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Substitute Chemical Program. Initial Scientific Review of Cacodylic Acid

Midwest Research Inst.

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December 1975

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Cacodylic acid was identified as a registered substitute chemical for certain cancelled and suspended uses of 2,4,5-T. The report covers all uses of cacodylic acid and is intended to be adaptable to future needs. Should cacodylic acid be identified as a substitute for a problem pesticide other than 2,4,5-T, the review can be updated and made readily available for use. The data contained in this report was not intended to be complete in all areas . Data searches ended in March, 1975.

The substitute chemical is reviewed for suitability considering all applicable scientific factors, such as chemistry, toxicology, pharmacology, environmental fate and movement, use patterns and efficacy.

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Cacodylic acid	cotton defoliant	food tolerances
2,4,5-T	tree-killer	acceptable intake
herbicide	daily intakes	environmental effects
arsenic	ionization constants	efficacy and performance
acute oral toxicity	white metal ions	
dermal toxicity	reduction reactions	
bark beetle control	sodium cacodylate	
uses on major crops in California	production and use	
	toxicity	
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SUBSTITUTE CHEMICAL PROGRAM

INITIAL SCIENTIFIC REVIEW OF CACODYLIC ACID

DECEMBER 1975

U.S. ENVIRONMENTAL PROTECTION AGNNCY
OFFICE OF PESTICIDE PROGRAMS
CRITERIA AND EVALUATION DIVISION
WASHINGTON, D.C., 20460

EPA-540/1-75-021

This report has been compiled by the Criteria and Evaluation Division, Office of Pesticide Programs, EPA, in conjunction with other sources listed in the Preface. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

The Alternative (Substitute) Chemicals Program was initiated under Public Law 93-135 of October 24, 1973, to "provide research and testing of substitute chemicals." The legislative intent is to prevent using substitutes which in essence are more deleterious to man and his environment than a "problem" pesticide suspected of causing "unreasonable adverse effects to man or his environment." The major objective of the program is to determine the suitability of potential substitute chemicals which now or in the future may act as replacements for those uses (major or minor) of pesticides that have been cancelled, suspended, or are in litigation or under internal review for potential unreasonable adverse effects on man and his environment.

The substitute chemical is reviewed for suitability considering all applicable scientific factors, such as chemistry, toxicology, pharmacology, environmental fate and movement, use patterns and efficacy. EPA recognizes the fact that even though a compound is registered, it still may not be a practical substitute for a particular use or uses of a problem pesticide. The utilitarian value of the "substitute" must be evaluated by reviewing its biological and economic data. The reviews of substitute chemicals are carried out in two phases. Phase I conducts these reviews based on data bases readily accessible at the present time. An Initial Scientific Review is conducted to make a judgment with respect to the "safety and efficacy" of the substitute chemical. The Phase II Integrated Use Analysis examines the situation resulting from possible regulatory action against a hazardous pesticide for each of its major and critical uses. This Phase II analysis considers the suitable substitutes reviewed during Phase I in conjunction with alternative management practices to evaluate current and projected environmental, health, and economic impacts of potential changes in pest management practices.

The report summarizes rather than interprets scientific data reviewed during the course of the studies. Data is not correlated from different sources. Opinions are not given on contradictory findings. This report contains the Phase I Initial Scientific Review of Cacodylic Acid. Cacodylic acid was identified as a registered substitute chemical for certain cancelled and suspended uses of 2,4,5-T. The report covers all uses of cacodylic acid and is intended to be adaptable to future needs. Should cacodylic acid be identified as a substitute for a problem pesticide other than 2,4,5-T, the review can be updated and made readily available for use. The data contained in this report was not intended to be complete in all areas. Data searches ended in March, 1975.

The review was coordinated by a team of EPA scientists in the Criteria and Evaluation Division of the Office of Pesticide Programs. The responsibility of the team leader was to provide guidance and direction and technically review information retrieved during the course of the study. The following EPA scientists were members of the review team: John Bowser (Team Leader); Stewart Colten (Chemistry); Merry Lou Alexander (Chemistry); Clinton Fletcher (Chemistry); Roger Gardner (Pharmacology and Toxicology); John Leitzke (Fate

and Significance in the Environment); Richard Petrie (Registered Uses); Jeff Conopask, Ph.D. (Economics).

Data research, abstracting, and collection were primarily performed by Midwest Research Institute (MRI), Kansas City, Missouri (EPA Contract #68-01-2448) under the direction of Mr. Thomas L. Ferguson. RvR Consultants, Shawnee Mission, Kansas, under a subcontract to MRI, assisted in data collection. The following MRI scientists were principal contributors to the report: James V. Dilley, Ph.D., David F. Hahlen, Alfred F. Meiners, Ph.D., William J. Spangler, Ph.D., Frank E. Wells, Ph.D. Rosmarie von Rumker, Ph.D. (RvR Consultants) also contributed to the report.

Draft copies of the report have been reviewed by the scientific staffs of EPA's National Environmental Research Centers and their associated laboratories. Comments and supplemental material provided by the following laboratories were greatly appreciated and have been incorporated into this report: Gulf Breeze Environmental Research Laboratory, Gulf Breeze, Florida and National Ecological Research Laboratory, Corvallis, Oregon. The Ansul Company, a manufacturer of cacodylic acid, reviewed the draft of this report and made certain comments and additions.

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PART I. SUMMARY

CONTENTS

This section contains a summary of the "Initial Scientific Review" conducted on cacodylic acid (dimethylarsinic acid). The section summarizes rather than interprets data reviewed.

Production and Use

Cacodylic acid, the common name for dimethylarsinic acid [$(CH_3)_2$ As(O)OH], is manufactured in the United States by The Ansul Company, Marinette, Wisconsin, and Vineland Chemical Company, Inc., Vineland, New Jersey. Both the acid and its monosodium salt are used for herbicidal purposes.

The sodium salt of the acid (sodium cacodylate or sodium dimethylarsinate) is manufactured by a synthesis involving 5 reactions.

$$As_2O_3 + 6NaOH \longrightarrow 2Na_3AsO_3 + 3H_2O \quad (1)$$

Arsenic Trioxide — Sodium Arsenite

$$Na_3AsO_3 + CH_3Cl \longrightarrow CH_3AsO(ONa)_2 + NaCl \quad (2)$$

Methyl Chloride — DSMA

$$CH_3AsO(ONa)_2 + SO_2 \xrightarrow{H_2O} CH_3AsO + Na_2SO_4 \quad (3)$$

$$CH_3AsO + 2NaOH \xrightarrow{H_2O} CH_3As(ONa)_2 + H_2O \quad (4)$$

$$CH_3As(ONa)_2 + CH_3Cl \xrightarrow{H_2O} (CH_3)_2AsO(ONa) + NaCl \quad (5)$$

Sodium cacodylate

Cacodylic acid is then made by acidification of the sodium salt:

$$(CH_3)_2AsO(ONa) + HCl \xrightarrow{H_2O} (CH_3)_2AsO(OH) + NaCl \quad (6)$$

Cacodylic acid

Cacodylic acid is a colorless, odorless, crystalline compound. It is very soluble in water and can be used as a buffer. The cacodylate anion [$(CH_3)_2AsO_2^-$] is very stable and easily interchanges cations to form a wide variety of other salts. Cacodylic acid is very stable toward chemical oxidation. Cacodylic acid reacts with thiols but the reaction products are unknown. Cacodylic acid is amphoteric and reacts as a base with stronger acids.

The technical product is 65% aqueous cacodylic acid, and contains salts, including sodium chloride. Water is the principal solvent in formulations, which usually have sodium cacodylate as the principal active ingredient and cacodylic acid as the minor active ingredient. Generally, the formulations are 20 to 30% strength (cacodylic acid equivalent), but the tree-killer formulation is 50%, and contains only the acid form. At least two formulations are available that contain cacodylic acid in combination with monosodium methanearsonate (MSMA) as active ingredients. No dry powder or granular formulation of cacodylic acid are available.

Cacodylic acid (and its sodium salt) is a contact herbicide, capable of defoliating or dessicating a wide variety of plants. It is currently registered in the United States for general weed control in noncrop areas, for weed control by directed application* in nonbearing citrus orchards, for lawn renovation, for defoliation of cotton, and for crown kill of undesired trees.

Cacodylic acid is also used by professional foresters and entomologists only for the control of bark beetles.

The estimated domestic use of cacodylic acid in 1973 was 1,300,000 to 1,700,000 lb acid equivalent. About 50% of that quantity was used for nonselective weed control, 40% for cotton defoliation, about 1% for forest management, with the remainder being used for all other purposes, including lawn usage.

Toxicity and Physiological Effects

Specific information on acute, subacute, or chronic toxicity of cacodylic acid to man by oral, dermal, or respiratory routes was not found. A potential occupational hazard for forestry workers using cacodylic acid in tree-thinning operations has been suggested, although toxic effects in these workers were not evident. Exposures were monitored by increases in urinary excretion of arsenic.

In tests on rats, the acute oral toxicity (LD_{50}) reported for cacodylic acid herbicide formulations ranged from 0.7 to 2.6 g/kg of body weight. Significant sex differences were not indicated (LD_{50} of 1.4 g/kg for males versus 1.28 g/kg for females). When weanling rats were fed at dietary levels equal to 10, 20, and 40% of the estimated oral LD_{50} (0.70 g/kg), little effect was noted on various tissues examined except for reduced activity of spermatogonia cells at the 40% treatment level.

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* "Directed application" means that this herbicide is not allowed to contact the leaves, stems, or bark of the crop in which weeds are to be controlled.

Subacute toxicity tests (90 days) indicated that dietary cacodylic acid was nontoxic at 30 ppm to dogs and at 100 ppm to rats.

Rabbits treated by dermal application of cacodylic acid (77%) exhibited mortality at lower dose levels when the skin was abraded than when it was intact. With abraded skin a dose of 1.0 g/kg was lethal for the rabbit, but with intact skin death did not occur until the dose reached 2.5 g/kg.

Skin and eye irritation tests with rabbits appeared to indicate that cacodylic acid formulations could be considered essentially nonirritating to both skin and eyes.

Subacute toxicity was the only area in which reports were found for domestic animals. Cattle given cacodylic acid (by capsule) at 25 mg/kg for 10 days exhibited no ill effects. When cacodylic acid was given by drench at 50 mg/kg, toxic signs appeared after the first dose and death after the seventh. Sheep treated for 10 days at 50 mg/kg (capsule) exhibited signs of toxicity after the second dose but did not die after 10 doses. A weight loss of 22% resulted from the treatment.

Chickens were fed for 10 weeks at dietary levels up to 30 ppm arsenic (cacodylic acid) without any apparent toxic effects. Eggs from the hens fed at the 30-ppm level contained 0.22 ppm arsenic after 1 month and 0.23 ppm after 2 months feeding.

In other studies chickens fed 10 daily doses of 100 mg/kg of body weight exhibited no toxic signs. However, chickens treated at 500 mg/kg had only a 13% weight gain compared to a 53% gain for controls.

Metabolic studies specifically designed to determine mammalian absorption, distribution, excretion, and residual potential of cacodylic acid are lacking. One study on absorption was reported on the rat. The mechanism by which cacodylic acid was absorbed appeared to be simple diffusion; the absorption half-time was calculated to be 201 min. In the cow, cacodylic acid was excreted primarily in the urine and residues were not found in milk.

Nonavailability of tissue-bound arsenic was shown by studies in which animal products that contained arsenic were fed to rats, chickens, and man. It appears that trivalent arsenite is oxidized to pentavalent arsenate in mammals. Most of the organic arsenicals (the pentavalents) are excreted essentially unchanged so that their toxic effect is unlikely to be related to conversion to an inorganic arsenic compound.

Rapid clearing of tissue residues of arsenic after animals are removed from feeds containing various arsenicals was demonstrated for cattle, chickens, and swine. Only studies on the mutagenic effects in bacteria have been reported for cacodylic acid; in this system, a mutagenic potential was not found. Reproductive and teratogenic effects have not been reported for cacodylic acid in any species. EPA laboratories at Research Triangle Park, North Carolina, are currently studying the teratogenic effects of cacodylic acid on rats and mice.

Dietary tests to determine the tumorigenic effect of cacodylic acid in mice were conducted for 18 months; the treatment did not cause any increase in hepatomas, pulmonary tumors, lymphomas, or in total numbers of mice with tumors over the values found for untreated control animals.

Food Tolerances and Acceptable Intake

Analytical methods which distinguish residues of specific arsenical compounds in plant materials are not presently being used in the analysis of food and feed. Rather, samples are analyzed for total arsenic (as As_2O_3). Results, therefore, include naturally occurring arsenic levels in addition to pesticide residues.

There are currently tolerances for cacodylic acid (calculated as As_2O_3) of 0.7 ppm in cattle (meat, fat, and meat by-products except kidney and liver), 1.4 ppm in beef kidney and liver, and 2.8 ppm in cottonseed.

Investigators who have monitored the levels of arsenic in food and feed for a 6-yr period have concluded that the dietary intake of arsenic from pesticide residues is not significant.

An acceptable daily intake (ADI) has not been established for cacodylic acid.

Environmental Effects

The data available on the toxicity of cacodylic acid to fish is limited to acute toxicity. The 96-hr TL_m of a 23.4% cacodylic acid formulation for bluegill (Lepomis macrochirus) is reported to be 80 ppm. The 96-hr LC_{50} for a second formulation (percent cacodylic acid not stated) was reported to be 16 ppm for bluegill.

One field study was made of the effect on fish populations of cacodylic acid in runoff. Only one of the 20 species monitored was found to decrease significantly in population between pre- and post-treatment counts. The random effects on the species and the low levels of arsenic in the runoff water (<0.05 ppm), however, led the investigators to conclude that variations in populations were not due to the cacodylic acid. During this study, the population levels of several benthic organisms were also monitored, including crayfish (Orconectes species), dragonfly naiad (Gomphus species), freshwater snail (Neritian species), and an unidentified immature freshwater clam. Observations were also made to detect possible morphological effects on eelgrass (Vallisneria americana). None of these organisms exhibited any gross changes in population levels; all remained abundant throughout the study period.

No effects were noted when pink shrimp (Penaeus duorarum) and longnose killifish (Fundulus similis) were exposed to 40.0 ppm active ingredient (AI) of cacodylic acid for 48 hr or in Eastern oyster (Crassostrea virginica) exposed to 1.0 ppm AI for 96 hr.

Information from controlled studies concerning the effects of cacodylic acid on wildlife is limited to studies of its oral toxicity to 3 avian species and 1 species of deer. The 8-day dietary LC_{50} for mallard ducklings (Anas platyrhynchos) is greater than 5,000 ppm. A material containing 29% sodium cacodylate and 5% cacodylic acid was also calculated to have an 8-day dietary LC_{50} for bobwhite quail (Colinus virginianus) of greater than 5,000 ppm.

The LD_{50} of a formulation containing 54.3% cacodylic acid for mallard hens is greater than 2,000 mg/kg and equal to or greater than 2,000 mg/kg for the chukar partridge (Alectoris graeca).

Studies have been made of the fate and environmental impact of organic arsenical herbicides, including cacodylic acid, used in the forest environments of the Pacific Northwest. More than 400 determinations were made of arsenic residues in specific tissues and whole body samples from animals trapped at various intervals after use of the arsenicals. About 50% of the animals captured between 2 and 30 days following treatment contained arsenic residues between 0.5 and 9.8 ppm. One animal collected 1 day after treatment contained arsenic residues ranging from 17 to 30 ppm in various body parts. Few animals collected more than 30 days after treatment contained detectable arsenic residues.

Conflicting results have been reported from studies of the toxic effect of cacodylic acid to honeybees (Apis mellifera). Cacodylic acid was classified as "relatively nontoxic" in tests designed to measure the herbicide's contact effect; application of 152.12 ug/bee produced only 5.6% mortality after 48 hr of exposure. However, both oral dosing (10, 100, and 1,000 ppm in 60% sucrose) and spraying with an aqueous solution at a rate of 4 lb cacodylic acid, 20 gal/acre, were found to be highly toxic.

Soil microorganisms appear to be capable of degrading organic arsenical herbicides, including cacodylic acid. Pennicillium brevicaule and Methanobacterium have been shown to produce methylarsines from methylarsonates. Three fungi isolated from raw sewage (Candida humicola, Gliocladium roseum, and Penicillium sp.) have been shown to produce measurable quantities of trimethylarsine from cacodylic acid.

Cacodylic acid does not appear to affect soil microorganisms adversely under actual field conditions, even at concentrations much higher than those likely to result from commercial use in accordance with label directions. Investigators disagree, however, on the relative interaction of cacodylic acid with fungi and bacteria. In some studies, cacodylic acid appeared to inhibit the growth of fungi more than bacteria, whereas in others cacodylic acid (as well as other organic arsenicals) was more toxic to bacteria than to fungi. One investigator suggested that the toxicity of cacodylic acid to fungi may be due to reaction with sulfhydryl groups of essential proteins, whereas the fungitoxicity of arsenates and arsenites seems to be due to the competitive interference of arsenic with phosphorus in oxidative phosphorylation.

The pathways of degradation of cacodylic acid in soil have not been extensively investigated. One study has been reported in which degradation in

volatile organoarsenical within 24 weeks and was lost from the soil system; under aerobic conditions, 35% was converted to volatile organoarsenical compounds.

The effect of repeated applications of cacodylic acid on arsenic residues in the soil has been evaluated. After 6 annual applications at rates of 2.5 and 7.5 lb of acid equivalent per acre, statistically significant buildup of arsenic was detected in the top 6 in of soil for both rates (2.4 to 4.5 ppm above the average background of 11 ppm). Arsenic concentrations in the 6- to 12-in layer were increased by the higher rate, while the 12- to 18-in layer was not affected by either rate.

Available data indicates that herbicidally effective concentrations of cacodylic acid "disappear" rather rapidly from field soils after application. Microbial activity appears to some extent to contribute to their degradation. Several different chemical reactions also seem to be involved. A number of crops have been tested in order to evaluate the effect of cacodylic acid on their respective arsenic content. Snap beans, potatoes, sweet potatoes, carrots, Chinese cabbage, field corn, and soybeans were planted in plots which had been treated with 5 lb of cacodylic acid per acre. No significant uptake of arsenic was detected in the edible parts of the crops. In a companion study, no uptake of arsenic was detected in alfalfa or ryegrass from plots that had been similarly treated.

Regarding the effects of cacodylic acid in water, one study was reported in which 5 lb of cacodylic acid per acre were applied to irrigation canals. The highest arsenic concentration detected in the water was 0.86 ppm; this level dropped to less than 0.1 ppm in less than 2 hr.

There were no reports found on the presence, fate, persistence, or significance of cacodylic acid in the air. However, some investigators have suggested that cacodylic acid (and other organic arsenicals) may be reduced and methylated to form volatile compounds which escape from treated areas into the air.

Studies have been made in a model ecosystem in which mosquitofish (Gambusia affinis), Daphnia magna, Physa snails, and algae (Oedogonium cardiacum) were exposed for 3, 29, 32, and 32 days, respectively, to ^{14}C-labeled cacodylic acid at a concentration of 11.5 ppb. In this system, algae were found to be the primary sink in which cacodylic acid residues accumulated. Algae and daphnids bioaccumulated more cacodylic acid residues than did the two higher food chain organisms, snails and fish, indicating that cacodylic acid did not biomagnify between food chain organisms.

Other tests have shown that fish and snails accumulated 2 to 10 times more cacodylic acid from solution than from consuming cacodylic-treated Daphnia or algae.

In still another aquatic ecosystem, bottom-feeding organisms (catfish, Ictalurus punctatus; and crayfish, Procambarus clarki), and duckweed (Lemna minor) were exposed to 3 soils containing ^{14}C-labeled cacodylic acid. Based on the results from this study, the investigators concluded that cacodylic

acid does not bioaccumulate in the aquatic organisms studied. However, crayfish did accumulate arsenic, particularly in their soft tissue, in the 3 different tests.

The data regarding the behavior of cacodylic acid in soil and water, although limited, indicates that movement of cacodylic acid from treated land to water by leaching or surface runoff appears to be minimal.

Efficacy and Performance

Cacodylic acid is a nonselective herbicide used for control of weeds and grasses along ditch banks and rights-of-way, for cotton defoliation, for control of hardwood trees, and for suppression of bark beetles.

Cacodylic acid has shown up to 100% crown kill when applied to quaking aspen, red maple, paper birch, jack pine, and oak. Poor crown kill was observed on hickory and blackgum. Although it gives good crown kill, most trees survived when measured over a 2-year period.

Use of the Hypo-Hatchet® to apply cacodylic acid does not appear to increase the rate of tree kill, but it has been shown to be 2 to 3 times as efficient as other application methods.

Control of the bark beetle in spruce, ponderosa pines, and loblolly pines can be as high as 99% when these trees are treated with cacodylic acid. The use of attractants to lure the insect to the treated tree has been successful in increasing the number of insects killed. However, some doubts exist if cacodylic acid is translocated in the southern pine to provide control of the southern pine beetle.

Although cotton defoliation is a significant use of cacodylic acid, a search of the literature did not produce any information on its efficacy. Additional contacts at selected extension agencies also revealed a lack of this type of information.

PART II. INITIAL SCIENTIFIC REVIEW

SUBPART A. CHEMISTRY

CONTENTS

This section reviews available data on cacodylic acid's chemistry and presence in foods. Eight subject areas have been examined: Synthesis and Production Technology; Physical Properties of Cacodylic Acid; Composition and Formulation; Analytical Methods; Chemical Properties; Occurrence of Residues in Food and Feed Commodities; Acceptable Daily Intake; and Tolerances. The section summarizes rather than interprets scientific data reviewed.

Synthesis and Production Technology

Cacodylic acid, the common name for dimethylarsinic acid [$(CH_3)_2$ As(O)OH], is used in the control of weeds, cotton defoliation, forest management, and lawn restoration.

