivative. This method, outlined in Figure 2, involves extraction of paraquat from the filter by sonication with 6N HCl, concentration and centrifugation to remove insoluble materials, and dissolution of soluble matter in saturated ammonium biocarbonate. The latter solution was taken to dryness, including evaporation of the volatile ammonium bicarbonate, in a sand bath; the residue was then dissolved in aqueous sodium hydroxide and derivatized by reduction with sodium borohydride. The reduced product, a mixture of mono- and diunsaturated tertiary amines, was extracted in hexane and quantitated by gas chromatography using NP-selective thermionic detection. Recoveries of paraquat dichloride spiked to glass fiber filters

were 96, 87, 81, and 74% for 1.0, 0.5, 0.1, and 0.05 μg fortifications. Considering these recovery data and the background from an air sample lacking paraquat, the limit of detection of the method was estimated to be 0.5 ng/m^3.

This method is considerably more sensitive than the colorimetric assay applied to fall-out or high volume filter samples. We applied it to a determination of paraquat residues in air collected over 200 m from a spraying operation, both during and for several hours following treatment. Additionally, the method may be used to measure the quantity of paraquat associated with various particulate size fractions collected by cascade impaction.

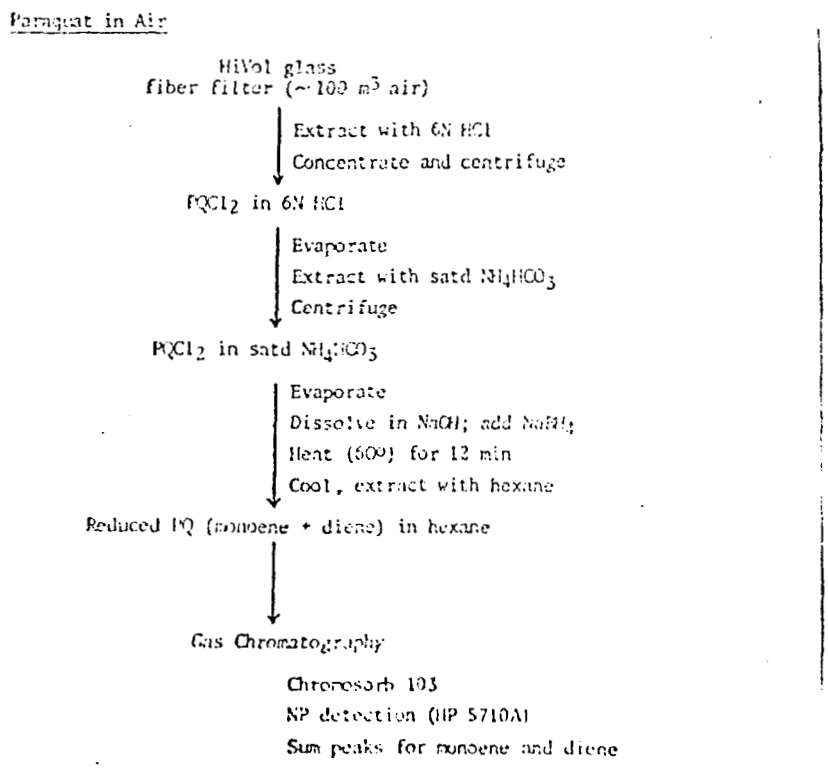


Figure 2. Schematic for the determination of airborne residues of paraquat.

C. Field Monitoring for Airborne Levels

Field analyses were carried out at two sites using high or low-volume air samplers deployed at several points around the field. Some samplers had glass-fiber filters to trap paraquat while other samplers contained XAD-4 resin to trap DEF, a component of the harvest aid mixture. Application was by fixed-wing aircraft at 0.1 kg/ha of paraquat.

The total volume of air processed by each sampler was corrected for the time the wind blew toward the sampler from some segment of the treated field. This yielded the "effective volume" sampled, that is, the product of sampler flow rate and time the wind blew toward the sampler from the field. From this the effective concentrtion of paraquat in each air sample was calculated (Table X).

For each field, a relatively smooth drop of effective concentration with downwind distance was observed during spraying. The profile for the Southlake field is shifted toward higher concentrations at comparable sampling sites which may reflect more drift than at the Devil's Den field since the average windspeed for Southlake was greater.