It was introduced as a herbicide in 1958 by The Ansul Company, Marinette, Wisconsin. However, the chemical has been known for over 130 years. Bunsen (1843) was one of the earliest researchers to work with the compound. The only known present domestic manufacturers of this compound are The Ansul Company and Vineland Chemical Company, Inc., Vineland, New Jersey. However, one patent on a manufacturing process was issued to O. M. Scott and Sons Company (Schanhals 1967).

A process flowsheet for cacodylic acid is presented in Figure 1. Cacodylic acid is manufactured from disodium methanearsonate (DSMA), $CH_3AsO(ONa)_2$, which is also a commercial herbicide. The following equations illustrate that DSMA is initially synthesized in a two-step reaction sequence:

$$As_2O_3 + 6NaOH \longrightarrow 2Na_3AsO_3 + 3H_2O \qquad (1)$$

Arsenic Trioxide — Sodium Arsenite

$$Na_3AsO_3 + CH_3Cl \longrightarrow CH_3AsO(ONa)_2 + NaCl \qquad (2)$$

Methyl Chloride — DSMA

Reaction equations for the subsequent manufacture of cacodylic acid are as follows:

$$CH_3AsO(ONa)_2 + SO_2 \xrightarrow{H_2O} CH_3AsO + Na_2SO_4 \qquad (3)$$

DSMA — Sulfur dioxide — Methylarsine oxide

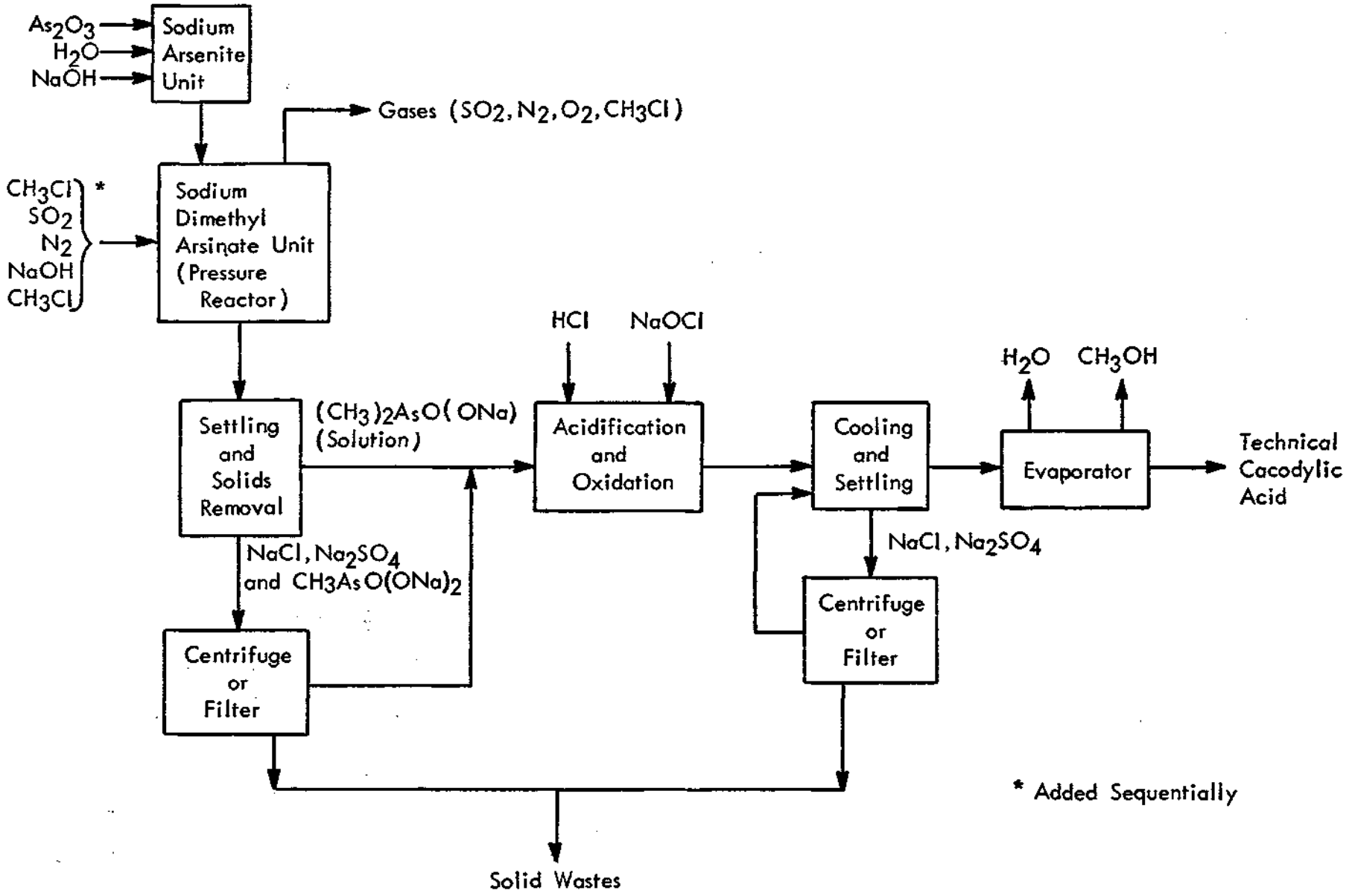

Figure 1. Patented production method for cacodylic acid.

$$CH_3AsO + 2NaOH \xrightarrow{H_2O} CH_3As(ONa)_2 + H_2O \quad (4)$$

Sodium hydroxide — Disodium methylarsonite

$$CH_3As(ONa)_2 + CH_3Cl \xrightarrow{H_2O} (CH_3)_2AsO(ONa) + NaCl \quad (5)$$

Methyl chloride — Sodium dimethylarsinate

$$(CH_3)_2AsO(ONa) + HCl \xrightarrow{H_2O} (CH_3)_2AsO(OH) + NaCl \quad (6)$$

Cacodylic acid

Reaction (3) is very rapid at temperatures below 200°F, and at any pressure. The reaction is complete in 5 to 15 min (Schanhals 1967).

Reaction (4) is the most critical step in yield efficiency. After Reaction (3), the excess SO_2 is purged using a gas which is inert to the methylarsine oxide. Nitrogen is preferred, but CO_2 or other inert gases may be used. Two alternates are: use of the alkylating agent as the purge gas or evacuation of the oxygen, followed by purging. The evacuation-purge cycle is repeated several times (Moyerman and Ehman 1965).

A low oxygen content is required in order to prevent the following oxidation reaction from occurring (Schanhals 1967):

$$2CH_3AsO + O_2 + 2H_2O \longrightarrow 2CH_3AsO(OH)_2$$

Methylarsonic acid

Moyerman and Ehman (1965) specify the following conditions related to oxygen concentration.

	Oxygen content of atmosphere on reaction mixture (moles/liter)	Ratio of oxygen to CH_3AsO (moles/mole)
"Should be" less than	300×10^{-5}	200×10^{-5}
"Preferably" less than	160×10^{-5}	125×10^{-5}
"Especially good results" when less than	70×10^{-5}	55×10^{-5}

A second important condition for Reaction (4) is the pH. Moyerman and Ehman (1965) report that, above a pH of 10.5, the following side reactions occur, but may be avoided by excluding air.

$$3CH_3AsO \longrightarrow As_2O_3 + (CH_3)_3As \qquad (7)$$

Trimethyl-
arsine

$$4CH_3AsO \longrightarrow [(CH_3)_2As]_2O + As_2O_3 \qquad (8)$$

Cacodyl
oxide

Noller (1957) reports the following reactions:

$$[(CH_3)_2As]_2\ O + 2\ NaOH \rightarrow H_2O + 2\ (CH_3)_2As\ O\ Na \qquad (9)$$

$$(CH_3)_2AsONa + CH_3CL \rightarrow (CH_3)_3\ As\ O + NaCL \qquad (10)$$

Trimethyl arsine

The formation of trimethylarsine is undesirable because of the resultant decrease in yield. In addition, $(CH_3)_3As$ is flammable, toxic and has a disagreeable odor.

The specific recommendations of Moyerman and Ehman (1965) in regard to pH are quoted directly from the patent as follows.

> In carrying out the reaction, it is desirable that the aqueous solution of the arsenoso substituted organic compound (for example, methyl arsineoxide) be maintained at a pH less than about 10 and preferably less than about 7, until the oxygen content has been reduced to the desired level. Following removal of the oxygen, the pH of the reaction mixture is adjusted to the alkaline range, as by the addition of an alkalimetal hydroxide. Preferably, the pH may be regulated following oxygen removal by adding an alkali metal hydroxide such as sodium, potassium or lithium hydroxide. Enough of the alkali metal hydroxide is added to insure a large stoichiometric excess, based upon the arsenoso substituted hydrocarbon. Because of the large excess of alkali metal hydroxide employed, the pH of the reaction mixture at the start of alkylation will ordinarily be about 14. As the alkylation reaction progresses, the pH gradually falls until the akylation is complete, at which time the pH is between about 5.5 and 6.5.

In Reaction (5) the alkylating agent is usually CH_3Cl, but Ch_3Br, CH_3I, or $(CH_3)2SO_4$ may be used (Moyerman and Ehman 1965). According to Schanhals (196.), Reaction (5) is carried out by bringing the disodium methylarsonite up to reaction temperature (75 to 200°F) and treating the reaction mixture with superheated CH_3Cl. Pressures may range from 40 to 175 psig. The best temperature and pressure for the reaction are 175°F and 150 psig. The above 3 process reactions are all carried out in the same pressure reactor.

Reaction (5) is the production of the sodium salt of cacodylic acid. Whether the salt form is to be used directly or converted to the acid, the following steps are taken, as quoted from Schanhals (1967):

> The products . . . are present in a slurry which is pumped out of the reactor. The solids are then removed by conventional methods, preferably by pumping the reaction products to a settling tank and cooling them. Most of the Na_2SO_4, some NaCl, and some reaction by-products have precipitated in the pressure reactor. Residual amounts remaining in solution precipitate out in the settling tank as the solution cools. The precipitated solids may then be dewatered using a filter, centrifuge, or similar unit. The mother liquor and the liquid phase remaining in the settling tank are pumped to a second reactor. The liquid phase pumped into that reactor is a solution of the sodium salt of dimethylarsinic acid (sodium dimethylarsinate).

According to Ottinger et al. (1973), there is no liquid effluent from this process because all the liquid streams are recycled for reuse. A number of multiple effect evaporators are employed in the solution recycling systems. The process does, however, create a solid waste which is a mixture of sodium chloride and sodium sulfate containing 1 to 1-1/2% cacodylate contaminants.

If the sodium salt is to be converted into cacodylic acid, Reaction (6) is a simple addition of hydrochloric acid, done at ambient condition. Sulfuric, nitric, or phosphoric acids could also be used (Schanhals 1967). Acidification is not carried to completion.

Schanhals (1967) recommended an additional oxidation step to reduce the toxicity and odor of the reaction mass. This may be performed on the sodium salt or cacodylic acid itself. Possible oxidation agents are sodium hypochlorite, hypochlorous acid, hydrogen peroxide, and others. The preferred oxidizing agent is said to be sodium hypochlorite. Typical reactions which occur in this oxidation step are as follows:

$$CH_3AsO + H_2O + NaOCl \longrightarrow CH_3AsO(OH)_2 + NaCl \quad (11)$$

$$As(ONa)_3 + NaOCl \longrightarrow AsO(ONa)_3 + NaCl \quad (12)$$

$$As(OH) + NaOCl \longrightarrow AsO(OH) + NaCl \quad (13)$$

$$As_2O_3 + NaOCl \longrightarrow As_2O_5 + 2NaCl \quad (14)$$

$(CH_3)_3As + [O] \rightarrow (CH_3)_3AsO$ (15)*, **

$[(CH_3)_2As]_2\ O + O_2 + H_2O \rightarrow 2(CH_3)_2\ As\ (O)\ OH$ (16)** See also below

Ambient conditions are also used for this reaction.

Schanhals (1967) described the manufacturing process as follows:

> The arsinic acid or salt solution is pumped to an evaporator or similar device and water . . . removed, precipitating additional quantities of NaCl and Na_2SO_4. The solids may be removed from the solution by any conventional means. In the preferred process, the hot concentrate is first cooled in a settling tank and the insoluble impurities then removed. Additional solution is then removed from the solids by conventional devices such as filters or centrifuges and the mother liquor added to the solution removed in the settling tank.

An alternate method of production was described by Melnikov (1971):

$$4CH_3COOK + As_2O_3 \xrightarrow[\text{dist.}]{\text{dry}} [(CH_3)_2As]_2O + 2K_2CO_3 + 2CO_2 \qquad (17)$$

Potassium acetate (anhydrous) — Cacodyl oxide

$$[(CH_3)_2As]_2O + H_2O + O_2 \longrightarrow 2(CH_3)_2As(O)OH$$

Cacodylic acid

However, Schanhals (1967) concluded that the method is uneconomical commercially because of expensive starting materials and a relatively low conversion.

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* Noller (1957, p. 900) gives:
$(CH_3As + O_2 \rightarrow (CH_3)AsO$: (15a)

CRC Handbook of Chemistry and Physics (1969) shows:
$2ClO^- + 2H_2O + 4e \rightleftharpoons 2Cl^- + 4OH^-$ 0.90 Volt

$4OH^- \rightleftharpoons 4e + O_2 + 2H_2O$ -.401 Volt, so that overall

$2ClO^- \rightleftharpoons O_2 + 2Cl^-$ .499 Volt (15b)

At 25° the equilibrium constant of this reaction is $\log^{-1}(.499(4) \div .059) = \log^{-1}(E°nF/RT)$ or about 10^{34}. Thus, it may be safely assumed that the hypochlorite will be releasing substantial free oxygen for reaction (15a).

** The trimethylarsine and cacodyl oxide for reactions (15) and (17) would be present, for example, if the by product reactions (7) and (8) could not be prevented.

Laboratory Preparation - Conversion of methylarsine oxide to cacodylic acid, as reported by Moyerman and Ehman (1965), is 98%.

Physical Properties

Chemical name: Dimethylarsinic acid
Hydroxydimethylarsine oxide

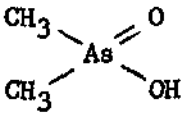
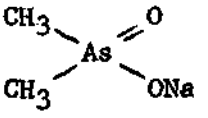
Common name: Cacodylic acid

Derivation of name: Cacodylic acid has been known for many years. The prefix cac- or caco- comes from the Greek word kakos, meaning bad. The Greek word kakodes meant ill-smelling. Cacodyl refers to an arsenical radical $As(CH_3)_2$ whose compounds are noted for their vile smells and poisonous properties, or to the compound with 2 radicals joined, $As_2(CH_3)_4$.

Cacodylic acid, $(CH_3)_2As(O)OH$, contains the cacodyl radical with a double bonded oxygen and a hydroxyl group attached to the arsenic atom. The acid itself is odorless, despite the name.

Other names: Phytar® 138, Chexmate®, Rad-E-Cate®, Silvisar® 510.

Pesticide class: Herbicide, arsenical.

Empirical formula:	Cacodylic acid	Sodium cacodylate
	$C_2H_7AsO_2$	$C_2H_6AsO_2Na$
Structural formula:		
Molecular weight:	137.99	159.98

Analysis	Percent	Percent
C	17.41	15.01
H	5.11	3.78
As	54.29	46.83
O	23.19	20.00
Na		14.37

Structural data: Cacodylic acid crystals are triclinic, with unit-cell dimensions of a = 6.53 nm, b = 6,82 nm, c = 6.61 nm, $\alpha = 77°30'$, $\beta = 98°45'$, $\gamma = 55°9'$ (Trotter and Zobel 1965).

Smith et al. (1970b) listed different unit-cell dimensions; a = 8.34 nm, b = 6.82 nm, c = 10.16 nm, α = 59.5°, β = 89.3°, γ = 106.0°.

The configuration is tetrahedral about the arsenic atom; the bond angles are in the range of 106 to 115° (Trotter and Zobel 1965).

Bond	Bond length (nm)
As - C	1.91 ± 0.04
As - O(both)	1.62 ± 0.03
O-H• • •O(hydrogen bond)	2.57

Physical state: Colorless, odorless crystals. Hygroscopic.

Technical product is 65% pure, containing NaCl as an impurity (Martin 1971). The sodium salt is deliquescent.

Density: 1.95 g/ml (Smith et al. 1970b). From unit-cell volume, not actual measurement.

Melting point (°C): 195-196 (crystals from alcohol ether) (Merck 1968)
192-198 (Martin 1971)
200 (Weed Society of America 1970)
200 (Frear 1969)

Enthalpy of fusion: 4.96 kcal/mole (Smith et al. 1970a).

Solubility: Very soluble in water, 83 g acid to 100 g water at 22°C. Solubility in ethyl alcohol, 28.5 g/100 ml at 15°C (Bailey and White 1965), 20.6 g/100 ml at 20°C (Herbicide Handbook 1970). Soluble in acetic acid, but not in ethyl ether.

Sodium salt: 82 g of salt is soluble in 100 g of water.

pH: 7.7 to 8.0 (4% solution of sodium cacodylate). (Masucci and Moffat 1923.)

3.1 [1 molar solution of acid, calculated from pKa given by Jacobson et al. 1972].

Corrosivity: Aqueous solution is mildly corrosive.

Analytical Methods

This subsection reviews analytical methods for cacodylic acid. The review describes (a) multi-residue methods, (b) residue analyses, and (c) formulation analyses. Information on the sensitivity and selectivity of the methods is also presented.

Information Sources - The primary information sources for the analytical methods are as follows: (1) The Pesticide Analytical Manual (PAM 1967), published by the Food and Drug Administration (FDA), is designed to bring together procedures and methods used by the FDA laboratories to examine food samples for the presence of pesticide residues. PAM is published in 2 volumes. Volume I contains procedures for multi-residue methods (for samples of unknown history which may contain more than one pesticide). Volume II contains analytical methods used for specific pesticide residues and for specific foods. (2) Official Methods of Analysis of the Association of Official Analytical Chemists (AOAC 1970) is a methods manual published about every 5 yr. The reliability of the methods must be demonstrated by a published study showing the reproducibility of the method by professional analysts. Methods and collaborative studies are published in the Journal of the Association of Official Analytical Chemists.

Multi-Residue Methods - There are no multi-residue methods which specifically detect cacodylic acid. The residue analyses performed by FDA do not detect cacodylic acid as an individual chemical; all forms of arsenic are converted to arsenic trioxide (As_2O_3).

Residue Analysis - The Diamond Shamrock Chemical Company (1970) explains the difficulty in detecting residues of arsenical pesticides as follows:

> Analytical methods which can distinguish residues of specific arsenical compounds in plant materials are not available. Gas chromatography and thin-layer chromatography methods do not have sufficient sensitivity to quantitatively analyze methanearsonate herbicides.

There have been some recent developments which may lead to practical, specific methods for the determination of cacodylic acid residues. These are discussed below.

Sachs et al. (1971) developed a paper chromatographic separation method for cacodylic acid and other arsenicals. Four solvent elution systems were employed. Aqueous extraction of plant tissues removed essentially all of the arsenicals applied. The paper chromatographic procedures were followed by colorimetric determinations of the separated arsenicals. The silver diethyldithiocarbamate colorimetric method was useful for detecting as little as 0.6 to 20 µg of arsenic (the color is caused by the formation of an arsine-silver diethyldithiocarbamate complex).

Soderquist et al. (1974) have reported a procedure whereby cacodylic acid and its salts can be determined rapidly with a detectability limit below 0.05 ppm in water and 0.5 ppm in soil. The method, which excludes other arsenicals, is based upon conversion of cacodylic acid to iododimethylarsine with hydriodic acid:

$$Me_2AsO_2H \xrightarrow{HI} Me_2AsI$$

The iododimethylarsine is determined by means of electron-capture gas chromatography. Recoveries of cacodylic acid from water and soil are as follows.

	Cacodylic acid		
Sample	Added (ppm)	Found (ppm)[a/]	Recovery (%)[a/]
Distilled water	0.15	0.137 (± 0.012)[a/]	92.3 (± 7.4)
Rice water	0.15	0.150 (± 0.004)	100 (± 2.6)
Rice water (blank)	0	< 0.050	0
Dinuba soil	1.5	1.22 (± 0.11)	81.3 (± 5.1)
Dinuba soil (blank)	0	< 0.50	0

a/ Standard deviation from 3 samples.

Interferences in the water analyses were not serious and, according to the authors, the detectability limit of 0.05 ppm could be lowered further by using a larger water sample. Attempts failed to lower the detectability limit in soil (about 0.5 ppm) by prior extraction of the cacodylic acid with methanol or aqueous methanol probably due to binding with soil particles.

Braman and Foreback (1973) developed a method for analyzing various forms of methylated arsenic acids in the environment at low concentration. This method depends upon reduction of cacodylic acid to dimethylarsine, $(CH_3)_2AsH$, by sodium borohydride at pH 1 to 2. This volatile arsine is then scrubbed out with helium gas and frozen in a liquid nitrogen trap. The arsine gas is then volatilized from the trap and a recording is made of the intensity of arsenic emission lines (234.9 nm or 228.8 nm) produced by an electrical discharge in the carrier gas. The limit of detection is very low, 0.5 ng. Braman and Foreback's method is also applicable to arsenite ion, arsenate ion, and MAA. Since arsine, methylarsine and dimethylarsine will volatilize from the trap in the order of their boiling points, the compounds pass through the detector at different times and the analysis readout is similar in appearance to a gas chromatogram. Thus, the two methylated arsenic acids can be distinguished from one another and from inorganic arsenic. The authors applied this method to the analysis of water samples, bird eggshells, seashells and limestone, and adapted this method to the analysis of urine samples.

Specific residue methods are outlined below:

Gutzeit Method - (Official Final Action) - (For total arsenic) - The sample is oxidized to As_2O_5 with a sulfuric and nitric acid mixture, then reduced to AsH_3 by Zn-HCl in $SnCl_2$ and KI. A paper strip soaked in $HgBr_2$ and placed in a narrow tube develops a stain of a length which can be calibrated for As content in the sample. A preabsorber with lead acetate removes any H_2S evolved. Special separation techniques are needed following the oxidation step where interfering substances are present (for example, pyridine in tobacco) or where the As is difficult to convert to As_2O_5, as in shrimp (AOAC 1970).

Samples of fresh fruits, dried fruit products, vegetables or other materials, are treated with nitric and sulfuric acids to convert arsenic compounds to arsenic pentoxide (As_2O_5). According to PAM (1967), the sensitivity of the method is 0.01 to 0.03 mg or about 0.1 ppm.

Colorimetric Methods - (Official Final Action) - For each of the 2 colorimetric methods, the arsenic compound in the sample is converted to arsine (by reduction with zinc) and the arsine is absorbed in a reagent which produces a color (AOAC 1970).

Buttrill (1973) described a colorimetric method for determining arsenic residues that has been adopted by AOAC as "official first action" for arsenic in meat and poultry. The method uses the molybdenum blue complex for a spectrophotometric readout and involves ashing with magnesium nitrate at 600°C. Six groups of 4 samples were analyzed. The average recoveries for 0.28 to 2.41 ppm arsenic were 87.6 to 109.3%; the standard deviations ranged from 0.037 to 0.225. The method is based on the work of Kingsley and Schaffert (1951), whose glassware design is used, and on the sample preparation techniques of Evans and Bandemer (1954).

Molybdenum Blue Method - (For total arsenic) AsH_3, produced as in the Gutzeit method, is absorbed in $NaOBr_1$ and mixed with a solution of $(NH_4)_2MoO_4$ and hydracine sulfate. The color produced is determined spectrophotometrically (at 845 nm) and is compared to a series of blanks prepared similarly. According to PAM (1967), the molybdenum blue method has a working range between 0.01 and 0.06 mg of arsenic; the sensitivity of the procedure is 0.1 ppm.

Diethyldithiocarbamate Method - (For total arsenic) The arsine is absorbed in a solution of silver diethyldithiocarbamate. The color intensity is determined spectrophotometrically (at 52 nm) and the concentration of arsenic is determined from a standard curve. According to PAM (1967), the silver diethyldithiocarbamate procedure has a working range of between 1 and 15 µg of As_2O_3. The sensitivity of the method is estimated to be 0.01 ppm As_2O_3.

Dry-Ash Methods - Evans and Bandemer (1954) demonstrated that biological materials with magnesium nitrate can be ashed in an electric furnace without loss of arsenic. Stone (1967) modified this procedure to allow arsenic analysis in animal tissues at a sensitivity of less than 0.1 ppm.

Hudley and Underwood (1970) investigated a simple, sensitive, and reproducible procedure for the determination of total arsenic in composite food samples. The samples are dry-ashed in the presence of magnesium oxide and magnesium nitrate. Arsenic is then evolved from an acid solution as its hydride. The arsine is reacted with silver diethyldithiocarbamate to give a red complex that is measured spectrophotometrically. The absorbance of this complex is proportional to arsenic over a wide range of concentrations (1 to 20 µg arsenic). The method is sensitive to 0.05 ppm arsenic. The procedure of Hundley and Underwood utilized the dry-ash procedure of Stone. According to Hundley and Underwood, their method was comparable to the wet-ash procedure and colorimetric determination used as the "official method." However, they noted that the official method requires an average of 80 hr for the analysis of the 12 food categories specified in the total diet program; the same number of analyses may be accomplished in 20 to 24 hr using the method of Hundley and Underwood. Furthermore, a substantial improvement in recovery is obtained by this method.

Atomic Absorption Methods - There have been significant developments in the analysis of arsenic by atomic absorption methods. The basis of the new method is the generation of arsine by treatment of the arsenic sample with sodium borohydride. The arsine generated is introduced directly into the flame. The method has been recently described by Thompson and Thomerson (1974) and by Duncan and Parker (undated). The method apparently has not been used yet for organoarsenic pesticides, but it would appear suitable for both formulation and specific residue analyses. The organoarsenic pesticides would require initial conversion into arsenic oxide by conventional wet digestion or dry-ashing procedures, then reduction to arsine by aqueous sodium borohydride.

Thompson and Thomerson (1974) reported that the detection limit for arsenic is 0.8 ng/ml. In precision studies, these investigators observed that a concentration of 100 ng/ml in 10 separate measurements produced a relative standard deviation of 5.7%.

Duncan and Parker (undated) report a sensitivity of 0.1 ng/ml and an absolute sensitivity of 2 ng. In a check for accuracy, these investigators used NBS standard reference material SRM 1571 (orchard leaves) which is certified to contain 14 ± 2 µg/g of arsenic. Their results showed an analysis of 14.9 ±0.4 µg/g with a relative standard deviation (based on 5 determinations) of 2.6%.

Formulation Analysis - Only limited information is available concerning analysis of cacodylic acid formulations. However, any of the residue analysis methods for arsenic could probably be adapted for formulation analyses. They are summarized below:

AOAC Method for Arsenic in Sodium Cacodylate - Official Final Action - A method for the determination of arsenic in sodium cacodylate is described. The method involves a digestion of the sodium cacodylate sample with potassium sulfate, starch and sulfuric acid. The digested material is subsequently analyzed using the conventional iodometric procedure (AOAC 1970).

Four other methods, with Official Final Action status, provide analysis for total arsenic in pesticide formulations. However, the methods either specify that they are used for inorganic arsenate or arsenites, or only mention inorganic arsenicals. These methods are the hydrazine sulfate distillation method, the iodometric method, an ion exchange method, and a water-soluble arsenic method.

Potential Formulation Analysis Method - Carey (1968) proposed a formulation analysis method involving a fusion procedure in which the arsonate is decomposed to pentavalent arsenic by a potassium bromate-nitric acid solution. He tested the method on MSMA (commercial formulation), DSMA (technical grades), and several other arsenicals, including arsanilic acid, $H_2NC_6H_4AsO(OH)_2$. Thus, the method appears to be applicable to cacodylic acid. The fusion temperatures are preferably kept below 300°C. Color in the fusion mass indicated interferences; these can be removed using an ion exchange procedure. Carey (1968) presented actual results for each compound, but did not include an overall accuracy of the method.

Composition and Formulation

Technical grade cacodylic acid is 65% pure and contains sodium chloride (Martin 1971). Water is the principal solvent in cacodylic acid formulations. These usually contain a surfactant. Based upon patented production methods (Moyerman and Ehman 1965; Schanhals 1967), technical cacodylic acid also contains sodium sulfate, sodium chloride, methylarsonic acid, and arsenic acid. No information is available concerning the quantities of these impurities in commercially available formulations. Both the DSMA feed and the final product in the Ansul process are free of trivalent arsenic and have none of the garlic odor characteristic of cacodyl compounds, arsines, and arsine oxides. Analyses of the process on a bench scale (Ansul 1975) have shown that neither cacodyl oxide or arsines are present under the reaction conditions used by Ansul. (See equations 7, 8, 10, and 15, pp. 13, 15.) Field reports refer to garlic odors from treated forest sites after 48 hr (Wagner and Weswig 1974) but not from the formulated products themselves. According to Ansul (1975), it is also possible that reducing conditions at surfaces of metals, such as iron in storage vessels could produce traces of cacodyl oxide and a garlic odor. (See equation 22 and 35, pp. 27, 28.)

The formulation used as a tree killer is 50% cacodylic acid (6 lb/gal). Formulations are also available with sodium cacodylate and cacodylic acid as the minor herbicidal ingredients. (See subsection on Formulations, p. 110.)

Chemical Properties, Reactions, and Decomposition Processes

Acidic and Chemical Properties - Cacodylic acid is normally considered to be an acid, but it is actually an amphoteric electrolyte. Reported values of the ionization constant are presented in Table 1. Definitions for the letter designations are as follows:

pk_a Negative log of k_a

k_a For the equation $Me_2AsOOH + H_2O \longrightarrow Me_2AsOO^- + H_3O^+$,

$$k_a = \frac{[Me_2AsOO^-]\,[H_3O^+]}{[Me_2AsOOH]}$$

k_b For the equation $Me_2AsOOH + H_3O^+ \longrightarrow Me_2AsOOH \cdot H^+ + H_2O$,

$$k_b = \frac{[Me_2AsOOH \cdot H^+]}{[Me_2AsOOH]\,[H_3O^+]}$$

$K_B = \frac{k_h}{k_w}$, where

k_w = ionization constant of water = 1×10^{-14} at 24°C.

The pk_a value of Juillard and Simonet (1968) in Table 1 was that obtained in a series of determinations using water-methanol mixtures. Other pk_a values at various methanol concentrations were: 20%, 6.47; 40%, 6.77; 60%, 7.14; and 80%, 7.64.

According to Hantzsch (1904) (cited by Raiziss and Gavron 1923), conductivity measurements with cacodylic acid show that, when treated with an excess of caustic alkali, it does not react strictly as a monobasic acid, but partly as the sodium salt of a tribasic acid. He concluded that in the presence of one molecule of sodium hydroxide, the acid is monobasic, but with an excess of alkali it forms the molecular aggregate $Me_2As(OH)(ONa)_2$ so that the acid is capable of functioning in the tribasic form, $Me_2As(OH)_3$.

Plumel (1948) suggested the use of sodium cacodylate as a buffer for the pH range of 5.2 to 7.2 in experiments where salts of other weak acids cannot be used.

Table 1. IONIZATION CONSTANTS OF CACODYLIC ACID*

pk_a	k_a(°C)	k_b(25°C)	K_B	Reference
	4.2×10^{-7}(25)	3.4×10^{-13}**	34	a/
	6.4×10^{-7}(25)	3.2×10^{-13}**	32	d/
	7.5×10^{-7}(25)	5.1×10^{-13}**	51	b/
	5.66×10^{-7}(30)			c/
	5.33×10^{-7}(25)	3.73×10^{-13}	37.3	d/
	6.2×10^{-7}(5)			e/
6.26	5.5×10^{-7}(25)			f/
6.15	7.1×10^{-7}(24)			g/

* The ionization constants and related values are defined in the text of this report.

** Calculated by Midwest Research Institute (Kansas City, Missouri) using modern value of k_w, 1×10^{-14}. References cited used a value of 1.2×10^{-14}.

a/ Zawidzki (1903).
b/ Holmberg (1910).
c/ Morton (1928).
d/ Kilpatrick (1949).
e/ Dhar (1913).
f/ Juillard and Simonet (1968).
g/ Jacobson et al. (1972).

Because it is amphoteric, cacodylic acid will react with some acids; with hydrochloric acid it will form $Me_2AsO_2H \cdot HCl$. This compound crystallizes into leaflets which are readily dissociated into their constituents by water (Kaiziss and Gavron 1923). The structure of this product was examined by Simon and Schumann (1973). With hydrobromic acid the corresponding product is a very unstable, syrupy mass. The hydrofluoride corresponds to the formula $(Me_2AsO_2H \cdot HF)Me_2AsF_3$ (Raiziss and Gavron 1923). Moyermann and Ehman (1965) also reported that cacodylic acid reacts with nitric and sulfuric acids, but gave no details concerning reaction products.

Petit (1941) examined the interaction of hot, concentrated sulfuric acid with cacodylic acid and other arsenical compounds. The reaction of sulfuric acid with cacodylic acid was studied at temperatures ranging from 190 to 315°C. The complex reaction is apparently complete within 10 min at 315°C, but is not complete after 5 hr at 190°C. Petit was primarily interested in the mechanism of this reaction; he states that the reaction proceeds as shown in the following equations.

$$Me_2AsO_2H + H_2SO_4 \longrightarrow Me_2As(OH)_2SO_4H$$

$$Me_2As(OH)_2SO_4H \longrightarrow MeSO_4H + MeAs(OH)_2$$

$$MeAs(OH)_2 + H_2SO_4 \longrightarrow MeAsO(OH)_2 + SO_2 + H_2O$$

$$MeAs(OH)_2SO_4H \longrightarrow MeSO_4H + As(OH)_3$$

Ahrens and Maass (1968) determined the rate constants for proton transfer between various acceptor ions and donor molecules. For the reaction:

$$\underset{\text{Acetate}}{C_2H_3O_2^-} + \underset{\text{Cacodylic acid}}{Me_2AsO_2H} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \underset{\text{Acetic acid}}{C_2H_3O_2H} + \underset{\text{Cacodylate}}{Me_2AsO_2^-}$$

at an ionic strength of 1 M and 20°C, k_1 was 6.2×10^7 $\ell mol^{-1} sec^{-1}$ and k_2 was 1.7×10^9 $\ell mol^{-1} sec^{-1}$.

Clifford (1959) determined an electronegativity value for a large number of ions. For the cacodylate ion, $Me_2AsO_2^-$, the electronegativity was 3.15 (relative scale, 0 to 4).

For possible applications in analysis, Pietsch (1958) determined the pH at which various metal ions began to precipitate with cacodylic acid at 0.02 molal concentration. The results are shown in Table 2.

Table 2. pH AT WHICH METALLIC IONS ARE PRECIPITATED WITH CACODYLIC ACID

pH	Ion precipitated
1	Sn^{+4}
2	VO_2^{+2}, Bi^{+3}
2.5	Fe^{+3}
3	Hg^{+}
4	Hg^{+2}
5	Zr^{+4}, Sn^{+2}, Ti^{+4}, Cr^{+3}
6	Pb^{+2}, Be^{+2}, Y^{+3}, La^{+3}, Mn^{+2}, Cu^{+2}, Al^{+3}
6.5	Fe^{+2}, Ni^{+2}, Zn^{+2}
7	Ce^{+3}, Pd^{+4}
7.5	Co^{+2}, Cd^{+2}, In^{+3}
8	Mg^{+2}, Th^{+4}
8.5	Ca^{+2}
10	Sr^{+2}, Ba^{+2}

Metal ions not precipitated were: V^{+5}, Cr^{+6}, Mo^{+6}, W^{+6}, Rv^{+3}, Rh^{+3}, In^{+4}, Pt^{+4}, Av^{+3}, Tl^{+}.

Source: Adapted from Pietsch (1958).

Oxidation and Reduction Reactions - Cacodylic acid is very stable toward oxidizing agents. Reports indicate that cacodylic acid is not decomposed by the action of fuming nitric acid, aqua regia, or potassium permanganate, even upon heating (LaCoste 1881, cited by Raiziss and Gavron 1923). Cacodylic acid is not oxidized by bromine water (Braman and Foreback 1973). However, as discussed in the Analytical Methods subsection of this report, it is oxidized to As_2O_5 by fuming nitric acid in the presence of concentrated sulfuric acid. When electrolyzed in alkaline solution, cacodylic acid is also oxidized to arsenic acid [H_3AsO_4 or $AsO(OH)_3$] (Fichter and Elkind 1916, cited by Raiziss and Gavron 1923).

Cacodylic acid is also unaffected by sulfurous acid, oxalic acid, ferrous sulfate, nascent hydrogen or other milder reducing agents (Raiziss and Gavron 1923). Noller (1957), however, reported that sodium dimethylarsinate is reduced by sulfurous acid to give cacodyl oxide. The reported reduction reactions of cacodylic acid are shown (in unbalanced equation form) in Table 3.

Braman and Foreback (1973) reported that cacodylic acid is reduced to dimethylarsine, Me_2AsH, by sodium borohydride at pH 1 to 2. According to the authors, the pH requirement indicates that the acid must be in the undissociated form before it can be reduced to the arsine.

Reactions of Cacodylic Acid and Sodium Cacodylate to Form Other Salts - Cacodylic acid and sodium cacodylate react with many substances to form a variety of salts. These salts and methods for their preparation are presented in Table 4. Raiziss and Gavron (1923) also reported that cacodylic acid salts of lithium, barium, magnesium, iron, strychnine, codeine, and antipyrine have been prepared.

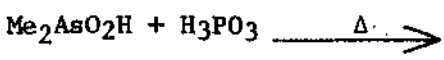
Other Reactions - Jacobson et al. (1972) noted that cacodylic acid is often used with an appropriate cation to buffer enzyme-catalyzed reactions. They investigated the interaction of cacodylic acid with thiols, which are commonly used in enzyme-catalyzed reactions. Although they did not determine the structure of any of the products formed, they concluded that cacodylic acid and thiols do react. Compounds studied included 2-mercaptoethanol, cysteine, glutathione and dithiothreitol. The authors indicated that the reaction was extremely complex, but concluded that more than one thiol group reacts with each molecule of cacodylic acid.

Heinemann (1919) reported that, at 120°C, the acid reacts with easily-meltable condensation products of phenols and formaldehyde, forming resinous substances in which the arsenic is held in an esterlike combination. These form water-soluble salts with alkalis, and are soluble in the same solvents as the parent phenolic condensation compounds, upon which their melting points are also dependent.

According to Moyermann and Ehman (1965) arsinic acids (which would include cacodylic acid) form esters with alcohols and organic acid anhydrides. Levskaya and Kolomiets (1967) also studied the esterification of arsonic acids. When

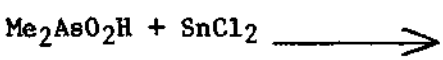
Table 3. REDUCTION REACTIONS OF CACODYLIC ACID

(Equations are not balanced)



(22) Source

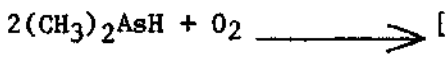
Phosphorous acid — Cacodyl oxide — a,b/



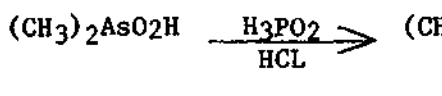
(23)

Stannous chloride — Dimethyl-chloroarsine — a,b/

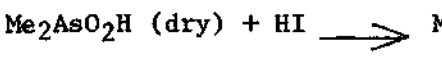
(24) a,b/



(25) a,b/

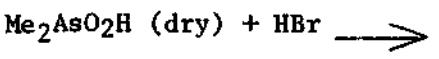


(26) a,b/



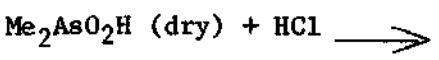
(27)

Dimethyliodoarsine — a,b/



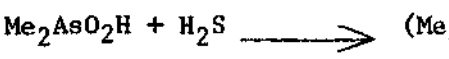
(28)

Dimethylbromoarsine — b/



(29)

Methyldi chloroarsine — Methyl chloride — b/



(30)

Cacodyl sulfide — b/

Table 3. (Continued)

		Source
$Me_2AsO_2H + H_3PO_3$ in HCl $\longrightarrow$ Me_2AsCl	(31)	c/
$Me_2AsO_2H + H_3PO_3$ in HBr $\longrightarrow$ Me_2AsBr	(32)	c/
$Me_2AsO_2H + SO_2$ in H_2SO_4 in presence of KI $\longrightarrow$ Me_2AsI	(33)	c/
$Me_2AsO_2H + SO_2 + HCl \xrightarrow{KI} Me_2AsI$	(34)	d/
$2\ Me_2AsO_2Na + 2\ H_2SO_3 \longrightarrow (Me_2As)_2O + H_2O + 2\ NaHSO_4$ (cacodyl oxide)	(35)	e/
$3\ Me_2AsO_2H + 4PCl_3 \longrightarrow 3\ Me_2AsCl + 3\ POCl_3 + H_3PO_2$	(36)	f/
$Me_2AsO_2H + 2\ Zn + 4HCl \xrightarrow[40\text{-}45°]{N_2\ atm.} Me_2AsH + 2\ ZnCl_2 + 2H_2O$	(37)	g/

a/ Fichter and Elkind (1916).
b/ Raiziss and Gavron (1923).
c/ van der Kelen and Herman (1956).
d/ Feltham et al. (1967).
e/ Noller (1957).
f/ Laughlin (1965).
g/ Feltham and Silverthorn (1967).

Table 4. REACTIONS OF CACODYLIC ACID OR SODIUM CACODYLATE

Product	Starting materials	Conditions, type of reaction or nature of product	Reference
Me_2AsO_2Ag	Acid and Ag_2O or Ag_2CO_3	Dissolve pure oxide or carbonate in acid; forms long needles which are soluble in water and darken in sunlight. Product reacts with free acid to form $Me_2AsO_2Ag \cdot 2Me_2AsO_2H$	a,b/
$(Me_2AsO_2)_2Hg$	Acid and freshly precipitated Hg	Dissolve HgO in an excess of a concentrated solution of the acid. Crystallizes in fine white needles which yield mercury when heated.	a,b/
$(Me_2AsO_2)_2Cu \cdot 7CuCl_2$	Alcoholic solutions of acid and $CuCl_2$	Mix solutions; shiny green sediment forms at first which becomes granular on boiling. Soluble in water. Decomposes on heating to yield cacodyl, copper chloride, copper arsenite, arsenic, and carbon.	a,b/
$(MeAsO_2)_3Bi \cdot 8H_2O$ Bismuth cacodylate	Strong, hot, saturated solution of acid with Bi_2O_3	Product deposits on cooling, m.p. 82°, 21% soluble in H_2O at 12°, soluble in alcohol and glycerol.	c/ e/
$Zn(Me_2AsO_2)_2$ and zinc cacodylate	Acid and Zn		b/
$(Me_2As)_2O$ cacodyl oxide			
$S{=}CNHC_3H_5 \cdot Me_2AsO_2H$ NH_2 Thiosinamine cacodylate	Acid and thiosinamine $CH_2CHCH_2NHCSNH_2$	Product is a crystalline compound, m.p. 74°; readily soluble in water or alcohol.	b/
Me_2AsCl_3 Cacodyl trichloride	Acid and PCl_5		b

Me = Methyl group (CH_3)
Acid = Cacodylic acid = Me_2AsO_2H
Salt = Sodium cacodylate = Me_2AsO_2Na

Table 4. (Continued)

Product	Starting materials	Conditions, type of reaction or nature of product	Reference
$Me_2AsO_2Ag \cdot AgNO_3$	Salt and $AgNO_3$	Double decomposition.	d/
Me_2AsO_2Ag Silver cacodylate	Wet Ag_2O into 88% aq. acid	After 12 hr, add 3 vol of C_2H_5OH, filter off first crop of crystals after 24 hr.	d/
$Zn(Me_2AsO_2)_2 \cdot 7H_2O$	Acid, ZnO, and water	Septahydrate formed when evaporated at 15°.	e/
$Zn(Me_2AsO_2)_2 \cdot H_2O$		Monohydrate formed when crystallized after evaporating the solution to half its volume at 50°, under 70 mm pressure.	
$(Me_2AsO_2)_2Ca$	Acid and $Ca(OH)_2$	Mono- and nona-hydrates, anhydrous precipitate.	f/
$(Me_2AsO_2)_2Sr$	Acid and $Sr(OH)_2$	Mono-, tri-, and tridecahydrates.	
$(Me_2AsO_2)Cd \cdot 10H_2O$	Acid + $Cd(OH)_2$	Fine, silky, colorless crystals separate. Various hydrated forms can form under different conditions of temperature and pressure.	g/
$(Me_2AsO_2)_2SnMe_2$	Acid + Me_2SnCl_2	Product soluble in water and acids. Decomposes at 330°.	h/
$Me_2AsO_2Pb(C_6H_5)_3$	Salt trihydrate + $(C_6H_5)PbCl$	Refluxed in MeOH, 73% yield.	i/
$Me_2AsO_2PbCl(C_6H_5)_2$	Salt trihydrate + $(C_6H_5)_2PbCl_2$	Refluxed in dimethylformamide, 77% yield.	i/

Table 4. (Continued)

Product	Starting materials	Conditions, type of reaction or nature of product	Reference
Me_3AsS (I), $(Me_2As)_2S$ (II), and Me_2AsSO (III)	Acid and CS_2	Heated at 150° for 18 hr. Crystallization from hexane gave I (11% yield). Removal of solvent and distillation gave II (51% yield) and III (25% yield).	j/
$(Me_2AsO_2)_2Zn$	Acid + Zn SO_4	Reaction in ethyl alcohol, becomes polymerized in C_6H_6	k/

a/ Bunsen (1843).
b/ Raiziss and Gavron (1923).
c/ Clausmann (1923).
d/ Zappi and Manini (1929).
e/ Tiollais and Perdreau (1937).
f/ Tiollais (1936).
g/ Tiollais et al. (1939).
h/ Chamberland and MacDiarmid (1961).
i/ Henry (1962).
j/ Reichle (1962).
k/ Ciana (1967).