The concentrations-distance profiles could be used to calculate air concentrations at locations where no sampler was set up. For example, we estimated the effective concentration 1 m from the downwind edge of the treated area to be 4 $\mu g/m^3$ for the Devil's Den site and 11 $\mu g/m^3$ for the Southlake site during spraying.

Effective paraquat air concentrations sampled 2 hours after treatment at the two fields were 1-10% of those recorded at corresponding sampler stations during spraying. No paraquat was detectable at any of the sampling stations 5 hours after spraying. This reflects the negligible volatility of paraquat and the apparent lack of significant wind erosion of paraquat from surface

deposits under the climatic conditions of our tests. This contrasts sharply with the behavior of moderately volatile compounds such as DEF for which evaporation from surface deposits may occur for several hours or days following treatment. For DEF, total airborne residues (particulate plus vapor) decreased only moderately at the same stations in the 2-4 hours post spraying while paraquat, as noted previously, fell off dramatically with time. This was reflected also in the DEF/paraquat ratio increase with time, which occurred at two sampling stations, and a greater settling rate for particulate paraquat than for DEF, for which the bulk of the airborne residue is vapor.

Table X. Paraquat Residues in Air Samples Collected Downwind During an Application of 0.1 kg/ha to Cotton

Location	Amt (W)	Flow Rate (Q)	Time Drift To Sampler (t)	Effective Volume (Qt)	Conc. (W/Qt)	Average Windspeed
Devil's Den						
10m NW	56 ng	0.019 m^3/min	6.75 min	0.13 m^3	430.8 ng/m^3	1.0 m/sec
50m NW	750	1.26	6.75	8.50	88.2	1.0
91m S	656	1.24	11.6	14.38	45.6	1.0
161m SW	918	1.54	21.7	33.5	27.4	1.1
Southlake						
70m S	193	0.028	45.0	1.26	153.2	1.7
100m N	38	0.028	12.7	0.36	105.6	1.6
216m S	2000	1.40	28.9	40.4	49.5	1.7

We also determined paraquat in the dust generated during harvesting of seed cotton. Air samplers were placed on the outside platform of the harvester and inside the cab in the front corner opposite the door with the intake in the breathing zone; the samplers were operated for 4 hours. While most harvesters operated in California have enclosed cabs, it is fairly common

practice for the operators to leave the cab doors open, a possible source of exposure to paraquat-containing dust.

The highest concentrations, in the range 470-1,200 ng/m^3, were recorded in samples taken just outside the harvester cab and inside the cab when the door was left open. When the cab door was closed a considerably lower concentration, 13.7 ng/m^3, was recorded inside the cab. Thus, the harvesting operation generated air concentrations of paraquat comparable to those present just downwind from the field during spraying even though harvesting took place 4 weeks after defoliation.

Calculating from the highest air level of paraquat found in the harvest air, 1.2 μg/m^3, and the "light work" average male human breathing rate of 1.7 m^3/hr, the maximum exposure for harvester operators in this study by inhalation was 16 μg/8 hr day. This assumes that all of the paraquat in the dust entered and was entrained in the lungs; in fact, cascade impactor results indicated that nearly 70% of the harvest dust was in the respirable range. This also assumes that all of the paraquat in the dust is biologically available; this is questionable, since paraquat is known to be tightly bound to soil and plant particles. The calculated exposure is far below the 8 hour TLV for paraquat, 7000 μg/8 hr day.

Assuming that all airborne paraquat was ingested orally following deposition in the upper respiratory tract, we calculated an exposure of 0.24 μg/kg/day. This value is far below the acute oral or subacute, chronic oral LD_{50} values in the rat. It is, thus, difficult to envision an exposure circumstance for harvester operators by inhalation or oral routes, either singly or in combination, which would violate a reasonable factor of safety from acute or chronic toxicity data in laboratory animals, although

substantial dermal contact with the dust (not measured in our study) could mitigate this statement considerably.