Me_2AsO_2H was heated with butyl alcohol (BuOH) and refluxed in C_6H_6, the ester, Me_2AsO_2Bu, was formed.

Coates and Mukherjee (1964) treated trimethylgallium (Me_3Ga), with cacodylic acid dissolved in benzene. The product was dimethylgallium dimethylarsinate, $(Me_2AsO_2GaMe_2)_2$. The melting point of this product was 144 to 145°C after sublimation at 110°C and 0.01 mm pressure.

Occurrences of Residues in Food and Feed Commodities

FDA monitors pesticide residues in the nation's food supply through 2 programs. One program, commonly known as the "total diet program," involves the examination of food ready to be eaten. This investigation measures the amount of pesticide chemicals found in a high-consumption varied diet. The samples are collected in retail markets and prepared for consumption before analysis. The other program involves the examination of large numbers of samples, obtained when lots are shipped in interstate commerce, to determine compliance with tolerances. These analyses are complemented by observation and investigations in the growing areas to determine the actual practices being followed in the use of pesticide chemicals.

A majority of the samples collected in these programs are categorized as "objective" samples, which are not considered to contain excessive residues or misused pesticide chemicals. All samples of imported foods and fish are categorized as "objective" samples even though there may be reason to believe excessive residues may be found on successive lots of these food categories.

Market-basket samples for the total diet studies are purchased from retail stores, bimonthly, in 5 regions of the United States. A shopping guide listing 117 foods for all regions is used, but all foods are represented differently because of differences in regional dietary patterns. The food items are separated into 12 classes of similar foods (including dairy products; meat, fish and poultry; legume vegetables; and garden fruits) for more reliable analysis and to minimize the dilution factor. Each class in each sample is a "composite." The food items and the proportion of each used in the study were developed in cooperation with the Department of Agriculture's Household Economics Research Division and represents the high consumption level of a 16- to 19-year old male. Each sample represents a 2-week supply of food.

Surveillance samples are generally collected at major harvesting and distribution centers throughout the United States and examined in 16 FDA district laboratories. Some samples may be collected in the fields immediately prior to harvest. Surveillance samples are not obtained in retail markets. Samples of imported foods are collected when offered for entry into the United States.

The residue analysis currently being used by FDA does not detect cacodylic acid as an individual chemical. Residue analyses are made for total arsenic in the form of As_2O_3, but the analytical method does not distinguish between naturally occurring arsenic or arsenic resulting from the presence of any of the arsenical pesticides.

Table 5 presents the results of total diet program for a 6-yr period. The number of composites which were found to contain arsenic and the concentration ranges (ppm) are illustrated. Although the FDA has continued the analytical program, results have not been reported since the 1969 to 1970 study was published in 1972.

The information in Table 5 was used to calculate the daily intake of arsenic shown in Table 6. Duggan and Corneliussen (1972) drew the following conclusion for the 6-yr period:

> The incidence and levels of As_2O_3 have remained low during the 6 years of this study. While there is a wide variation in the actual annual range, the differences generally are due to higher values for a few samples examined during a particular year. There is a natural low-level background of arsenic in foods, and the values reported during this period are within or slightly above the natural background. The dietary intake of arsenic from pesticide use does not appear to be significant.

Acceptable Daily Intake

The acceptable daily intake (ADI) is defined as the daily intake which, during an entire lifetime, appears to be without appreciable risk on the basis of all known facts at the time of evaluation (Lu 1973). It is expressed in milligrams of the chemical per kilogram of body weight (mg/kg).

The ADI for pesticides is established jointly by the Food and Agricultural Organization Committee on Pesticides in Agriculture and the World Health Organization Expert Committee on Pesticide Residues. However, an ADI for cacodylic acid (or for arsenic) has not yet been established.

Tolerances

Section 408 of the Food, Drug and Cosmetic Act, as amended, gives procedures for establishing U.S. tolerances for pesticide chemicals on raw agricultural commodities. Section 409 applies to food additives, including pesticide chemicals on processed foods. Tolerances for cacodylic acid, calculated as As_2O_3, are publisehd in the Code of Federal Regulations (Section 180.311). They are: 2.8 ppm in or on cottonseed; 1.4 ppm in the kidney and liver of cattle; and 0.7 ppm in the meat, fat, and meat by-products (except kidney and liver) of cattle.

Table 5. ARSENIC IN TOTAL-DIET SAMPLES[a/]

Year of study	1[b/]	2[c/]	3[d/]	4[e/]	5[f/]	6[g/]
Date of study[h/]	1964-1965	1965-1966	1966-1967	1967-1968	1968-1969	1969-1970
Number of composites	18	28	30	30	30	30
Dairy products	--	--	i/	i/	i/	i/
Meat, fish and poultry	1 (0.12)	5 (0.1-0.5)	9 (0.1-0.5)	16 (0.1-0.6)	15 (0.1-1.0)	14 (0.1-2.6)
Grain and cereal products	1 (0.10)	1 (0.1)	i/	5 (0.1-0.8)	7 (0.1-0.2)	--
Potatoes	1 (4.7)	--	--	8 (0.1-0.2)	3 (0.1)	2 (0.1)
Leafy vegetables	--	--	1	6 (0.1-0.3)	4 (0.1)	--
Legume vegetables	1 (0.11)	--	2 (max. 0.18)	1 (0.2)	3 (0.1)	--
Root vegetables	1 (0.10)	1 (0.1)	3 (max. 0.16)	2 (0.1)	3 (0.1)	1 (0.2)
Garden fruits	--	1 (0.1)	--	4 (max. 0.2)	4 (0.1)	1 (0.2)
Fruits	1 (0.18)	--	3 (0.1-0.2)	5 (0.1-0.5)	5 (0.1)	1 (0.2)
Oils, fats and shortening	--	--	2 (0.1)	3 (0.1-0.4)	2 (0.1)	--
Sugar and adjuncts	--	1 (0.1)	4 (max. 0.15)	6 (0.1)	5 (0.1)	--
Beverages	--	--	--	5 (0.1-0.2)	3 (0.1)	--
Totals (concentration ranges, ppm)	6 (0.1-4.7)	10 (0.1-0.5)	33 (0.1-0.4)	65 (0.1-0.8)	57 (0.1-1.0)	21 (0.1-2.6)

a/ The values are the number of composites which were found to contain arsenic. The concentration, range or maximum value of arsenic (in ppm) is given in parenthesis. The absence of a value in parenthesis indicates that this information was not available. A dash indicates that none of samples contained arsenic.

b/ Duggan et al. (January 7, 1966).

c/ Duggan et al. (September, 1967).

d/ Martin and Duggin (March 1968).

e/ Corneliussen (March 1969).

f/ Corneliussen (December 1970).

g/ Corneliussen (March 1972).

h/ June of first year to April of second year, samples taken bimonthly.

i/ Arsenic was stated to be present, but neither the number of composites nor the concentration range was given.

Table 6. DAILY INTAKE OF ARSENIC RESIDUES[a/]

Date of study[b/]	1964-1965[c/]	1965-1966[c/]	1966-1967[d/]	1967-1968[d/]	1968-1969[e/]	1969-1970[e/]
Dairy products	--	--	< .001	0.008	0.005	0.006
Meat, fish and poultry	< .001	0.003	0.004	0.045	0.034	0.048
Grains and cereals	0.002	0.001	0.004	0.029	0.011	--
Potatoes	0.063	--	0.003	0.007	0.002	0.001
Leafy vegetables	--	--	0.001	0.002	0.001	--
Legume vegetables	0.001	--	0.001	0.001	0.001	--
Root vegetables	0.001	< .001	0.001	0.001	< .001	< .001
Garden fruits	--	0.001	< .001	0.004	0.001	0.001
Fruits	0.002	--	0.004	0.012	0.004	0.001
Oils, fats and shortening	--	--	0.004	0.002	< .001	--
Sugar and adjuncts	--	0.001	0.001	0.002	0.001	--
Beverages	--	--	0.010	0.024	0.015	--
Total daily intake	--	--	0.033	0.137	0.075	0.057

a/ Expressed in milligrams of As_2O_3/day. Includes naturally occurring amounts. A dash indicates that the food class contained no detectable quantities of arsenic.
b/ Samples collected from June of first year to April of second year.
c/ Duggan and Weatherwax (September 1, 1967).
d/ Duggan and Lipscomb (1969).
e/ Duggan and Corneliussen (1972).

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PART II. INITIAL SCIENTIFIC REVIEW

SUBPART B. PHARMACOLOGY AND TOXICOLOGY

CONTENTS

This section reviews data on the acute, subacute and chronic toxicity of cacodylic acid in laboratory and domestic animals. Symptomology and Pathology in animals and man is discussed. The metabolism of cacodylic acid is also reviewed. Mutagenic and oncogenic effects are presented. The section summarizes rather than interprets data reviewed.

Acute, Subacute, and Chronic Toxicity

Toxicity to Laboratory Animals -

Acute Oral Toxicity - Rats - Male albino rats were tested for toxic susceptibility to a herbicide formulation that contained 77% cacodylic acid. The material was administered by stomach tube to rats that weighed 200 to 300 g. The animals were observed for 14 days after treatment. An LD_{50} of 700 mg/kg was calculated from the results of this test (Nees 1960).

The toxicity to rats of a herbicide composed of 61.29% cacodylic acid as the active ingredient has also been reported. Sprague-Dawley albino rats were used in this study. Six dose levels were administered to male and female rats in test groups of 8 animals each (4 males and 4 females for each dose). The herbicide was given to the rats as a 20% aqueous solution administered directly to the stomach by a syringe. The animals were observed for 14 days following treatment. The LD_{50} for males was 1.4 g/kg (1.15 to 1.71) and for females was 1.28 g/kg (0.93 to 1.75).

Within 1 hr, some animals developed diarrhea, which continued for 24 to 48 hr; after 48 hr, survivors were all normal. Death occurred in susceptible animals within 24 hr. Necropsy did not reveal any gross pathological changes (Kay 1961).

An approximate LD_{50} was determined for a cacodylic acid herbicide (Ansar® 160) to rats. The material tested contained 24.78% sodium cacodylate and 8.76% cacodylic acid (cacodylic acid equivalent = 30.13%). Adult albino rats (200 to 300 g Sprague-Dawley strain) were used in the tests. Their reactions, following treatment by intubation, were observed for 2 weeks. An approximate oral LD_{50} of 3.2 ml/kg was calculated from the mortality data. Two animals were used at each dose level (Nees 1965).

A herbicide formulation containing 25.1% cacodylic acid was tested for toxicity to young albino rats (150 g). Four males and 4 females were used in each group at each dosage level. The material was given by intubation and the animals were observed for 14 days following treatment. An acute oral LD_{50} of 2.6 g/kg (2.1 to 3.2) was calculated from the mortality data. An $LD_{0.01}$ of 0.92 g/kg and an $LD_{99.99}$ of 7.4 g/kg were also reported.

A slight loss of body weight was noted during the surveillance period. Necropsy of dead animals did not reveal any gross pathological alteration in any tissue or organ that could be attributed to treatment (Palazzolo 1965).

Charles River strain rats were given doses of a formulation containing 27.38% sodium cacodylate and 4.67% cacodylic acid (32.05% cacodylic acid equivalents). The LD_{50} value was found to be 2,480 mg/kg, with standard deviation of 412.0 mg/kg. Necropsy examination of animals that died showed hemorrhaging in the gastrointestinal tract. No gross pathology was seen in animals sacrificed after the 14-day observation period (Industrial Bio-Test Laboratories 1975).

A summary of the acute oral toxicity data of various cacodylic acid formulations to rats is given in Table 7.

Table 7. ACUTE ORAL TOXICITY TO RATS

Formulation: % cacodylic acid	Sex	LD_{50} (95% CI) (g/kg)	$LD_{0.01}$ (g/kg)	$LD_{99.99}$ (g/kg)	Reference
25.1	M and F	2.6 (2.1-3.2)	0.92	7.4	Palazzolo (1965)
32.05	M and F	2.48 (4.2.0) approximately	----	---	Industrial Bio-Test Laboratories (1975)
30.13	M and F	3.2 ml	----	---	Nees (1963)
77.0	M	0.70	----	---	Nees (1960)
61.29	M	1.4 (1.15-1.71)	0.82	2.41	Kay (1961)
61.29	F	1.28 (0.93-1.75)	0.38	4.3	Kay (1961)
61.29	M and F	1.35 (1.11-1.64)	0.48	3.9	Kay (1961)

Subacute Oral Toxicity - Rats - Weanling rats (Sprague-Dawley strain, 40 to 50 g) were fed a basal ration containing a herbicide that consisted of 77% cacodylic acid. Three groups of 10 rats each were diet-fed cacodylic acid at levels equal to 40, 20 or 10% of the estimated LD_{50} (0.7 g/kg). A control group was fed only basil ration. Feeding was continued daily for 20 days. At the end of the feeding period, all animals were sacrificed for histological examination. The tissues examined were the cerebrum, cerebellum, heart, lungs, liver, spleen, kidney, adrenals, pancreas, stomach, small bowel, large bowel, testes, urinary bladder, and bone.

Changes in tissues were not seen in animals fed at the 20% or lower level or in controls. There was some evidence in animals fed at 40% of the LD_{50} of reduced activity of spermatogonia cells and some atrophic changes in the seminiferous tubules (Nees 1960).

Subacute (Dietary) Toxicity - Rats - Weanling rats (Sprague-Dawley strain) were given cacodylic acid at dietary levels of 3, 15, 30 and 100 ppm for 30 days. Both male and female rats were treated at each of 6 dietary levels; a control group fed an untreated diet was also included.

After 90 days of feeding, urinalysis and hematological studies were done on 5 animals of each group. All animals were sacrificed for gross pathology. A comparison of the responses of each group of animals indicated that there were no significant differences in body weight or food consumption between the controls and the test animals. Variations in the results of the hematological examinations and the urinalysis could not be attributed to cacodylic acid treatment. There were no differences between treated and control animals in organ weights. The histological alterations that were observed were minimal and were reported to be of a type generally found in laboratory rats of the age of those tested (Nees 1968).

Acute Dermal Toxicity - Rabbits - A group of 2 male and 2 female albino rabbits had shaved skin of their backs exposed to 3,000 mg/kg Bolls Eye (32.05% cacodylic acid) for 24 hr. The animals were wrapped with impervious plastic and tape to prevent oral ingestion of test material. After 24 hr, the plastic tape and test material were removed.

An acute dermal LD_{50} value of greater than 3000 mg/kg was estimated. All rabbits lost a slight amount of weight during the first week after exposure, but they showed normal weight gain during the remainder of the 14-day observation period. No toxic signs were noted, and skin changes were seen as moderate edema at 24 hr and slight desquamation at days 7 and 14. With the exception of skin changes, there were no other pathological changes observed (Industrial Bio-Test Laboratories 1975).

Eye Irritation - Rabbits - A 0.1 ml amount of undiluted Bolls Eye (32.05% cacodylic acid equivalent) was instilled into the conjunctive sac of the right eye of each albino New Zealand strain rabbit tested. The left eye was used as a scoring control. Injuries and their persistance in the conjunctiva, cornea, and iris were used to score, with 110 representing maximum irritation and 0 representing no irritation. Classifications into corrosive, irritating, and nonirritating were made, and the Bolls Eye formulation was considered nonirritating (Industrial Bio-Test Laboratories 1975).

In another study, New Zealand albino rabbits were used in eye irritation tests in which test animals were constrained during the test period so they could not rub their eyes. A 0.1 ml portion of a formulation which contained

77% cacodylic acid and 22.8% sodium chloride was placed in one eye of each test animal. The untreated eye was used as a control. Six rabbits were treated; 3 had the eye washed with 20 ml of water 2 to 4 hr after introduction of the herbicide. Under test conditions, the herbicide formulation containing 77% cacodylic acid had an ocular irritation score of 2.0. The author concluded that a score of 2.0 placed the material in the "essentially nonirritating" category (Nees 1960).

Skin Irritation - Rabbits - In one study, 4 areas were clipped on the backs of albino rabbits (10 cm apart) and used as test sites for determining dermal irritation. Two areas on each rabbit were left intact and 2 were abraded. A formulation containing 77% cacodylic acid was applied to 6 immobilized rabbits, and the treated areas were covered for 24 hr. Under test conditions, the herbicide had a primary irritation index of 0.3 and, at this level, was considered "essentially nonirritating" to the skin (Nees 1960).

Primary Skin Irritation - Rabbits - Albino New Zealand strain rabbits were used to determine the primary skin irritation resulting from exposure of clipped intact and abraded skin to Bolls Eye (32.05% of cacodylic acid equivalent). A 0.5 ml amount of undilute Bolls Eye was applied to each test site, and the site was immediately occluded by a 2 in square gauze patch secured by masking tape. The rabbit's trunk was then wrapped in plastic. The tests were observed at 24 and 72 hr. The study demonstrated that Bolls Eye is nonirritating (Industrail Bio-Test Laboratories 1975).

Subacute Dermal Toxicity - Rabbits - Adult male albino rabbits (2 to 3 kg) were used to test whether or not a cacodylic acid herbicide caused skin irritation, sensitization, or mortality. Two animals were tested at each dosage level under 2 conditions: normal skin (clipped) and abraded skin (clipped). A herbicide formulation containing 77% cacodylic acid was used in the test, and it was applied to the skin as an aqueous suspension by inunction. Exposure was continued for 12 hr. Each animal was treated 5 days a week for 3 weeks, and observations were carried out for 2 weeks following the final treatment.

Sensitization was tested by 1 application of the herbicide to new skin areas of survivors after 10 to 14 days. Necropsies were performed on all dead animals. Two tests were run in this series, 1 at dose levels of 3.9, 6.0, and 9.4 g/kg; and the other at 1.0, 1.6, and 2.5 g/kg.

The clinical signs of intoxication noted were: rapid loss of conditioning, diarrhea, and mild hyperemia on application areas on intact skin and severe hyperemia with apparent cyanosis on margins of abrasions.

A summary of the mortality associated with the various doses is shown in Table 8.

Table 8. DERMAL TOXICITY (MORTALITY) OF A HERBICIDE (77% CACODYLIC ACID) TO RABBITS

Condition of skin	Dose (g/kg) 1.0	1.6	2.5	3.9	6.0	9.4
Normal	0/1[a]	0/1[a]	1/1 (13)[b]	1/1 (13)	1/1 (5)	1/1 (4)
Abraded	1/1 (5)	1/1 (3)	1/1 (2)	1/1 (9)	1/1 (5)	1/1 (2)

a/ Weight loss noted.
b/ Figures in parentheses are days of death.

Necropsy indicated that fluid accumulation in the intestinal tract was the most commonly found sign of intoxication. The spleen often showed vascular congestion, and there was distention of the large bowel in many instances. Animals that died from the heavier dosage had a heavy inflammatory infiltrate of a mixed type directly beneath the epithelium and parenchymatous degeneration deep in subcutaneous tissue. No evidence was obtained for sensitization (Nees 1960).

Subacute (Dietary) Toxicity - Dogs - Thirty-two beagle puppies were divided into 4 groups of 4 males and 4 females each. One group was used for controls, and the other 3 were given dietary levels of cacodylic acid (100%) of 3, 15, or 30 ppm. Body weights were recorded weekly. Kidney and liver function tests and urinalyses were conducted after 90 days feeding.

Mortality was not noted in any of the test groups. No differences in body weights at 30 ppm were observed with the exception of a slower weight gain for females. Hematological differences between treatment and control groups were not detected, and there were no real differences apparent between control and treated animals. Some lesions were noted in brain, heart, liver, kidney, spleen, intestine, and other organs, but the lesions were randomly scattered in both control and test animals and were not considered to be due to diet supplementation with cacodylic acid (Derse 1968).

Toxicity to Domestic Animals -

Acute Toxicity - Cattle - Holstein dairy calves were treated with acute oral doses of Ansar 160 (24.78% sodium cacodylate and 8.76% cacodylic acid) and Ansar 560 (22.73% sodium cacodylate and 3.88% cacodylic acid) to determine minimum lethal dose or LD_{50} values. One animal per dose was used, and treatment levels were increased until lethal dose was found. Three additional calves were treated

with he "minimum lethal dose," and signs of toxicity were noted. Dosages were determined on the basis of milligram elemental arsenic per kilogram body weight.

The value found for Ansar 160 was 254.0 mg/kg and 200.0 mg/kg for Ansar 560. Treated calves had diarrhea accompanied by general listlessness and inanition. Signs appeared 24 to 36 hr after treatment and persisted from 4 to 5 days in the surviving animals (The Ansul Company undated).

Subacute Oral Toxicity - Cattle - Two cows were fed for 60 days on cottonseed meal ration containing 10 ppm of cacodylic acid. At a feeding rate of 5.4 lb of cotton seed meal per day, the animals received a daily intake of 24.5 mg cacodylic acid. At this level of intake, mortality did not occur. When the animals were slaughtered after 60 days feeding, tissue levels of arsenic were low, with the principal sites of storage being the liver, spleen, and pancreas. Cacodylic acid residues were not detected in the milk. Excretion of cacodylic acid was primarily by urine (75 to 80%) and a balance between intake and output was established after 30 days feeding. (Peoples 1963).

Cattle were also treated by capsule or by drench with a commercial herbicide formulation (26.5% cacodylic acid) at dosages from 5 to 50 mg/kg body weight. Doses were given daily up to 10 days. When dosing was done by capsule, no ill effects were noted up to the maximum dose given (25 mg/kg). When dosing was accomplished by drench, an irritation effect was reported for the 10 mg/kg level after the second dose (unrelated to toxicity action) and a 5% weight loss occurred after 10 doses. At 25 mg/kg, the drench resulted in apparent poisoning after 8 doses; however, the animal survived 10 doses. Drenching at 50 mg/kg resulted in obvious poisoning after the first dose, and death occurred 4 days after the seventh dose (U.S. Department of Agriculture 1972).

In another study, 6 Holstein dairy calves (2 per dose) were fed doses of 200.3, 400.6, and 1201.8 mg/kg Ansar 560 (22.73% sodim cacodylate and 3.88% cacodylic acid) for 7 days. Dose levels corresponded to 10%, 20%, and 60% of the estimated LD_{50} value and are expressed on the basis of mg of product per kg of body weight.

All calves fed cacodylic acid showed decreased feed consumption. Calves given the 10% diet continued eating some of their daily ration throughout the 7 day test. Calves on the 20% diet refused their feed after the fifth day; those on the 60% diet refused feed after the fourth day. One calf given the 60% diet had diarrhea, and the other in the group died. The authors attributed the death to "the rapidity of feed consumption." When the calves were returned to pretreatment diets their feed consumption rapidly returned to a normal daily rate (The Ansul Company undated).

Another study is considered in the Fate and Significance in the Environment section on the exposure of cattle grazing in forest areas treated with MSMA and other arsenical herbicides.

Subacute Oral Toxicity - Sheep - Mortality or poisoning was not observed in sheep when dosed from 10 to 25 mg/kg (26.5% cacodylic acid) whether the dose was given by capsule or drench. Treatment by capsule at 50 mg/kg, however, resulted in an apparent poisoning in one animal after 3 daily doses. The animal survived 10 doses but exhibited a 21% weight loss. A second sheep dosed at 50 mg/kg by capsule also survived 10 doses but suffered a 22% weight loss. Signs of poisoning were observed after the second dose (U.S. Department of Agriculture 1972).

Subacute Oral Toxicity - Chickens - Three groups of 23-week-old white leghorn chickens (7 females and 3 males per group) were fed cacodylic acid in a basal diet for 10 weeks. Three levels of cacodylic acid were tested: (a) 0.3 ppm dietary arsenic, (b) 3.0 ppm dietary arsenic, and (c) 30 ppm dietary arsenic. After 1 month of feeding, eggs were collected from each hen for a 3-day period; after 2 months, additional eggs were gathered. After 10 weeks, 3 females and 2 males from each group were sacrificed, and selected tissues were analyzed for arsenic. The animals not sacrificed were then placed on a cacodylic-free diet for 7 days; these animals were sacrificed after the 7-day recovery period, and selected tissues (fat, abdominal; liver, all; muscle, 50% white and 50% dark; and kidney) were analyzed for arsenic content. Eggs from hens fed at 30 ppm dietary arsenic contained 0.22 ppm at 1 month and 0.23 ppm at the end of the second month (Bodden 1968).

A commercial herbicide containing 26.5% cacodylic acid was administered (by pipette) to chickens in doses ranging from 50 to 500 mg/kg body weight. Ten daily doses were given; 5 chickens were used at each dose level. During the time this experiment was in progress, the untreated controls exhibited a 53% weight gain. The chickens treated with up to 100 mg/kg appeared to match the gain of the controls. The 2 groups treated at 175 and 250 mg/kg had a lowered weight gain (33 and 36%, respectively) and the group treated at 500 mg/kg exhibited the lowest gain of all (13%). While weight gain was affected, there were no mortalities, even at the highest treatment level (USDA 1972).

Toxicity to Man - No specific information was found on acute, subacute or chronic toxicity of cacodylic acid to man by oral, dermal, or respiratory routes.

Occupational Hazards - The occupational hazard to forestry workers in the use of cacodylic acid for tree-thinning operations was reported by 2 groups of investigators. Tarrant and Allard (1972) used 3 tree-thinning crews in one study to determine the exposure hazard related to the use of cacodylic acid and another arsenical over a 9-week period. The study was carried out during the summer. In order to minimize variation in exposure, all subjects in the study were required to wear similar clothing and to follow recommended safety practices. Urine samples were collected on Monday mornings before work was begun, and again on the following Friday afternoon at the end of the working day.

Six men were assigned to each test crew; one did not work with any of the chemicals and served as a reference. The other 5 crewmen used either cacodylic

acid or another organic arsenical herbicide and applied it by use of an injector hatchet, an injector tool, or by the hack-squirt method.

There was no statistical significance in differences in urinary levels of arsenic among crewmen using cacodylic acid, those using another organic arsenical herbicide, and those using alternative application methods.

The levels of arsenic in the urine of the workers were elevated after 1 week of exposure. The values were higher on Fridays but in most instances were normal by the following Monday. There was no indication of a continuing increase over the 9-week study period.

All but one of the 15 men applying the chemicals in this study had urine arsenic levels in excess of 0.3 ppm at least once during the test. The highest level recorded was 2.5 ppm. No health problems were observed that could be related to arsenic poisoning.

Wagner and Weswig (1974) examined forestry workers exposed to cacodylic acid during tree-thinning operations for evidence of arsenic accumulation in urine. It appeared that urinary excretions were adequate for use as an index of exposure, but blood levels correlated poorly with exposure. This study indicated that workers exposed to organic arsenicals will show positive evidence of exposure by analysis of the 24-hr urinary excretion during the first week of exposure. In contrast to the results of Tarrant and Allard (1972), none of the workers in this study exceeded a urinary concentration of 0.3 ppm.

Accidents - Accidental exposure to cacodylic acid during its use is apparently quite limited. Data from the EPA Pesticide Episode Review System (PERS) shows that only one episode, including those involving humans, animals, and plants as well as episodes involving area contamination, was reported from 1972 to 1974.

Symptomology and Pathology -

Animals - Some or all of the following signs may be observed in animals acutely or chronically affected by arsenic compounds: loss of condition (rough hair coat), loss of body weight, diarrhea, evidence of abdominal pain, cutaneous hyperemia, increased sensitivity of the skin, teeth grinding, stiffness of limbs, loss of coordination, posterior paresis, and quadriplegia (Ledet et al. 1973; Jones 1958; Weaver 1962).

Gross pathological examination of animals may lead to an observation of liver and kidney alteration with small areas of kidney herrhages evident, and perhaps some liver degeneration. The heart may be congested. There will likely be extensive fluid accumulation in the intestinal tract, and this will probably be the most commonly found condition.

Man - In man, the usual signs of organic arsenic poisoning will probably be those most often noted in cases of poisoning by inorganic arsenicals. Some of these are: burning pain in esophagus and stomach, nausea and vomiting, diarrhea followed by bloody discharges, muscular cramps, vertigo, cold clamy skin and cold extremities, numbness of feet which may spread to upper limbs, burning sensation in limbs or other affected areas, tenderness in muscles or lack of joint sense, pigmentation of skin (raindrop), hyperkerotosis of palms and soles, stupor, circulatory collapses, convulsions, coma, polyneuropathy (2 to 3 weeks), development of Mee's lines (6 weeks) (Merck 1966; Munasingle et al. 1969).

Metabolism

Most of the studies reporting on the metabolism of arsenic compounds were concerned with arsenicals other than cacodylic acid. Some of the more pertinent of these reports have been included in this section because the results may hold some indirect evidence for the metabolic fate of cacodylic acid.

Absorption and Excretion - The results of a study by Hwang and Schanker (1973) indicate that cacodylic acid is absorbed from the small intestine of rats at rates such that 50% of a dose will be absorbed in 1.5 to 3.4 hr.

The mechanism by which cacodylic acid was absorbed appeared to be simple diffusion. The absorption process did not show evidence of saturation when the concentrations tested ranged from 1 to 100 mM (100-fold increase). Absorption rates of cacodylic acid and other organic arsenicals did not appear to be related to molecular size; therefore, it was unlikely that passage through membrane pores was an important pathway.

Absorption reportedly takes place by diffusion through lipoid regions of the intestinal boundary, a pathway reported to be utilized by a great many drugs and other organic substances. This pathway was suggested because the absorption process did not show evidence of saturation and the absorption rate of the arsenicals ranked in the same order as the $CHCl_3$ to water partition coefficients of the compounds. The absorption halftime (minutes) was 201 for cacodylic acid.

Peoples (1971) reported on older pharmacological literature comparing cacodylic acid and another arsenical as tonics, in which reference was made to the disadvantage of cacodylic acid, namely the foul odor of "cacodyl" on the breath.

Peoples (1975) and Irgolic (1975) suggested that the odor of cacodyl may have been confused with that of another arsenical. According to Doak and Freedman (1971), cacodyl is too unstable in moist air and too toxic to be the material detected. Peoples (1975) noted that since cacodylic acid is still used as a popular tonic in some parts of Europe, there is a potential data source for future study.

Goodman and Gilman (1958) reported that sodium cacodylate is metabolized to cacodyl oxide and inorganic arsenic. It is also possible that trimethylarsine $(CH_3)_3As$ is one of the detected materials.

In the cow, excretion of cacodylic acid was found to occur primarily by urine (75 to 80%). A balance between intake and output was established after 30 days feeding at 24.5 mg/day (Peoples 1963).

The nonavailability to the rat of arsenic bound in swine liver was demonstrated by Overby and Frost (1962). Three diets were used. The control diet was prepared using acetone-dried liver powder. The tissue-arsenic diet consisted of liver powder obtained from arsanilic-acid-fed swine, and the inorganic-arsenic diet consisted of control liver powder plus 3.3 mg of As_2O_3/100 g.

The amounts of elemental arsenic contained in these diets were less than 0.1 ppm for the control, 6.0 ppm for the tissue arsenic, and 6.5 ppm for the inorganic arsenic diet.

Rats were fed on the 3 (ad libitum) diets in a 7-day cycle. Feeding was continued with some animals up to 42 days. The diets and daily feces and urine collections were analyzed for total arsenic.

The metabolic inertness of liver-bound arsenic was demonstrated by the fact that 97% of the tissue arsenic was excreted during the feeding period and the following 7-day control period. However, only about 50% of the inorganic arsenic was excreted during the same period under the same test conditions.

The results of this investigation appear to parallel the results of an earlier study (Coulson et al. 1935) in which "shrimp arsenic" was reported to be retained by rats at much lower levels than was inorganic arsenic.

The strength of the tissue-arsenic bond is emphasized by the fact that liver arsenic was not easily solubilized in vitro by the usual chemical or biochemical digestion methods. Ashing was necessary to convert tissue arsenic to a form that could be readily reduced and distilled as arsine.

Calesnick et al. (1966) demonstrated that when the tissues of chickens which have been fed ^{74}As-labeled arsanilic acid were eaten by human volunteers, there was a rapid excretion of ^{74}As. Differences between urinary and fecal recoveries of tissues ^{74}As and pure ^{74}As-labeled arsanilic acid were not statistically significant. According to the authors, this suggests that the arsenicals in tissues of chickens fed arsanilic acid is absorbed and excreted in humans in much the same manner as is pure arsanilic acid.

The excretion and distribution of pentavalent and trivalent arsenicals were studied in adult male albino rats. Nonfasted and 24-hr fasted animals were given a single intravenous dose of one of the test materials. Urine and bile collections were made for 1 hr, and then the liver, kidney, heart, spleen, and RBC's were removed. Total arsenic was determined on these tissues.

Twenty-one to 64% of the pentavalent arsenicals were excreted in the urine; only 9 to 24% of one trivalent arsenical was excreted, and this primarily in bile. Arsenite-injected rats had the highest arsenic accumulation in the liver. The pentavalent arsenicals tended to accumulate to their higher levels in the kidney. Differences in accumulation between trivalent arsenic and pentavalent arsenic were not observed in heart, RBC's, and nonfasted spleen (Schreiber and Brouwer 1964).

When arsenite was given as an intravenous injection to man, it was recovered in the urine as a mixture of arsenite and arsenate with the latter predominating. This suggested in vivo oxidation and preferential excretion of arsenic in the urine as the arsenate (Mealey et al. 1959).

Tissue Accumulation - In cattle, the principal sites of storage of cacodylic acid arsenic were the liver, spleen, and pancreas. However, even in these principal sites, the tissue levels were low (Peoples 1963).

After 1 week of feeding on a cacodylate-free ration following 10 weeks feeding on diets containing the acid, tissue residues of arsenic in chickens were found to have been reduced. Data from this test is shown in Table 9.

Ledet et al. (1973) found that arsenic levels decreased rapidly in the organs and skeletal muscles of pigs after removal of the animals from a diet containing arsanilic acid. This result indicated that irreversible accumulation of organic arsenic in tissues does not occur.

Mutagenic Effects

Histidine-requiring mutants of Salmonella typhimurium were used by several investigators to test the mutagenic properties of cacodylic acid as well as other herbicides. Cacodylic acid was evaluated by measuring its effect on bacterial genetics by the induction of reversion to histidine independence. Test results indicated that cacodylic did not possess a mutagenic potential in this system (Andersen et al. 1972).

Table 9. ARSENIC IN TISSUES OF CHICKENS FED CACODYLIC ACID (30 ppm)

Sample interval	ppm in Tissues Fat	Liver	Muscle	Kidney
After 10 weeks 30 ppm dietary	<0.05	0.23	0.23	0.23
10 weeks dietary at 30 ppm + 7 days arsenic-free diet	<0.05	<0.05	0.082	<0.05

Source: Bodden (1968).

Early studies reported a similarity in the mitotic effects of cacodylic acid and colchicine, a cytokinetic agent (Hartwell et al. 1946; King and Ludford 1950; Anso 1953). However, Salzgeber (1955) indicated that sodium cacodylate is less cytoxic in its effects than colchicine.

Oncogenic Effects

Pathogen-free mice were used in studies aimed at determining tumorigenicity by oral administration of cacodylic acid. A daily dosage of 46.4 mg/kg of cacodylic acid was given in distilled water from 7 to 28 days. Thereafter, the test material was incorporated in feed at a level of 121 ppm and fed *ad libitum* for nearly 18 months. The positive controls (7 tumorigenic compounds) and the cacodylic-acid-treated groups were compared with the grouped negative controls. Analyses were performed with 4 tumor groupings: hepatomas, pulmonary tumors, lymphomas, and total mice with tumors. From these tests it was determined that cacodylic acid did not cause a significant increase in tumors (Innes et al. 1969).

A complete review of the relationship of oncogens in all arsenic compounds is beyond the scope of this review.

Teratogenic Effects

A study of the teratogenic potential of cacodylic acid in the CD rat and CD-1 mouse is now in progress. Groups of rats and mice intubated with cacodylic acid during the critical period of organogenesis will be evaluated for weight gain, liver/body weight ratio, percent mortality, number of inseminations, number of term pregnancies and number of implantations. Litters from these animals will be examined for defects and will be evaluated with respect to percent mortality, body weight and lung/body weight ratio. (Chernoff 1975).

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PART II. INITIAL SCIENTIFIC REVIEW

SUBPART C. FATE AND SIGNIFICANCE IN THE ENVIRONMENT

CONTENTS

This section contains data on the environmental effects of cacodylic acid and other closely related arsenicals, including effects on aquatic species, wildlife, and beneficial insects and interactions with lower terrestrial organisms. Residues in soil, water and air are discussed. Data is also included on bioaccumulation and biomagnification of cacodylic acid and on the environmental transport mechanisms of arsenicals. This section summarizes rather than interprets data reviewed.

Effects on Aquatic Species

Fish and Amphibia -

Laboratory Studies - In studies on bluegill sunfish (Lepomis macrochirus), Hughes (1969) reported a commercial formulation that contained 23.4% cacodylic acid (as well as surfactant) had a 96 hr TL_m of 80 ppm. Another formulation containing sodium cacodylate, made up of 30% cacodylic acid equivalent (AE) was reported to have a 96 hr TL_m of 750 ppm.

In another study, Cope (1969) reported the 96 hr LC_{50} of the commercial herbicide Phytar (unknown percentage of cacodylic acid) to be 16 ppm for bluegill.

McCann (1969) reported that no deaths had occurred in bluegill exposed to Phytar (99.3% cacodylic acid) at 100 ppm AI within 72 hr at 65°F, although all bluegills exposed to 22.6% cacodylic acid at 210 ppm AI died within the test period (hr not specified).

The 24 hr TL_m of Phytar 560 (22.6% sodium cacodylate and 3.9% cacodylic acid) for rainbow trout (Salmo gairdneri) was reported to be 145 ppm at 55°F. The 48 hr TL_m was 130 ppm, and the 196 hr TL_m was 96 ppm AI.

Woodward (1974) reported the 96 hr LC_{50} of cacodylic acid to cutthroat trout (Salmo clarki) and lake trout (Salvelinus namaycush) as between 10,000 and 100,000 µg/liter.

Miller and Lowe (1966) reported no effects to longnose killifish (Fundulus similis) when exposed to 40.0 ppm AI of cacodylic acid for 48 hr.

Field Studies - Lehn et al. (1970) studied the effects of repeated applications of cacodylic acid on the populations of fish in 3 freshwater streams that drained an area in which the herbicide was applied. In July and August, 1969, 2,085 gal of the cacodylic acid formulation "Military Defoliant Blue" were sprayed on a 1 mi^2 test area. The formulation contained 4.7% cacodylic acid, 26.4% sodium cacodylate, 3.4% surfactant, 5.5% sodium chloride, 59.5% water and 0.5% antifoam agent. One gallon of this formulation contains approximately 3.1 lb of cacodylic acid equivalent per gallon, or 15.4% of elemental arsenic. The total quantity applied was equivalent to about 10 lb of cacodylic acid per acre.

The test area is on the Eglin Reservation, approximately 2 miles north of Choctawhatchee Bay in Walton County, Florida. The test area and the surrounding range area had been mechanically cleared of almost all vegetation prior to the test. The soil in the test area was of the Lakeland-Eustis-Blanton Association, consisting of 90.1 to 93.1% sand, 2.8 to 4.3% silt, 3.6 to 5.6% clay, and 0.0 to 0.46% organic matter. The cation exchange capacity was low, ranging from 0.69 to 1.19.

The cacodylic acid applications occurred during the period of heaviest rainfall; July precipitation in the test area was 14.92 in, 10.40 in was recorded for August. Total annual rainfall in 1969 was 59.9 in.

Six sampling stations were established on 3 freshwater streams which drain the test area. Periodic counts of 20 different species of fish were made at the sampling stations during 3 months preceding the applications (10 counts), during the 2 months in which applications were made (4 counts) and during 3 months following the applications (8 counts). Species diversity was determined by an equation which expresses the relationship between the number of species and the logarithm of the total number of individuals. Changes in the proportions of any one species present at each station before and after the spraying were also studied.

Seven species of fish were found at all 6 sampling stations, i.e., the sailfin shiner (Notropis hypselopterus), the mosquitofish (Gambusia affinis), the blackbanded darter (Percina nigrofasciata), the brown darter (Etheostoma edwini), the spotted sunfish (Lepomis punctatus), the speckled madtom (Noturus leptacanthus), and the pirate perch (Aphredoderus sayanus). When all pre- and post-treatment counts at all sampling stations were compared, it was found that the numbers of sailfin shiners decreased markedly in 8 instances. The numbers of all other fish in this group showed marked increases when pre- and post-exposure counts were compared. Mosquitofish increased in 7 observations, speckled madtom in 6 observations, spotted sunfish in 4 observations, black-banded darters and pirate perch in 2 observations and brown darter in 1 instance.

Of the remaining 13 species of fish, the distribution was as follows: 1 American eel, Anguilla rostrata, was found at 4 of the 6 stations; 1 Southern brook lamprey, Ichthyomyzon gagei, was found at 3 stations; 3 species (the weed shiner, Notropis texanus; the redfin pickerel, Esox americanus; and the spotted sucker, Minytrema melanops), were found at 2 stations each and 8 species were found at only 1 station, (the chain pickerel Esox niger, the rock bass Ambloplites rupestris, the black madtom Noturus funebris, the Okefenokee pigmy sunfish Elassoma okefenokee, the tadpole madtom Noturus gyrinus, the lake chubsucker Erimyzon sucetta, the spotted bass Micropterus punctulatus and the starhead topminnow Fundulus notti). There were no statistically significant changes in the numbers of any of these 13 species when pre- and post-treatment numbers were compared.

Of the 6 sampling stations, one showed a slight decrease in diversity of species, in a comparison of diversity indices before and after spraying. The diversity indices for the other stations either remained constant or increased after spraying.