However, it should be stressed that the literature records that lesions can form quickly at much lower paraquat exposure than reflected in acute or subacute toxicity measurements. Also, long-term effects of exposure to low levels of paraquat on the human body and, particularly, the human lung have not been evaluated. For example, the possibility that small quantities of paraquat could cause or aggravate asthma and emphysema-like symptoms in exposed individuals may have been overlooked in the past.

Considering the analytical findings and toxicity data in the literature, it would seem prudent to advise that agricultural workers and human residences not be situated within 400 meters downwind of paraquat spraying operations, which is in agreement with a recent EPA advisory opinion. During harvesting, cab doors should be closed and air filtration systems operated within the cabs, since both operations will sustantially reduce exposure to paraquat in airborne dust. As residues of other harvest aid chemicals, such as DEF, may be present in defoliation drift or harvest air samples at much higher levels than paraquat, the prudence of adopting such safety precautions is reinforced.

In this WRPIAP-supported project we did not undertake a thorough worker-exposure study among applicators, mixer-loaders, and other field workers. A separate, WRPIAP-supported project is now underway (1982-83) in which patch, handrinse and air samples were collected from workers involved in paraquat application; the results of this study, when completed, will be given in a separate report.

IV. CACODYLIC ACID

A. Background.

Cacodylic acid (CA) is an organometallic arsenical compound used as a non-selective post-emergence herbicide. Its principle use in California is as a cotton defoliant. Because residues of CA after field treatment represent a potential health hazard, it is desireable to develop a method for analysis of this compound. The method should include a scheme for separating cacodylic acid from three other common arsenical contaminants, namely monomethylarsonic acid (MMA), arsenic acid (As^{5+}), and arsenous acid (As^{3+}).

$(CH_3)_2As(O)O^-$	$CH_3As(O)O_2^=$	$As(O)O_3^{\equiv}$	$AsO_3^{\equiv}$
dimethylarsinate (cacodylate)	monomethyl arsonate	Arsenate (Arsenic acid)	Arsenite (Arsenous acid)

The ionic nature, high water solubility, and low vapor pressure of these acid/salt forms of arsenic suggest that airborne residues will be almost entirely associated with the particulate phase.

These properties also suggest anion chromatography as a method for separating these compounds. Among the previously reported methods of analysis of specific arsenic compounds, two of them use high-performance liquid anion exchange chromatography. One involved a separation of arsenite, cacodylic acid, and monomethylarsonic acid using a strong anion exchange column (Brinkman and Irgolic, 1980). This method does not fully resolve cacodylic acid from arsenite, and arsenate is absorbed to the column. Woolson and Ahranson (1980) reported a separation of all four arsenic compounds using a Dionex polystyrene-based weak anion exhange column. Although a satisfactory separation was achieved, it was very sensitive to the salt content of

environmental samples because no buffer is used in the column during the first part of the gradient elution. These two methods, and more recent modifications (Morita et al., 1981; Iadevaia et al., 1980; Chem Eng. News, 1981), employ flameless atomic absorption spectroscopy to detect arsenic in the HPLC fractions.

We pursued development of an analytical method similar to those reported in the literature, but using a weak anion exhange HPLC. It appears that it would be preferable to use a weak anion exchange column that allowed the use of a buffer to stabilize the ionic strength of the solvent during elution. A primary alkylamino column was useful in this respect because it has a lower exchange capacity than a strong anion exchange column, but a higher one than the Dionex column. Furthermore, its capacity is pH dependent. Our work was brought successfully to the point of demonstrating HPLC resolution of the three arsenic species of most interest (cacodylate, MAA, arsenite) with GFAA detection. We did not, however, analyze field air samples

B. Analytical Procedure

Reagents - Standard solutions of the four arsenic compounds were made at concentrations of 50 μg/ml in deionized water. The eluting buffer for the chromatography needed to be one that did not interfere with the graphite furnace atomic absorption analysis. Ammonium acetate was found to be satisfactory. ACS grade ammonium hydroxide, ACS grade acetic acid, and Baker HPLC grade water were used. The buffer was prepared by first making a .005 M NH_4OAc solution (pH=7), and then adjusting it to the desired pH by adding additional acetic acid. The buffers were prepared at pH's ranging from 3.3 to 6.7.