Water and silt samples were taken from the 3 streams before, during and after spraying and were found to contain arsenic concentrations of less than 0.05 ppm, the lower detection limit of the analytical procedure employed. The authors point out that these arsenic residue levels are lower than background levels found in many aquatic organisms and systems, as reported by other investigators. Since the arsenic levels found in the water and silt were too low to have an immediate effect on fish, the authors suggest that the decrease in the relative numbers of Notropis hypselopterus found at one sampling station, and other variations in fish population levels were probably due to 1 or more extraneous variables, rather than to the cacodylic acid applications.

Literature searches, contacts with basic producers of cacodylic acid and contacts with 5 U.S. Department of the Interior and Environmental Protection Agency laboratories known to be engaged in fish toxicity studies with pesticides, failed to produce any further data or reports on the effects of cacodylic acid on fish under field conditions.

As with all pesticides having 24-hr LC_{50} values for fish greater than 1.0 ppm, commercial labels of formulated pesticides containing cacodylic acid as an active ingredient do not carry any direct warnings regarding fish toxicity, except for the general statement, "Do not contaminate waters used for domestic consumption, or by animals, wildlife and aquatic life or for irrigation purposes."

Special Laboratory Studies - Oliver et al. (1966), in a field study of the effect of cacodylic acid on specific floral ecotones, also described the direct effect of cacodylic acid on pond fauna in laboratory bioassays. The results were too heterogeneous for a statistical evaluation but the authors reported that the 48-hr LD_{50}'s for Gambusia affinis (mosquitofish), Notropis maculatus (tailight shiner), and Bufo terrestris tadpoles (Southern toad) approached 1000 ppm. Over a 2-week period Micropterus salmoides (largemouth bass) were fed mosquitofish that had been previously exposed to 1000 ppm cacodylic acid for 24-hr. There was no apparent effect on the bass. The authors noted that fauna would not be directly affected by field concentrations of cacodylic acid. However, damage to vegetation from the pesticide would indirectly affect the fauna, especially the highly specialized species which are unable to adapt to environmental modification.

In another study, Rostand (1950) studied teratogenicity in the tadpoles of the red frog (Rana temporaria) exposed to sodium cacodylate as well as 4 known teratogens. The tadpoles were exposed to 1/10,000 (100 ppm) sodium cacodylate for 3 weeks at the age of one month, when the buds of posterior members began to appear. No quantitative results were given other than that 10 to 25% of the 100 to 150 tadpoles in each test exhibited abnormalities.

In sodium cacodylate the only abnormality observed was rigidity of posterior appendages without structural anomalies.

Lower Aquatic Organisms -

Laboratory Studies - The toxicity of cacodylic acid to estuarine animals was studied in 1966 at the then existing Gulf Breeze, Florida biological laboratory of the U.S. Bureau of Commerical Fisheries (Miller and Lowe, 1966). Test organisms were exposed for 24 or 48 hr to cacodylic acid concentrations of 1.0 ppm in natural flowing seawater at a temperature of 19°C, and a salinity of 24 to 28% (parts per thousand). There were no effects from cacodylic acid or pink shrimp (Penaeus duorarum) after 48 hr exposure, nor on the Eastern oyster (Crassostrea virginica) after 24 hr exposure. Effectiveness (or lack thereof) on shrimp was determined by the percent of the population exhibiting paralysis or loss of equilibrium, and the effects on oysters by percent decrease in shell deposition.

Sanders (1970) studied the toxicity of a number of herbicides, including cacodylic acid, to freshwater crustaceans. Cacodylic acid was one of several herbicides that were not toxic to scud (Gammarus fasciatus) after 96 hr exposure at a concentration of 100 ppm.

Cox and Alexander (1973a) investigated the production of trimethylarsine gas from various arsenic compounds, including cacodylic acid, by 3 sewage fungi isolated from raw sewage, i.e., Candida humicola, Gliocladium roseum and Penicillium species. Aliquots of raw sewage were added to culture media and exposed to successively higher concentrations of cacodylic acid, ranging from 100 to 2,000 µg/ml. The enrichment cultures obtained in this manner were incubated for 1 month at room temperature, and the headspace gas of each incubation bottle was then tested for the presence of trimethylarsine gas by odor analysis and gas chromatography. In addition to cacodylic acid, 3 other arsenic compounds were tested in the same manner, each at pH 5, 6 and 7. The typical garlic odor of trimethylarsine was detected in cultures containing cacodylic acid at all 3 pH levels.

The aforementioned 3 species of fungi were isolated from these cultures and tentatively identified. Each of these organisms was grown on different media in the presence of the 4 different arsenic sources, including cacodylic acid, to determine the extent of their ability to produce trimethylarsine gas. Candida humicola produced trimethylarsine with all 4 arsenicals, the greatest amounts (87 and 41 nmoles, respectively) with cacodylic acid at pH 5 and 6. Gliocladium roseum produced 2,970 to 3,700 nmoles of trimethylarsine with one arsenical with no appreciable effect of pH. By contrast, this organism produced only 10 nmoles of trimethylarsine from cacodylic acid under the same conditions at pH 5, 52 nmoles at pH 6 and 253 nmoles at pH 7. The third organism, an unidentified species of Penicillium, also produced a small amount of trimethylarsine gas with cacodylic acid.

Based on their data, the authors suggest that acid conditions in sewage might be conducive to trimethylarsine production by certain fungi from several arsenic sources.

In further studies, Cox and Alexander (1973b) investigated some of the variables affecting the formation of trimethylarsine from cacodylic acid and several other arsenicals by Candida humicola. Phosphate inhibited the formation of trimethylarsine gas by growing cultures of C. humicola from other arsenicals, but not from cacodylic acid. Phosphite suppressed the production of trimethylarsine by the fungus from one arsenical but not from cacodylic acid. Cox and Alexander correlate these observations with the report by Da Costa (1972), concluding that phosphate failed to reduce the fungitoxicity of cacodylic acid to several fungi, while it did overcome the fungitoxicity of other arsenicals. Cox and Alexander postulate that phosphate may suppress gas evolution by blocking the conversion of the arsenicals to trimethylarsine at a stage between the mono- and dimethylarsenic compounds.

Field Studies - In their studies on the effects of cacodylic acid applications on 3 freshwater streams draining the target area, Lehn et al. (1970) included observations on lower aquatic organisms.

On each sampling date at each sampling station, the population levels of several benthic organisms, including crayfish (Orconectes species), dragonfly naiad (Gomphus species), freshwater snail (Neritian species) and an unidentified immature freshwater clam were monitored. Observations were also made to detect possible morphological effects on eelgrass (Vallisneria americana), the only species of vascular aquatic plants that was common to all sampling stations. None of these organisms exhibited any gross changes in population levels; all remained abundant throughout the study period.

Effects on Wildlife

Laboratory Studies - The only laboratory studies on the effect of cacodylic acid on wildlife deal with its oral toxicity to 3 avian species and one species of deer.

For 5 successive days, 10 bobwhite quail chicks (Colinus virginianus) were fed a standard diet containing 5,000 ppm of a material that contained 29% sodium cacodylate and 5% cacodylic acid. Fifty were fed an untreated diet (negative controls) and 50 chicks were fed a diet containing a chlorinated hydrocarbon (positve controls). A 9-day LC_{50} value was calculated to be in excess of 5,000 ppm cacodylate.

Abnormal behavior was not observed during the test nor were any signs of systemic toxicity noted. Necropsy revealed no adverse gross pathology (Industrial Bio-Test Laboratories, 1973a).

The subacute toxicity of sodium cacodylate to mallard ducklings (Anas platyrhynchos) was determined in an 8-day dietary test. The test material was administered to 10 ducklings in a laboratory ration for 5 days at a level of 5,000 ppm. Fifty untreated controls and 50 positive controls were used for comparison. The LC_{50} was calculated to be greater than 5,000 ppm.

No abnormal behavioral reactions or signs of systemic toxicity were noted in the cacodylate-treated ducks. Necropsy did not reveal any gross pathological lesions (Industrial Bio-Test Laboratories 1973b).

The LD_{50} of Silvisar 510 (54.3% cacodylic acid) for mallard hens was reported to be greater than 2,000 mg/kg by Tucker (1969). The LD_{50} for chukar partridges (Alectoris graeca) of mixed sex was reported as equal to or greater than 2,000 mg/kg (one died).

Signs of intoxication included regurgitation, polydipsia, ataxia and use of wings to aid in movement.

Tucker (1969) reported that 320 mg/kg of Silvisar given via stomach tube did not cause death of a 15-month-old mule deer doe (Odocoileus hemionus hemionus). Signs of intoxication included slight ataxia and imbalance, slowness, soft feces and anorexia; a weight loss was observed over a 19-day period.

Field Studies - Norris (1971) presented an interim report on comprehensive cooperative studies on the fate and environmental impact of organic arsenical herbicides in the forest environment. The studies were initiated following the death of 8 range cattle in forest areas where organic arsenical herbicides, including cacodylic acid, had been used. Arsenic residues had been found in hair and tissues from 4 of the dead cattle.

Schroedel et al. (1971) studied the effects of several arsenical herbicides on wildlife. Animals (numbers not specified) were trapped at various intervals after use of arsenical herbicides, including cacodylic acid, and arsenic residues were determined in specific tissues, or in the whole body. More than 400 determinations of arsenic residues were made on samples collected from 3 treatment areas in western Washington and 4 areas in eastern Washington. Several species of birds, mountain beaver and porcupines did not contain detectable arsenic residues. A single deer which was recognized by applicators as a long-time resident of one of the treated areas was also collected. Histopathological examination of tissues from this animal showed no arsenic-induced lesions and chemical analysis revealed no arsenic residues. Voles, shrews, mice and chipmunks contained low levels of arsenic shortly after thinning with arsenical herbicides began. About 50% of these animals had arsenic residues ranging from 0.5 to 9.8 ppm between 2 and 30 days following treatment. Most of the residues found were less than 5.0 ppm. Few animals (number not specified) collected more than 30 days after treatment contained detectable residues. Most ground squirrels that were collected contained arsenic residues, similar to those found in voles, shrews, mice and chipmunks, but 1 squirrel, collected 1 day after treatment, contained arsenic residues ranging from 17 to 30 ppm in various body parts.

A total of 11 dead snowshoe hares were found in one particular treatment area near Colville, Washington, between June of 1970 and February of 1971. High levels of arsenic in tissues from these hares indicated that arsenic poisoning was the cause of death, although postmortem degeneration prevented more detailed studies. Most of the dead hares were found within a few hundred yards of "wash areas," i.e., locations where crews would dispose of remaining herbicide at the end of the working day and where they washed their equipment and hands. The normal procedure at the time was to empty the remaining contents of "squirt cans" and all wash water on the ground. Severe damage to vegetation at these sites suggested high concentrations of arsenicals. When this method of disposal of excess herbicide and wash water was discontinued, no further mortality of hares was observed in this area. Samples of soil, forest floor material and vegetation from the "wash areas" contained high levels of arsenic.

Two hares were collected 2 and 42 days following treatment with arsenical herbicides in another area in eastern Washington. They did not contain detectable arsenic residues. Five other hares collected in western Washington 232 days after treatment contained either extremely low or undetectable residues of arsenic.

In comparison study, Maycumber (1971) observed the exposure of cattle which were grazing in areas treated with arsenical herbicides, including cacodylic acid. Pre- and post-exposure samples of hair were collected from 37 head of adult cattle grazing in 1970 in a forest area treated with cacodylic acid (Silvisar 510, 50% purity) which was also the same area where cattle mortality had been observed in 1969. Comparable pre- and post-exposure samples were collected from 28 other head of cattle which were grazed in another forest area being thinned with another arsenical herbicide during the grazing season when these studies were conducted (1970). There was a statistically significant (at the 5% level) increase in arsenic concentrations between pre- and post-exposure samples at both sites. There was no significant difference in arsenic levels between the two sites in samples collected at a given time. No cattle mortality was observed in either of the 2 test areas. The author emphasized that the animals from whom these tissue samples were taken were grazed in an area which had been subjected to chemical thinning with arsenicals during the same grazing season.

A report on the toxicology of Silvisar® 510 (cacodylic acid) tree killer by the Ansul Company (1968) points out that, in commercial tree-thinning use, about 4 g of the formulated product (containing 50% of cacodylic acid equivalent per gal) will be used per tree. Assuming that all of the cacodylic acid enters the foliage after treatment, a 150-lb animal would have to consume all of the foliage of about 10 trees to begin showing toxic symptoms. Furthermore, the animal would have to do this "in a relatively short time" (not further specified) since cacodylic acid is quickly excreted and does not accumulate in body tissues. It would be practically impossible, Ansul concluded, for any animal to consume enough foliage, fruits or nuts to show any toxic symptoms.

A report by Martin and Nickerson (1973) on arsenic, mercury, lead and cadmium residues in starlings is of marginal interest to the objectives of the

present study. In 1971, the authors collected starlings (Sturnus vulgaris) at 50 sites throughout the continental United States and analyzed them for residues of arsenic, mercury, lead and cadmium. Sampling sites were chosen to reflect varying environmental conditions, representing broad geographic areas and different degrees of human activity and related pollution sources. Each sample consisted of a "pool" of 10 starlings which were frozen immediately after collection and kept in frozen condition until analysis. After appropriate digestion, arsenic residues were determined by atomic absorption spectrophotometry. The minimum level of sensitivity for arsenic was 0.01 ppm. Residues found were expressed in parts per million of whole body, wet weight.

The arsenic residues found were generally much lower than those of the other 3 metals. Except for a sample from Michigan which contained 0.21 ppm of arsenic, all remaining samples had arsenic residues of 0.04 ppm or less, with no arsenic residues detected in 8 of the samples. The authors pointed out that arsenic residues in urban soil samples have been reported as high as 74.5 ppm, but that apparently this arsenic is either unavailable to the starlings, or is ingested in a form which is not retained in the body by this species.

Data from controlled investigations on the toxicity of cacodylic acid to laboratory animals indicates that the mammalian toxicity of this chemical is relatively low. Few reports are available on the effects of cacodylic acid on wildlife. The observations from the studies conducted in the Pacific Northwest as summarized by Norris (1971) indicate that misuse of organic arsenical herbicides or careless dumping of excess concentrates or spray mixtures must be avoided.

Effects on Beneficial Insects

In toxicity tests on honeybees (Apis mellifera), Atkins et al. (1973) summarized the effects of a large number of pesticides and other agricultural chemicals. In a laboratory procedure which primarily measures a pesticide's contact effect, pesticides are applied in dust form to groups of 25 bees per test level, with 3 replicates for each of 3 colonies for a total of 9 replicates per test level. The procedure permits determination of an LD_{50} value for each pesticide in micrograms of chemical per bee. Cacodylic acid is included in Group III as "Relatively nontoxic to honeybees." Cacodylic acid produced 5.6% mortality of bees at the rate of 157.12 ug/bee (by the authors' estimates equivalent to 152.12 lb/acre) after exposure for 48 hr at 80°F and 65% relative humidity.

Moffett et al. (1972) studied the effects of cacodylic acid and several other herbicides on honeybees. About 50 bees were collected by vacuum cleaner from entrances of colonies in an experimental apiary and placed in individual wire cages measuring about 2 x 2 x 6 in. The bees were brought into the laboratory and fed 60% sucrose syrup and distilled water. The next day, dead bees were removed, and the cages with the remaining live bees were sprayed with cacodylic acid in aqueous solution at a rate equivalent to 4 lb AI at 20 gal/acre. Dead bees were counted daily after spraying. Each treatment was

replicated 5 times. Cacodylic acid was highly toxic to the sprayed bees. Few bees sprayed with cacodylic acid died on the first day, but mortality reached almost 60% on the third day, and all bees were dead 10 days after spraying.

Morton et al. (1972) and Morton and Moffett (1972) studied the toxicity of herbicides, including cacodylic acid, when fed orally to honeybees. Ten g (approximately 100 individuals) of newly-emerged honeybees were placed in 2 x 6 x 6 in screened cages. All bees were less than 24 hr old at the time they were placed in the cages. The test herbicides were fed to the bees in 60% sucrose syrup at concentrations of 0, 10, 100 and 1,000 ppm by weight. Cacodylic acid was "extremely toxic" at the 100 and 1,000 ppm by weight concentrations. It was among the most toxic of all herbicides tested, producing high bee mortality at all 3 concentrations. At the rate of 10 ppm by weight, 50% of the test bees were killed in 4.1 days; at 100 ppm by weight, the bees' halflife was 2.6 days; and at 1,000 ppm by weight, 2.1 days.

The findings of Moffett et al. (1972), Morton et al. (1972) and Morton and Moffett (1972) regarding the bee toxicity of cacodylic acid appear to be at variance with those of Atkins et al. (1973). However, Atkins et al. applied the test pedticides to honeybees in dust form, whereas Moffett et al. (1972) applied the herbicides orally in sucrose syrup. It appears that cacodylic acid may be more toxic to honeybees in aqueous solution than in the form of a dry dust applied topically.

Commercial labels of formulated pesticides containing cacodylic acid (or its sodium salt) as an active ingredient are not required to contain any statements regarding toxicity to bees. A number of authors have investigated the effects of forest trees treated with cacodylic acid on bark beetles. While these insects are pests, rather than beneficial species, these observations are of some interest and will therefore be reviewed briefly.

Chansler and Pierce (1966) investigated the brood survival of 4 species of bark beetles (Dendroctonus adjunctus, Dendroctonus obesus, Dendroctonus ponderosae, and Dendroctonus pseudotsugae) in trees injected with cacodylic acid. Two different formulations containing cacodylic acid were employed. Both were injected undiluted into the sap stream of spruce and pine trees around the full circumference of the tree, about 5 to 10 in above the ground. Treatment was made soon after beetle attack. Three to 7 months after treatment, the number of live immature beetles in the treated trees was reduced by 84 to 98% compared with untreated trees.

Stelzer (1970) found that the Arizona 5-spined engraver (Ips lecontei) attacked ponderosa pine trees poisoned with a fast acting herbicide containing cacodylic acid. The density of attack and the mortality of different stages of the beetle varied with the time of the year the trees were treated. The density of live brood was reduced by about 70% in trees treated from April to July, as compared to untreated trees felled during the same period.

Trees poisoned from late July through August attracted more attacks than those treated at any other time of the year. Trees felled about 1 month after treatment in July were most effective as toxic trap trees.

Buffam and Yasinski (1971) studied the effects of cacodylic acid on the spruce beetle (Dendroctonus rufipennis), the most serious pest of Engelmann spruce in the United States. Spruce trees were frilled by hand hatchet, and cacodylic acid formulated as Silvisar 510 (containing 50%, or 1b/AI/gal) was applied to the trough by plastic squeeze bottle at the rate of 1 ml of formulation per inch of tree circumference. Some treated trees were felled at intervals after treatment; some were left standing.

Buffam and Flake (1971) applied cacodylic acid in the form of the Silvisar 510 formulation in the same manner (adding 1 ml of formulation per inch of tree circumference to a horizontal frill made completely around the tree by hand hatchet, using a plastic squeeze bottle) to pine trees that were recently attacked by the roundheaded pine beetle (Dendroctonus adjunctus). This method gave 100% reduction of the pine beetles; application of the silvicide to power saw-frilled trees, while significantly effective, was not nearly as effective as the hatchet method.

Buffam (1971) then undertook further studies to define the best method of producing lethal trap trees. By varying the timing and the cacodylic acid dosage rate, a combination was sought that would attract as many beetles as untreated checks, but would be lethal to them. It was found that trees frilled and treated in mid-June with one-half the concentration of Silvisar 510 used previously and felled 2 weeks later worked best as beetle traps. These trees showed about the same attack density as untreated, felled trees. Bark beetle broods survived in untreated trees, while they did not survive in the cacodylic acid-treated trees.

Frye and Wygant (1971) reported very similar results, using cacodylic acid (undiluted Silvisar 510 formulation) in frill girdles of Engelmann spruce against the spruce beetle (Dendroctonus rufipennis). They observed that other bark beetles, including Ips pilifrons, Polygraphus rufipennis and Scierus annectens, were also killed by the treated trap trees. Striped ambrosia beetles (Trypodendron lineatum) were attracted to the treated trees, but their development was not adversely affected by the treatment.

Newton and Holt (1971) reported on studies in which 60 yr-old Ponderosa pines were injected with cacodylic acid and a mixture of another arsenical compound. Treatments consisted of cacodylic acid at 5.7 1b/AI/gal: the other compound at 6.67 1b/AI/gal; and a 50:50 mixture of the 2 solutions, applied by injection with a Hypo-Hatchet tree injector at waist height. A volume of about 1.3 ml of undiluted material was applied in each injection. The experiment included 1,080 trees, treated with the 3 herbicides at 3

spacings on 6 treatment dates. In the treatment area, the presence of all insects under observation was confirmed in scattered, dead or dying trees. Plots thinned with other treatments which included felling and nonarsenical injection were also in the vicinity. All organic arsenical treatments resulted in lower attack levels on the treated trees than on the control trees by the insects studied, including the mountain pine beetle (Dendroctonus ponderosae) and the pine engraver (Ips pini). No larvae of these species were found alive. There was much evidence of larval mortality and hatch failure. The authors speculated that an endometatoxic reaction involving reduction of the organic arsenicals to arsines may be a possible explanation for the insecticidal effectiveness observed.

It is significant that the controls in the experiment consisted only of untreated, felled trees. The authors failed to take into account in their experimental design that these beetles preferentially attack dead, felled trees even over dead, standing trees (Nagel et al. 1957).

Copony and Morris (1972) combined the use of cacodylic acid (in the form of Sivisar 510) with the use of bark beetle attractant to trap emerging southern pine beetles (Dendroctonus frontalis) in a heavily infested stand of pines in eastern Virginia. The attractant was successful in luring beetles to properly located trap trees. Cacodylic acid was used at the average rate of 1.2 ml of the 50% formulation per in of tree diameter applied to a shallow frill girdling each tree. This treatment resulted in a 3.5-fold increase in aborted attacks and reduced the brood of successfully attacking beetles by 59.9%.