Apparatus - The anion exchange chromatography was performed using a Waters 30 cm μ-Bondapak NH_2 column (10 μm particles). The pump was a Milton Roy minipump operted at a flow rate of 1 ml/min. Samples (20 μl of individual standards or mixtures of standards were introduced into the column using a Rheodyne 7010 injector. Fractions (1 ml) of the column effluent were collected in 1.5 ml polyethylene sample cups using an Isco Model 1200 fraction collector.

For atomic absorption, a Perkin-Elmer Model 560 Atomic Absorption Spectrophotometer equipped with a HGA 2100 graphite furnace and a Model AS-1 Autosampler was graciously provided for our use by Professor Richard Burau. The sample cups from the fraction collector were transferred to the autosampler for analysis. The autosampler injected 20 μl aliquots from each sample cup into the furnace. The aliquots were dried at 100°C for 15 seconds, charred at 1200°C for 15 seconds, and atomized at 2700°C for 15 seconds, with the furnace operating in the interrupt mode with argon purge gas at 30 ml/min. The peak arsenic absorbance was read during a 10 second integration time at 194 nm, with a slit width of 0.7 nm. An arsenic electrodeless discharge lamp, operated at 9 watts, served as the light source.

C. Method Development Results

Arsenate is not included in the following discussion. Work not included here has shown that arsenate elutes either with monomethylarsonic acid or later, and does not interfere with the elution of cacodylic acid.

The pH of the ammonium acetate buffer was varied from 3.3 to 6.7. At the upper pH limit, retention of the compounds was insufficient to resolve them. At pH 5.6, arsenite was found to elute in the void volume as before, but cacodylic acid and monomethylarsonic acid were retained to some extent, and

peak elution occurred in fraction 15. Unfortunately, they were still unresolved from each other. At pH 4.7, all three compounds were well separated (Figure 3). Arsenate was still eluted in the void volume, cacodylic acid eluted second, peaking at fraction 12, followed by monomethylarsonic acid, peaking in fraction 25. As the pH was lowered further, the retention time of cacodylic acid decreased while that of monomethylarsonic acid continued to increase. At pH 3.3, MAA became adsorbed to the column, while CA eluted right after the void volume. The complete retention vs. pH profile is shown for the three compounds in Figure 4.

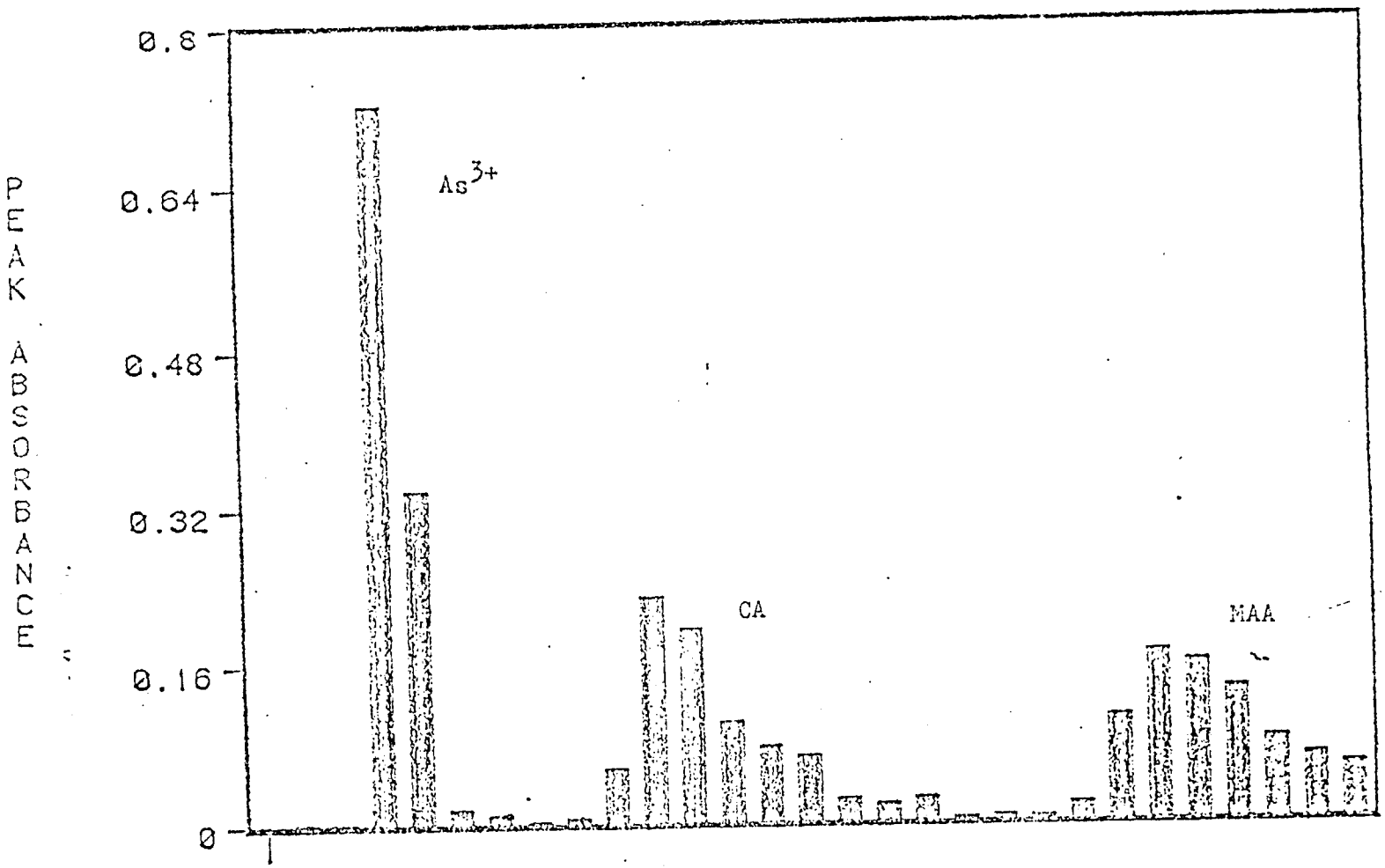
The separation of the three compounds on the μ-Bondapak NH_2 column can only be partially explained using the usual ion exchange arguments. In addition to ion exchange behavior, some form of reverse-phase partition chromatography is to be expected since the amino groups in the column are attached to alkyl chains which provide a somewhat hydrophobic surface for possible interactions with the methyl groups of CA and MAA. Also, adsorption to exposed silica in the column packing is possible. This may be responsible for the broadness of the peaks observed.

The behavior of arsenite is readily explained. It is seen that this compound always elutes in the void volume. Since the pKa of arsenite is 9.2, it is unionized at all pH's used in this study, and no ion-exchange retention would be expected. Furthermore, the compound contains no methyl groups, so partition type retention would not be expected either.