Buffam et al. (1973) and Coulson et al. (1973) report on further refinements of the "lethal trap tree technique" against the spruce beetle (Dendroctonus rufipennis), and the southern pine beetle (Dendroctonus frontalis). Variables studied included: the use of cacodylic acid at full strength and half strength; comparison of the treatment and felling of trap trees in the fall (preferable from an operation standpoint) and the spring; the number of trees treated with cacodylic acid; and the number of trees baited with beetle attractant. Buffam et al. (1973) analyzed phloem samples for arsenic and found that arsenic applied by way of cacodylic acid was translocated in this tissue. Check trees showed low levels, and treated trees generally higher, though variable, levels of arsenic. There was an inverse relationship between bark beetle larval numbers and arsenic concentrations in the phloem of treated trees.

Interactions with Lower Terrestrial Organisms

Studies on the interactions between arsenicals and microorganisms date back to the last century. Gosio, a nineteenth-century Italian scientist, observed that certain fungi produce a poisonous gas from moldy wallpaper due to arsenic in the pigment. In the subsequent literature, this gas became known as "Gosio-gas."

Challenger et al. (1933) and Challenger and Higginbottom (1935) identified "Gosio-gas" as trimethylarsine. They demonstrated that a strain of Penicillium brevicaule added to culture media containing cacodylic acid (free from inorganic arsenic) produced trimethylarsine. They conducted a large number of experiments in an effort to elucidate the mechanism of this biological methylation, but were unable to reach a definite conclusion. In the course of these studies, they found that 3 bacterial species, Bacterium mesentericus vulgatus, B. mensentericus ruber and B. subtilis did not give off the typical garlic odor of trimethylarsine when added to glucose-meat extracts which contained various arsenicals.

More recently, McBride and Wolfe (1971) showed that cell extracts and whole cells of a strain of Methanobacterium both methylate and reduce arsenate to dimethylarsine under anaerobic conditions. These preparations produced dimethylarsine from arsenate, arsenite and methylarsonic acid (MAA). The process involves a series of methylations and reductions, and requires adenosine triphosphate, hydrogen and a methyl donor (^{14}C-labeled methylcobolamin was used as methyl donor in these tests). In the pathway, arsenate is reduced to arsenite which is methylated to form MAA. Dimethylarsinic acid (cacodylic acid), formed by the reductive methylation of MAA, is reduced to dimethylarsine. The authors point out that pollution hazards exist when arsenic and its derivatives are introduced into an environment where anaerobic organisms are growing. They emphasize that the importance of organisms such as Methanobacterium which convert toxic molecules to more toxic derivatives should not be underestimated.

Newton (1971) also studied the microbial degradation of cacodylic acid and other arsenicals. Media were prepared from Czapek-Dox agar with a range of arsenical and glucose (as an energy source) concentrations, inoculated with a mixture of mold organisms cultured from wood, incubated for various periods of time, dried and analyzed by neutron activation. Each concentration of each arsenical was tested at glucose concentrations of 0.3, 1.0, 3.0 and 10.0% by weight. Cacodylic acid concentrations studied were 0, 100, 1,000 and 10,000 ppm in terms of organic arsenic. Thus, there were 16 combinations of arsenic and glucose for each herbicide studied. Each combination was replicated 5 times.

Substantial losses of arsenic occurred at all levels of glucose, and at all 3 concentrations of cacodylic acid tested. These arsenic losses occurred through volatilization at temperatures below 70°C. The author concluded that high concentrations of organic arsenicals are subject to attack by molds and perhaps other microorganisms. Arsines, most likely trimethylarsine, appear to be the principal metabolites responsible for escape of arsenic from the cultures. The findings suggest, in the author's opinion, that there may be substantial losses of arsenic through volatilization following application of organic arsenical herbicides, and that the role of organic arsenical herbicides as persistent compounds needs to be reexamined.

A series of tests were conducted to determine if soil microorganisms contributed to the degradation of cacodylic acid. The test herbicides were added to soil samples collected in California, Alabama, the Central Plains of

Texas and the Rio Grande Valley of Texas. Cacodylic acid (in the form of the product Phytar 560) was added to the soil samples at a concentration of 50 ppm of acid equivalent, or 27.6 ppm of elemental arsenic. One-half of the soil samples were sterilized by autoclaving prior to addition of the herbicide. All samples were again subdivided, and about 1 g of corn syrup was added to one-half of the samples to evaluate the effects of an energy source. All samples were exposed to sunshine. The weight of each sample was checked periodically, and water was added to bring the sample back to its original weight if a loss had occurred. Periodically, aliquots were analyzed for arsenic residues and evaluated for the composition of the microbial population present.

Isolations made from serial dilutions of soil samples indicated that there was no apparent toxicity to soil microbes due to the presence of cacodylic acid. Analysis of soil samples for elemental arsenic after 60 days showed considerable variations. No conclusions could be drawn regarding the effects of the microorganisms on cacodylic acid (May 1974).

Zabel and O'Neil (1957) studied the toxicity of 44 arsenicals, including cacodylic acid, to 4 common slime-forming organisms by a petri plate method. Some of the more complex organic arsenicals demonstrated considerable bactericidal and fungicidal activity. Generally, there was no correlation between toxicity to the microbes and the amount of arsenic in the molecule. Cacodylic acid and most of its salts, with the exception of silver cacodylate and 8-hydroxyquinoline cacodylate, revealed very low activity; they showed no slimicidal potential at concentrations of 2,000 ppm or above. Ineffective salts included the copper, zinc, lead, bismuth, sodium, potassium, magnesium, iron, calcium and barium cacodylates. Two bacteria and 2 fungi of importance in slime formation were used as test organisms, i.e., Aerobacter aerogenes, Bacillus mycoides, Aspergillus niger and Penicillium expansum. Silver cacodylate evidenced strong bactericidal and low fungicidal activity. This difference was apparent in many arsenicals and suggests that there may be basic metabolic differences in the handling of arsenic between fungi and bacteria.

Malone (1971, 1972) investigated the effects of cacodylic acid applied to a fescue meadow on soil microorganisms. Plots measuring 5 x 7 m were laid out in a meadow composed of about 90% fescue, the remainder consisting of approximately 30 different herbaceous species. Cacodylic acid was used in the form of the commerical formulation Phytar 560, containg 22.6% sodium cacodylate, 3.9% cacodylic acid and 73.5% of other ingredients, including surfactants. In June of 1970, plots received single applications of the herbicide at the rate of 9 and 27 lb/acre of the commercial product. A third treatment series consisted of 3 applications of 9 lb/acre, repeated 3 times at monthly intervals, for a total of 27 lb/acre throughout the growing season. Treatments and untreated controls were replicated 3 times. The single applications at 9 and 27 lb of product per acre reduced the fescue biomass by 38 and 89%, respectively. The repeated applications reduced fescue by 83%. Regrowth of vegetation began in August, and at the end of September, most plots had recovered to near original levels of fescue biomass.

The responses of soil microorganisms to these treatments were evaluated bi-weekly, beginning 1 week before the treatment date and continuing throughout September. Four soil samples were obtained from each plot, combined and used to prepare serial dilutions for plates of bacteria and fungi. The herbicide treatments increased the numbers of soil bacteria and decreased the numbers of fungi, but both effects were of short duration and did not persist throughout the growing season. It is not known whether the increases in the numbers of soil bacteria were caused directly by the herbicide, or secondarily by death of the vegetation. The results of laboratory tests, which examined the direct responses of soil bacteria and fungi to the herbicide, suggest that the herbicide affected the soil microorganisms directly, rather than secondarily by death of the vegetation. The results indicate, in the author's opinion, that the use of sodium cacodylate for nonselective control of fescue meadow vegetation will have no drastic effect on the gross numbers of soil bacteria and fungi, nor on the decomposition processes in the soil.

Macklin and Witkamp (1973) studied the rate of decomposition of leaf litter from tulip poplar trees defoliated with cacodylic acid at one-third, 1 and 3 times the normal rate of application used for crown-kill. Tulip poplar trees with a diameter of 2.5 to 2.9 in at breast height (DBH) were injected with a cacodylic acid formulation, Silvisar 510 (containing 50% of AI), at the rate of 1 ml of formulation (equivalent to 0.719 g of cacodylic acid) per 2-in DBH, and one-third and 3 times that rate. Leaf litter was collected from the treated and from comparable untreated trees and transported to an area of forest floor beneath a mature stand of second growth tulip poplars away from the collection area. Data was collected weekly on carbon dioxide evolution, litter breakdown, and on densities of fungal mycelia and invertebrate taxa associated with both the treated and untreated litter.

At the triple dose rate (2.517 g of cacodylic acid per 2-in DBH), there was a significant reduction in carbon dioxide evolution from the forest floor. At both the normal (0.719 g per 2-in DBH) and the triple rate, densities of Entomobryidae (Collembola) increased significantly, while there was a significant decrease in the densities of fungal mycelia. However, all statistically significant effects were transitory. Over a 4-month period, cacodylic acid had no overall effect on the microbial processes in the study area, including decomposition processes and carbon dioxide evolution.

Bollen (1974) investigated the toxicity of cacodylic acid to microorganisms in forest floor and soil. Six bacteria (Bacillus subtilis, Micrococcus caseolyticus, Enterobacter aerogenes, Pseudomonas fluorescens, Streptomyces antibioticus and Streptomyces olivaceus) and 4 fungi (Penicillium claviforme, Pennicillium restrictum, Aspergillus nidulans and Trichoderma viride) were grown in pure culture on media to which cacodylic acid at concentrations of 0, 1, 10, 100, 1,000, or 10,000 ppm of arsenic had been added. The 2 Streptomyces species and the fungi were grown on plates which were incubated at 28°C for 4 weeks, while the remaining 4 bacteria were grown in nutrient broth cultures incubated at 28°C for 7 days.

The effect of cacodylic acid on liquid or plate cultures resulted in a slight reduction in growth of Bacillus subtilis and Micrococcus caseolyticus at 1,000 ppm of arsenic.

In further tests, triplicate samples of soil and forest floor material were treated with cacodylic acid at concentrations of 0, 10, 100 and 1,000 ppm of arsenic. Treated samples were incubated in pint bottles at 28° C, and carbon dioxide evolution was measured 7, 14, 21 and 28 days after treatment. The rate of carbon dioxide evolution was much greater from forest floor material than from soil. Cacodylic acid had no significant effect on the rate of carbon dioxide evolution from soil. In forest floor material, the rate of carbon dioxide evolution declined with increasing concentrations of cacodylic acid. However, even at the highest rate tested (1,000 ppm of arsenic), the CO_2 evolution decreased by only 10 to 20%.

Bollen (1974) pointed out that in the use of cacodylic acid for pre-commercial thinning in forests, concentrations of arsenic greater than 10 ppm in forest floor and soil will occur infrequently and will then usually be restricted to only a few square feet, providing careful handling and application techniques are used. He concluded that cacodylic acid will not seriously affect forest microbial populations, their decomposition of organic matter, or other functions important in the maintenance of soil fertility.

Da Costa (1972) studied the toxicity of several arsenic compounds to microorganisms as affected by phosphate. Fungi, including Pori monticola and Cladosporium herbarum, were grown on solid nutrient media to which the appropriate quantities of arsenicals and/or phosphates were added. One of the arsenicals completely inhibited the growth of Pori monticola at a concentration of 0.0025 molar. The growth of C. herbarum was reduced by 36% at 0.08 molar potassium arsenate. When increasing quantities of phosphate in the form of KH_2PO_4 were added, the fungi were progressively less inhibited. The addition of phosphate reduced the fungitoxicity of arsenite in the same manner, but not that of sodium cacodylate. The counteracting effects of phosphate on arsenate toxicity occurred with every one of a wide variety of microorganisms tested in the same manner. The author suggested that the fungitoxicity of arsenate is due to its competitive interference with phosphorus in oxidative phosphorylation, rather than to a reaction with sulfhydryl groups of proteins. He further suggested that the latter mechanism is, however, probably operative with sodium cacodylate, which would explain the fact that its fungitoxicity was not reduced by phosphate.

The data reviewed in this subsection indicates that cacodylic acid does not adversely affect soil micoorganisms under field conditions, even at concentrations much higher than those likely to result from commercial use in accordance with label directions. Some microorganisms appear to be capable of degrading cacodylic acid, as well as other organic arsenicals. In some studies (Malone 1971), cacodylic acid appeared to inhibit the growth of fungi more than bacteria, whereas in others (Zabel and O'Neil 1957), cacodylic acid and other organic arsenicals were more toxic to bacteria than to fungi.

The findings of Da Costa (1972) suggest that the toxicity of cacodylic acid to fungi may be due to reaction with sulfhydryl groups of essential proteins whereas the fungitoxicity of arsenates and arsenites seems to be due to the competitive interference of arsenic with phosphorus in oxidative phosphorylation.

Residues in Soil

Laboratory and Field Studies - The degradation of organoarsenicals in the soil is a complex chain of events. Complete degradation would involve mineralization of the herbicide molecule (Woolson 1974). Arsenic compounds are normal soil components; they contribute about 4 ppm of arsenic (dry weight) to most plants. Consequently, most plants are not adversely affected until high arsenic concentrations are reached in soils. For instance, Woolson et al. (1970 a, 1973) reported that arsenic concentrations in the upper 6 in of the soil of about 250 ppm reduced the growth of 4-week-old corn by approximately 50%. Under these conditions, dry plant material contained about 10 ppm arsenic (dry weight). Generally, according to Woolson et al. (1970a), the arsenic level required for phytotoxicity is variable, and is influenced by the chemical form and water solubility of the arsenic residues; soil fertility and PH; iron, calcium, aluminum and phosphorus present; plant vigor; and other factors.

The organic portion of organoarsenicals can be metabolized. Metabolism may include reduction to a volatile compound which may escape to the air (Woolson 1974).

According to Woolson (1974), the degradation of cacodylic acid in soil has not been extensively investigated. Woolson and Kearney (1973) studied the persistence and reactions of ^{14}C-labeled cacodylic acid in soils, with special emphasis on the chemical distribution of cacodylic acid into water-soluble iron, aluminum and calcium fractions in different soils under aerobic and anaerobic conditions. Three soils (Lakeland loamy sand, Hagerstown silty clay loam and Christiana clay loam) were treated with radiolabeled cacodylic acid at 1, 10 and 100 ppm in 50-ml covered beakers. There were 3 replicates per treatment. The soils were brought to 75% of field capacity and incubated at 25° C for 32 weeks. Grab samples were taken periodically and analyzed for the chemical distribution of cacodylic acid, for total arsenic, and for total ^{14}C content. The concentration of cacodylic acid was highest in the water-soluble fraction, followed in decreasing order by the aluminum, iron and calcium fractions. By contrast, inorganic pentavalent arsenic was largely present in the iron and aluminum fractions.

The persistence of cacodylic acid was a function of soil type. After 32 weeks, the following amounts of ^{14}C were recovered from the 3 study soils by combustion: Lakeland, 62%; Hagerstown, 53%; and Christiana, 23%. The rate of application had no appreciable effect on the disappearance of cacodylic acid. Since the total ^{14}C- cacodylic acid content generally paralleled a disappearance of water-soluble cacodylic acid, the rate of degradation

appeared to be a function of the concentration of water-soluble cacodylic acid and, consequently, of the amount of cacodylic acid available for microbial action. The results also indicate that cacodylic acid is not bound as readily in the soil as inorganic arsenic and is therefore more likely to be leached. Total ^{14}C as well as total arsenic decreased in all soils with time. A pungent garlic odor was detected in soils treated at the highest rate, suggesting the evolution of a volatile alkylarsine.

The authors conclude that the degradation of cacodylic acid in soils proceeds by 2 mechanisms. Under anaerobic conditions, 61% of the applied cacodylic acid was converted to a volatile organoarsenical within a 24-week period and was lost from the soil system. Under aerobic conditions, 35% was converted to a volatile organoarsenical compound. In addition, the carbon-arsenic bond cleaved, yielding CO_2 and AsO_4^{3-}. The volatile organoarsenical derivative may be dimethylarsine, an extremely unstable compound that may be oxidized by air to the oxide or back to cacodylic acid and returned to the earth by fixation to plants or soils. Dimethylarsine may also be oxidized by rainfall. The ultimate environmental fate of the arsenic from cacodylic acid, according to Woolson and Kearney (1973), appears to be metabolism to inorganic arsenate which is bound in the soil in an insoluble form.

Ehman (1963b) studied the movement of cacodylic acid in treated soils. Samples of pasture sod 10-in thick were obtained from fields of clay, silt-loam, and sand. The samples were placed into 6 specially-constructed wooden boxes. Three boxes were lined with polyethyline and equipped with holes and drains at the bottom for collection of seepage samples. For several weeks, the samples were watered lightly and allowed to acclimate to artificial indoor lighting conditions. The 6 boxes were then each sprayed with cacodylic acid at a rate equivalent to 15 lb/AI/acre. Twelve hours after treatment, each of the boxes equipped for collection of seepage was watered with the equivalent of 1/2 in of rainfall. Subsequent waterings were at 1, 2 and 4 weeks. Twenty-four hours after each watering, soil samples were taken from the first and second 3 in and from the bottom 4 in of each type of sod. The soil samples were air-dried and analyzed for arsenic content. Seepage samples were also analyzed for arsenic, as well as for basicity or acidity.

The results indicated that after 4 weeks, essentially all of the arsenic added to each of the 3 soils in the form of cacodylic acid remained in the soil. Analysis of the seepage samples indicated that some leaching occurred in the first 24 hr after treatment. After that, all samples showed a very low leaching of arsenic in all soil types. The author concluded that cacodylic acid is quite strongly bound by all 3 soil types; that a small but steady leaching of cacodylic acid occurred in the watered soil; and that cacodylic acid, applied to a sod surface, distributed rather evenly in about 1 week to a depth of 10 in.

In a companion study, Ehman (1963a) observed the residual effects of cacodylic acid on 7 crops, including snap beans, potatoes, sweet potatoes, carrots, chinese cabbage, field corn and soybeans. Field plots were laid out, fertilized and sprayed with a cacodylic acid formulation (Ansar 138,

containing 65% cacodylic acid) at a rate equivalent to 5 lb/acre of cacodylic acid. One-half of the plots were sprinkled with the equivalent of 1/2 in rain 24 hr after treatment. Plots were then planted with 2 20-ft rows of each of the 7 study crops. Composite soil samples collected just before treatment showed an average arsenic content of 3.68 ppm. The average of all untreated samples was 3.98 ppm of arsenic. The cacodylic acid treatment resulted in an average increase in the soil arsenic content of 3 ppm at the 3-in depth. There was no significant uptake of arsenic by edible parts of the crops in the treated plots. Some elevated levels of arsenic were found in leaves and stems of snap beans. The watering just after treatment had no effect on the arsenic content of the soil samples.

In a similar study (Ehman 1964), alfalfa and ryegrass were planted on pastureland treated with cacodylic acid (Ansar 138 formulation) at a rate equivalent to 5 lb/AI/acre 3 days prior to planting. Two of the 4 treated plots were watered with the equivalent of 1/2 in of rainfall prior to planting. Composite samples of the first cutting of alfalfa and ryegrass, and pre- and post-treatment soil samples were analyzed for arsenic content. The arsenic content of the soil samples increased by about 3 ppm, but there was no uptake of arsenic by the 2 crops.

The effects of 6 annual applications of cacodylic acid on arsenic residues in soil have also been studied. Cacodylic acid (Phytar 560 formulation) was applied near Weslaco, Texas, for 6 consecutive years at the rates of 2.5 and 7.5 lb/AI/acre/yr. Soil cores were collected at the end of each growing season at 3 different depths ranging from 0 to 18 in. After 6 annual applications, both rates of cacodylic acid resulted in a statistically significant build-up of arsenic in the upper 6 in of soil (2.4 to 4.5 ppm arsenic above an average background of 11 ppm). Arsenic residues in the 6- to 12-in soil layer were increased only by the higher rate of cacodylic acid, and the arsenic residue levels at the depth of 12 to 18 in were not affected significantly by any of the cacodylic acid treatments.

During the 6-yr study period, a total of 8.1 and 24.0 lb of elemental arsenic were applied in the form of cacodylic acid at the 2 treatment levels. These figures were converted to parts per million of arsenic in the soil and added to the measured average background arsenic levels to arrive at the theoretical level of arsenic that would be expected in the soil after the 6 annual treatments. For the 2.5 lb/acre cacodylic acid rate, the total added arsenic was 4.1 ppm. When added to the 11.0 ppm background, the total arsenic level should have equalled 15.1 ppm; 13.4 ppm of arsenic were actually found.

For the 7.5 lb/acre cacodylic acid treatment series, the calculated level of arsenic when added to 11.0 ppm background was 12.2 ppm. The total arsenic level should have equalled 23.2 ppm; 18.1 ppm of arsenic were actually found, a deficit equivalent to 28.17% of the predicted concentration.

Speculating about possible reasons for these deficits, the investigators reject leaching losses because throughout the entire 6-yr test period there was no significant accumulation of arsenic residues in the 12- to 18-in soil horizon. Microbial reduction of organic arsenicals to gaseous methylarsines

appears to be a more plausible loss mechanism. The investigators further suggest that the rate of reduction depends on the amount of organic arsenicals applied to the soil. The amount of arsenic "lost" from the soil in this study was proportional to the amount of organic arsenic added. Less than 1% of the added organic arsenic was not recovered at the lowest rate of application, while at the highest rate of application, 28% of the applied arsenic was not recoverable in plots treated with cacodylic acid at 7.5 lb AI/acre. The 2 intermediate organic arsenic application rates resulted in intermediate percentages of arsenic not accounted for.

If their assumptions are correct, the investigators hypothesize that an equilibrium may eventually be reached in which loss mechanisms would remove arsenic from the soil at the same rate as it is applied.

The treatment rates of cacodylic acid selected for this study are equivalent to the recommended single treatment dose and 3 times the recommended single treatment dose. The low rate of cacodylic acid corresponds to the normal amount of this chemical that could be applied once during a growing season; the high rate corresponds to the cumulative seasonal dose of 3 separate applications (Sandberg et al. 1973).