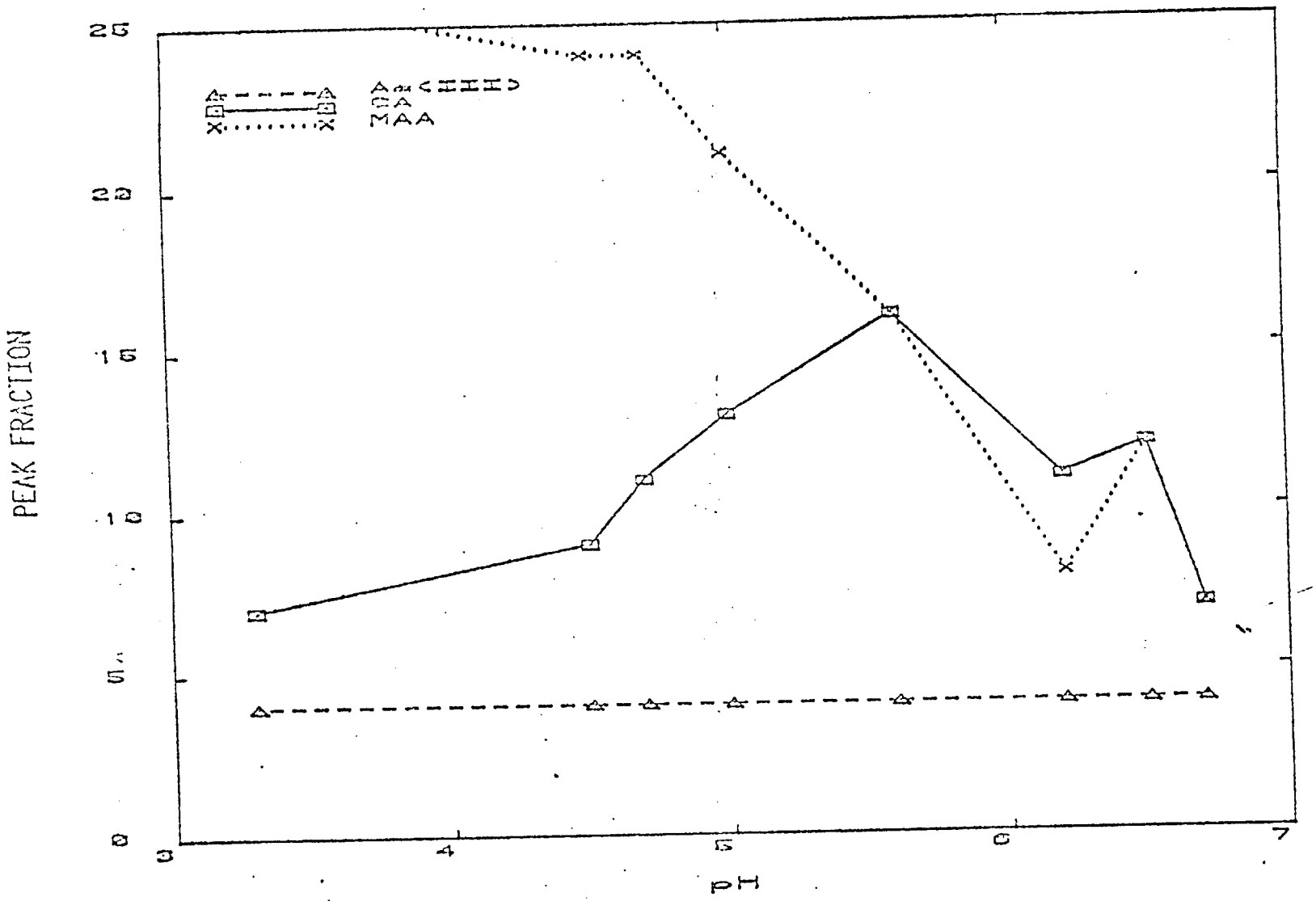
The increasing retention of CA and MAA between pH 6.7 and 5.6 can be explained by the pH dependance of the ion-exchange capacity of a primary amino column. The column capacity is increased as the pH is lowered from 6.7 to 5.6. Since both CA and MAA are ionized over most of this pH range, the retention of these compounds would be expected to increse as the pH is lowered.

FIGURE 5

RUN #107: As(III),CA,MAA - pH 4.7



PEAK FRACTION OF As(III), CA, AND MAA AS A FUNCTION OF pH



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At pH 5.6, CA is unionized (pKa = 6.2), and only partition type retention (and possibly adsorption) would be expected to occur. The decrease in retention of this compound as the pH is lowered from 5.6 to 3.3 is probably due to the increasing acetate concentration in the buffer.

Monomethylarsonic acid is ionized until the pH of the buffer is lowered below its pKa of 3.8. Throughout the whole range of pH's used in this study, the retention of this compound increased as the buffer pH was lowered, to the point where it was adsorbed to the column after the pKa of the compound was crossed. The reason for this behavior is not apparent.

D. Conclusions

A method has been developed for separating cacodylic acid from other arsenical compounds using ion exchange chromatography followed by graphite

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V. PROJECT SUMMARY AND CONCLUSIONS

This project was undertaken to assess airborne concentrations of four cotton harvest aid chemicals in and around sites of use, so that some estimate could be made of potential human exposures to atmospheric residues of these chemicals.

For the organophosphorus defoliants DEF and Folex (merphos), a method was developed for sampling and analyzing airborne residues of the three chemicals of interest -- DEF, butyl mercaptan, and dibutyl disulfide. Sampling was conducted at two fields in the San Joaquin Valley treated commercially by air with DEF or Folex. Residues of DEF were found in most air samples collected during spraying within 350 m of the fields whether sprayed with DEF or Folex (maximum, 6080 ng/m^3), and at many of the same stations for up to 4 days after spraying but at generally much lower concentrations. The origin of post-spray airborne DEF was by volatilization of DEF deposited from the spraying operation, or from DEF formed by oxidation of Folex deposits in the case of the Folex-treated field. Air concentrations of the odoriferous butyl mercaptan were generally higher in samples collected near the Folex treatment (maximum 1576 ng/m^3) than near the DEF-treated field (maximum 167 ng/m^3), apparently from the higher mercaptan content of technical Folex, the formation of butyl mercaptan when Folex formulation is diluted with water, and the further formation of butyl mercaptan when Folex residues are weathered. The butyl mercaptan-associated odor problem

can be minimized by restricting spraying to periods of good atmospheric ventilation, use of buffer zones, and imposing limits to mercaptan content of the formulation. For Folex, additional research is needed into ways to minimize formation of mercaptan when the formulation is added to water in the spray tank. The discomfort to sensitive individuals from inhaling mercaptan vapors is the principal ambient problem associated with the use of both DEF and Folex; no health hazard from the parent defoliants should exist for the ambient population as downwind air residues of the parent compounds are far below toxic levels.

Two series of experiments were carried out to assess the health effects for workers involved in applying DEF and Folex. In one series, carried out in collaboration with Dr. Barry Wilson, scaleless chickens were placed in and around fields treated by ground rig with DEF. Exposure of these birds, principally by the dermal route, resulted in measureable cholinesterase depression but no clinical symptoms of delayed neurotoxicity even under "worst case" situations. In the second series, carried out in collaboration with Drs. Charles Becker and Marcello Lotti, workers engaged in DEF applications were monitored for exposure, neurotoxic esterase levels, and nerve conduction. Workday exposures for mixer-loaders, flaggers, and ground rig operations, again principally by dermal contact, were frequently near 1 mg/kg/workday (not accounting for dermal absorption efficiency)--a level close to and perhaps in slight excess of the no observed effect level in hens. While neurotoxic esterase depression was observed in these workers, there was no detectable subclinical or electrophysiologic effects on their peripheral nervous system. We conclude that normal workplace contact with DEF is below the threshold level for delayed neurotoxicity in humans, although the margin of safety is apparently fairly low. Further research is needed in ways to decrease exposure levels, perhaps by protective clothing, and thus increase the margin of safety.

For the desiccant paraquat, an analytical method was developed for determining paraquat levels in air at very low concentrations (0.5 ng/m^3). The method was applied to air samples collected at two cotton fields in the San Joaquin Valley treated with paraquat. Maximum concentrations were 4 and 11 μg/m^3 in samples collected at the downwind edge of the fields, with a very rapid decline in residue both with distance from the field during spraying and with time following spraying. It was estimated that inconsequential levels of paraquat (<20 ng/m^3) exist in the air 400 m or more downwind from a field during spraying. We also found surprisingly high concentrations of paraquat in the air to which operators were potentially exposed during the harvesting of cotton previously treated with paraquat. The highest concentrations in this case were 470-1200 ng/m^3, arguing for enforcing the use of enclosed cabs in the harvesting operation. However, even at these maximum exposure levels, calculated 8 hr exposures were far below the TLV for paraquat for harvest operators. More research is needed on the long term effect of breathing dust contaminated with paraquat (and other chemicals of long residual lifetimes applied to cotton), particularly among individuals with a history of respiratory ailments who are engaged in the harvesting and ginning of cotton.

For the arsenical defoliant cacodylic acid, a method was developed for resolving cacodylic acid, monomethylarsonate, arsenate, and arsenite by ion-exchange chromatography, and their detection by graphite-furnace atomic absorption spectroscopy. The method was potentially applicable to air samples collected near cacodylate-treated cotton fields. However, this very laborious method was not applied to field samples because the samples collected for this purpose were outdated by the end of the lengthy method development period. Considering the increasing use of cacodylates in California, and their relatively high rates of application to cotton (2-4 × that of paraquat), further research should be done on cacodylate airborne residues associated with the treatment, harvesting, and ginning of cotton.