In the studies by Woolson and Kearney (1973), rates of application of cacodylic acid ranging from 1 to 100 ppm had no appreciable effect on its disappearance from 3 different soils. This observation would not support the hypotheses of Sandberg et al. (1973). However, the rate of degradation or disappearance of cacodylic acid varied considerably with different soil types in the test by Woolson and Kearney (1973). Furthermore, their studies were conducted under laboratory conditions over a time span of only 32 weeks, while the studies by Sandberg et al. were conducted in the field and extended over a period of 6 yr.

In an earlier study (Ehman 1967), plots of loamy fine sand in Fairfax, South Carolina, were sprayed with cacodylic acid (Phytar 138 formulation) at 50 lb/AI/acre. Three rates of another arsenical compound were studied comparatively (15, 50 and 100 lb/AI/acre).

On the day of treatment, cotton, soybeans, sorghum and peanuts were planted in these plots. The initial peanuts had to be replanted 1 month later because of excessive stunting of the first crop, especially in the cacodylic acid-treated plots. Four weeks after planting, cotton, soybeans and sorghum were also severely stunted in the cacodylic acid-treated plots. Eight weeks after planting, the 3 crops were still somewhat stunted in the cacodylic acid plots. The replanted peanuts were again somewhat stunted, but not as severely as the first crop. All crops were harvested at the appropriate times in the fall, and samples were analyzed. The same plots, without retreatment, were planted with cotton, soybeans, grain sorghum, peanuts, oats, corn, and tobacco the following year. There were no apparent adverse effects on these crops from the cacodylic acid treatment applied the previous year. Cottonseed, soybeans, sorghum grain and corn samples from the treated plots showed somewhat higher arsenic residues each year as compared to untreated control samples, with some reduction as time passed (Ehman 1967).

In summary, the reports reviewed in this subsection indicate that herbicidally effective concentrations of cacodylic acid "disappear" rapidly from soils under field conditions. Microbial degradation appears to contribute partially to this loss. Several different chemical reactions seem to be involved. According to Woolson (1974), cacodylic acid in the soil may undergo a number of different chemical and biological transformations, including formation of insoluble and biologically inactive arsenical salts; binding to soil-arsenic complexes by adsorption or ion exchange; oxidative demethylation to inorganic ortho arsenic acid; reduction to biologically active arsines; and reductive methylation to biologically active methylarsines.

Monitoring Studies - In the National Soils Monitoring program for pesticides (Stevens et al. 1970; Wiersma et al. 1971, 1972a, 1972b; and Carey et al. 1973), arsenic residues have almost never been found in the samples of cropland, noncropland and urban soils which were collected and analyzed. In general, it is believed that most of these arsenic residues come from natural sources; little or no correlation was found between high soil residue levels of arsenic and the geographical use patterns of organic arsenical herbicides, or of inorganic arsenical pesticides.

Cacodylic acid accounts for only a very small fraction of the total quantity of arsenic applied in various forms and formulations for pesticidal purposes in the United States. In view of the apparent lack of correlation between environmental arsenic levels found in monitoring studies and the use patterns of major arsenical pesticides, an attempt to correlate arsenic monitoring data with cacodylic acid use does not appear to be promising.

Residues in Water

Cohan (1971) studied the arsenic content in irrigation water following ditchbank application of cacodylic acid (sodium salt) to watered canals on the Rio Grande, Texas, project of the Bureau of Reclamation. One canal, 2.1 miles in length, was treated with cacodylic acid at the rate of 5 lb/acre. The spray rig moved downstream while applying the herbicide to both banks and the complete water surface. This is not the normal method for herbicide application to a ditchbank, but represents the maximum concentration of herbicide that could occur under similar operating conditions. The highest arsenic concentration found in the water in this canal was 0.86 ppm 10 min after spraying. The arsenic concentration declined rapidly thereafter and dropped to below 0.1 ppm within 110 min after spraying.

Two other canals, 2.25 and 2.2 miles in length, respectively, were treated at the same rate (5 lb/acre). The spray rig moved downstream spraying one bank, then turned around and, traveling upstream, sprayed the other bank. This represents normal herbicide application procedure. The maximum arsenic concentrations found were 0.16 ppm in one canal 5 min after spraying, and 0.17 ppm in the second canal 70 min after spraying. The arsenic concentration persisted only for short periods of time.

The arsenic concentration dropped to less than 0.1 ppm within 15 min after spraying the first canal, and within 100 min after spraying in the second canal.

Cohan's report does not analyze residues from canal bottoms or the effect on plants along the edge of the canal. There is no mention of possible effects on animals in and along the canals.

Lehn et al. (1970) studied the effects of aerial applications of cacodylic acid to a test area on 3 freshwater streams draining the test area. The experimental design and other study parameters employed by these authors are described in the subsection on Aquatic Effects. Lehn et al. reported that water and silt samples were taken from the 3 streams before, during, and after the spraying of cacodylic acid. The limit of sensitivity of the analytical method employed was 0.05 ppm. No detectable arsenic residues were found in any of the water or silt samples analyzed in this program. The authors pointed out that these levels are lower than background levels of arsenic in other aquatic systems and concluded that there was no appreciable migration of arsenic residues from the test area to any of the 3 streams draining it.

Braman and Foreback (1973) analyzed environmental samples, including samples of water from several rivers, ponds, and lakes, for arsenate and arsenite ions and methylarsenic acids in nanogram amounts. Dimethylarsinic acid (cacodylic acid) residues ranging from less than 0.002 to 0.6 parts per billion (ppb) were found in 7 natural waters (fresh waters) collected in and around Tampa, Florida. In 3 samples of saline waters, dimethylarsenic acid concentrations found ranged from 0.2 to 1.0 ppb. All of these samples also contained small, varying amounts of MAA, and of trivalent and pentavalent arsenic. The authors pointed out that dimethylarsinic acid is a major and ubiquitous form of arsenic in the environment, and that it is particularly involved in biological systems. MAA was generally found in smaller concentrations than dimethylarsinic acid, probably because it is only an intermediate in the the arsenic methylation sequence. Dimethylarsinic acid is very resistant to oxidation and could have considerable residence time in natural waters, unless subject to bacterial oxidation.

Woolson (1974) states that the organic arsenical herbicides, including cacodylic acid, are relatively nontoxic to fish and that, in addition, the movement of these compounds from treated areas to water containing fish is likely to be minimal because of fixation phenomena in plants, soils, and sediments.

Residues in Air

Some investigators have suggested that organic arsenicals, including cacodylic acid, may be reduced and methylated to form volatile, biologically active methylarsines which escape to the air from treated areas. No data was found on the possible presence and fate of such degradation products of cacodylic acid (or of other organoarsenicals) in air.

The Ansul Company pointed out that cacodylic acid has an extremely low vapor pressure so there is no possibility of movement in air by volatilization. There is some evidence of microbiological reduction and methylation of these organic arsenicals to trimethylarsine. The Ansul Company believes that this degradation is of a low order of magnitude since trimethylarsine is rapidly oxidized in air to a nonvolatile, pentavalent arsenical. Trimethylarsine is spontaneously inflammable in air, in contrast to the relative stability of dimethylmercury in air.

Newton (1971), based on his studies reviewed in the subsection on "Interactions with Lower Terrestrial Organisms," concluded that high concentrations of organic arsenicals are susceptible to attack by molds, and perhaps other microorganisms. Newton supported his conclusion by citing an experimental procedure where significant amounts of arsenic were lost with no possible opportunity for loss. He interpreted this as conclusive evidence of loss by volatilization. Because the boiling points of the organic arsines are 52.7°C (for trimethylarsine) or lower (Lange 1956), and because the other volatile arsenic compounds implicated (cacodyl and cacodyl oxide) have boiling points ranging above 150°C (Lange 1956), the conclusion is drawn that the arsines are the principal metabolite responsible for escape of arsenic from these cultures. The work of Challenger (1951) also supports this assumption that trimethylarsine constitutes an important fraction of the lost arsenic.

The work reported here, together with conclusions drawn by Challenger (1951), Newton and Holt (1971) and others, suggests that there may be substantial losses of arsenic through volatilization after application of organic arsenical herbicides. Because of this phenomenon, the role of the organic arsenical herbicides as persistent compounds needs to be reexamined.

Ehman (1963c) reported on the toxicity of smoke and vapors from burning grass previously treated with cacodylic acid. Plots were laid out in a field of good pasture grass in August of 1963. One plot was treated at the rate of 5 lb/acre of Ansar 138, a formulation containing 65% cacodylic acid; another plot was treated at the rate of 15 lb of cacodylic acid formulation per acre, and a third plot was left untreated. Five days after treatment, the grass in the treated plots was cut, and samples from all 3 plots were analyzed. The arsenic content of the 3 dried grass samples was as follows: untreated, 0.3 ppm; 5 lb/acre, 134 ppm; and 15 lb/acre, 197 ppm. After each grass sample was burned for the production of smoke, the ash was analyzed and found to contain 25 ppm arsenic following the 5 lb/acre treatment, and 96 ppm following the 15 lb/acre treatment.

Three groups of 10 albino rats each were then exposed to smoke produced by burning 3 of the grass samples in a series of tests. Three grams of grass was burned in a "bee smoker," and the smoke was pumped into a closed chamber (6 cu ft) containing the rats. The animals were subjected to the smoke for 15 min, and the chamber was opened for a 15-min ventilation period. This cycle, 30 min in length, was repeated 10 times, and a total of 30 g of one of the 3 grass samples was burned for each group of 10 rats. After the tenth exposure, 5 rats were sacrificed, and their lungs were removed for histological examination. Five untreated animals (not exposed to any grass smokes) were also

sacrificed as negative controls. The remaining test animals, 5 from each of the 3 grass smoke exposures, and 5 negative control animals were observed for a 2-week period. At the end of the period all surviving animals were sacrificed and lung tissues were collected and examined histologically.

All animals exposed to the smoke and vapors from the burning grasses showed signs of discomfort during the exposure periods, without significant differences between samples. The animals held over for observation were sick and gasped. Mortality was as follows:

Negative control	No deaths
Untreated grass	2 deaths at 10 days, 1 death at 12 days
5 lb/acre grass	1 death at 5 days, 1 death at 7 days
15 lb/acre grass	2 deaths at 1 day, 1 death at 4 days

Clinical observations of the animals during the 2-week post-exposure period did not show any marked variations between the positive control and test groups. Histological examination showed more acute degeneration of the bronchial epithelium in animals exposed to smoke from the grass treated at the highest rates, as compared to the animals exposed to the grass treated at the lower rate, or the untreated grass. This may indicate an increased irritation and inflammation of mucous membranes from smoke produced by burning grass treated with high rates of cacodylic acid.

In a second smoke inhalation study, the same test methods were employed, except that only 2 g of grass were used per exposure, in contrast to 3 g/exposure used in the first study. In the second study, no animals were sacrificed at the end of the exposure period, but all were observed for 14 days following exposure.

Some signs of irritation were again noted in all animals exposed to the smoke from burning the grass samples. Only animals exposed to smoke from the grass treated at 15 lb of cacodylic acid formulation per acre exhibited labored breathing after the 10 exposures, and one animal in this group died 4 days later. Histological examination showed an increased peribronchial lymphoid infiltration in tissue from the animals exposed to the smoke from burning the grass treated at the highest rate.

Ehman (1963d) also studied the toxicity to plant life of smoke from burning grass previously treated with cacodylic acid. Potted lima bean, corn, cotton, and wheat seedling plants were placed in a 6 cu ft chamber and exposed to smoke from a 3 g sample of pasture grass that had previously been treated with 15 lb/acre of Ansar 138, a formulation containing 65% cacodylic acid. After 20 min, 2 plants of each variety were removed from the chamber. The remaining plants were exposed to 2 additional grass-burning cycles. Two more plants were removed after each cycle. All plants were held for 1 week after exposure, at which time phytotoxicity was recorded. Beans exposed to the smoke of treated grass showed slight to severe damage; beans exposed to the smoke of untreated grass showed slight to moderate damage. Corn, cotton, and wheat showed no injury from exposure to the smoke of either treated or untreated grass.

Bioaccumulation, Biomagnification

Isensee et al. (1973) studied the distribution of ^{14}C-labeled cacodylic acid and dimethylarsine among aquatic organisms in a model ecosystem including mosquitofish (Gambusia affinis), Daphnia magna, Physa snails, and algae (Oedogonium cardiacum). The ecosystems were set up in glass aquariums 25.4 x 5.2 x 17.8 cm in size, each filled with 4 liters of "standard reference water" modified by increasing the NH_4NO_3 and K_2HPO_4 concentration 5-fold to obtain satisfactory growth of algae. The tanks were kept in the greenhouse in a shallow water bath maintained at 22 ± 1°C. Ten snails, a few strands of algae, about 30 daphnids, and a few milliliters of water from a previously set up aquarium (containing various diatoms, protozoa, and rotifers) were added to each tank. Five days later, duplicate tanks were treated with ^{14}C-labeled cacodylic acid at the rate of about 11.5 ppb added directly to the solution. After 29 days exposure to cacodylic acid, samples of daphnids were taken from each tank, and 2 fish were added. The experiment was terminated 3 days later since the fish had consumed all remaining Daphnia. Fish, daphnids, snails, and algae were thus exposed for 3, 29, 32, and 32 days, respectively. All organisms in both control and treated tanks prospered during the test period, indicating that the rate of cacodylic acid used was not toxic.

The concentration of cacodylic acid in the solution 24 hr after it was added was 10.6 ppb, based on radioactivity of the parent compound, equivalent to 92% of the original radioactivity placed in solution. The authors attributed the 8% loss of cacodylic acid radioactivity to initial absorption to algae or other organisms. After 32 days, the solution concentration of cacodylic acid had decreased to 6.1 ppb, a loss of 42% of the initial radioactivity measured at 24 hr. Seventy percent of this loss activity was accounted for in the biomass (sum of living and dead organic material). Algae accounted for 74% of the total biomass by weight, 95% of the radioactivity contained in the biomass, and 28% of the activity added at the beginning of the experiment. Thus, in this system, algae were the primary sink in which cacodylic acid residues accumulated. Algae and daphnids bioaccumulated more cacodylic acid than did the 2 higher food chain organisms (snails and fish), indicating that cacodylic acid did not biomagnify between food chain organisms.

Isensee et al. (1973) studied ^{14}C-labeled dimethylarsine in a parallel test series under the same experimental conditions. The rate of disappearance of the radioactivity introduced into the system by dimethylarsine and its accumulation in each organism were so similar to the behavior of cacodylic acid as to raise the question of compound identity. The tanks were aerated, providing oxidizing conditions that might convert dimethylarsine to cacodylic acid. To test this hypothesis, snail extracts were analyzed by thin layer chromatography. Radioautographs from both compounds had similar R_f values, but differed sufficiently with respect to tailing and ratios of mobile and nonmobile activity to indicate that several different chemical species were present.

A second experiment of shorter duration was performed to determine the relative importance of uptake from solution versus ingestion of one food chain organism by another in the distribution of cacodylic acid among food chain elements. Solutions containing 0.1, 1.0, and 10.0 ppm radiolabeled cacodylic

acid were prepared, and about 500 mg algae and 300 Daphnia were exposed to these concentrations for 2 days. Samples were taken for analysis, and the remaining algae and Daphnia were placed in separate solutions not containing cacodylic acid. Two fish were added to the untreated solutions containing Daphnia, and 4 snails were added to the untreated solutions containing algae. Two fish and 4 snails were also added to the treated solutions from which algae and Daphnia had been removed. All fish were harvested after 2 days, and 2 snails were harvested after 7 days.

Fish and snails accumulated 2 to 10 times more cacodylic acid from solution than they obtained by consuming cacodylic acid-treated Daphnia or algae. Only a limited supply of treated Daphnia was available to the fish, and it is not known whether or not a larger supply would have resulted in more accumulation of cacodylic acid residues. By contrast, the snails had an ample supply of algae, but after 7 days they also accumulated less cacodylic acid from algae than from treated solution. The authors concluded that under the conditions studied, uptake from solution was more important than consumption of one food chain organism by another, especially for the algae-snail part of the food chain.

The authors commented that there was considerable variability between replications, and that this seems to be an inherent problem in working with complex, multiorganism systems. Nevertheless, they consider the ecosystem a useful tool for indicating the likely behavior of compounds in the environment.

In response to the current concern over the distribution of pesticides in the environment, Schuth et al. (1974) reexamined the accumulation of cacodylic acid in an experimental aquatic ecosystem using different aquatic organisms. The model ecosystem used by Isensee et al. (1973) was considerably reorganized to include bottom feeding organisms (catfish, Ictalurus punctatus; and crayfish, Procambarus clarki) indigenous to cotton-producing areas, and duckweed, Lemna minor L. Three soils from a cotton-producing region in Texas, namely Hidalgo clay loam, Laredo silt loam, and Willacy sandy loam, were treated with a mixture of ^{14}C-labeled and unlabeled cacodylic acid so as to contain 21.4 ppm of cacodylic acid, a rate which approximately equals the concentration in the upper 3.8-cm layer of soil after application of the highest rate used in the field. After mixing, the soils were layered on the bottom of separate 110-liter glass tanks; covered with pea-gravel and aluminum window screen; flooded with 80 liter of distilled water; and allowed to equilibrate for 1 week without aeration. One control tank each of the Hidalgo and Laredo soils were also prepared, containing all components except the cacodylic acid. After 1 week, aeration was started and 7 catfish, 3 crayfish, several hundred daphnids, 10 snails, several hundred mg of filamentous algae, and 10 to 20 duckweed plants were added to each tank. Catfish and crayfish were fed brine shrimp and chopped perch, respectively, every 3 to 4 days. A screen was used to vertically bisect the tanks to protect the catfish from the predacious crayfish.

Twenty-three days after the organisms were added, an infestation of crayfish by parasitic Lerneus species made it necessary to harvest all organisms.

About 12.5 ppm of $KMnO_4$ was added to each tank 1 and 5 days later to kill the parasites. A second group of organisms was added 9 days later and harvested after 20-day exposure; no parasites were observed in this compliment. The ^{14}C and arsenic contents were determined intermittently in each component of the ecosystem over the 60-day experimental period.

After 59 days, 13.5% of the ^{14}C radioactivity and 40.0% of the arsenic from the cacodylic acid originally supplied remained in the soil (average of the 3 soils). The differential losses of ^{14}C and arsenic indicate that the carbon-arsenic bond of cacodylic acid is split in soil (Woolson and Kearney 1973). The cacodylic acid concentration in water, based on total radioactivity, increased almost linearly throughout the first 30 days, then leveled off, and finally decreased.

In another experiment, it was determined that $KMnO_4$ did not destroy cacodylic acid, even when being heated during distillation of arsine. Comparisons between the ^{14}C activity and the distribution of arsenite, arsenate, and total arsenic in the water at 5 different points in time during the experiment led to the conclusion that the cacodylic acid wad degraded in at least 2 or 3 of the soils studied. The aquatic organisms accumulated considerably more ^{14}C than arsenic, indicating that the cacodylic acid was degraded, with subsequent uptake of ^{14}C by the plant life. Autoradiographs of thin layer chromatograms of snail and algae extracts failed to show any parent cacodylic acid storage in these organisms. However, in the first harvest of organisms, crayfish did accumulate detectable amounts of arsenic. The arsenic was measured in terms of Bioaccumulation Ratio (calculated as the concentration of arsenic in tissue divided by the concentration of arsenic in water). Ratios for the first harvest of crayfish ranged from 4.2 to 5.2 (Isensee et al. 1973).

A material balance for the arsenic in the model ecosystem shows that 5, 31, and 48% of the arsenic initially added to the 3 soils was lost during the experiment. A garlic-like odor was observed above the tanks on day 25 of the experiment. The authors suggested that it may have been dimethylarsine which is known to have such an odor. Quantitative differences in arsenic lost from the different soils may reflect differences in the populations of microorganisms capable of reducing cacodylic acid to volatile derivatives, and/or differences in the ability of the soils to retain arsenical compounds. In relation to the total arsenic in the system, the biomass was an insignificant sink for arsenic.

The authors concluded that cacodylic acid does not bioaccumulate in the aquatic organisms studied. Cacodylic acid was degraded to ^{14}C-containing products and inorganic arsenate, and reduction to volatile organoarsenical compounds may account for the observed loss of arsenic from the system.

Environmental Transport Mechanisms

In a proposed environmental cycle for arsenic, Woolson (1974) stated that the major inputs into the system come from air and water pollution and from the use of pesticides. Soil is the sink to which arsenic ultimately returns.

Arsenic reaches man through air, water, and food. Arsenate which is ingested is eliminated and returns to the water or soil phases of the environment. Plants and animals receive arsenic from air or water pollution, from the soil, or from pesticide use. Arsenicals reaching the soil may begin the cycle of chemical transformation, precipitation and/or uptake once again.

According to McBride and Wolfe (1971), arsenate may be converted to dimethylarsine by a number of reduction and methylation steps in which MAA and cacodylic acid are intermediates. Cacodylic acid and MAA can also yield dimethylarsine when subject to the same conditions as arsenate. Woolson (1974) suggests that the arsines produced are probably oxidized back to MAA or cacodylic acid, or demethylated and returned to the arsenate form in the soil. Methylation as well as demethylation can occur in the soil medium.

Braman and Foreback (1973) recently reviewed the available information concerning methylated forms of arsenic in the environment, and analyzed nanogram amounts. They detected trivalent arsenic, pentavalent arsenic, MAA and dimethylarsinic acid in samples of freshwater, saline water, bird eggshells, seashells, and human urine. Since they are identical with the biologically produced methylarsenic acids, the detection of the effect of added methylarsenic pesticides will be difficult. The continued introduction of arsenic compounds into the environment via pesticides and other human activity may eventually result in a general increase in their concentrations in water and air due to the bacterial mobilization of all forms of arsenic. The authors emphasized the need for information on the effect of all forms of arsenic on ecological systems.

Woolson et al. (1970b) stated that the organic arsenates have about the same leaching and fixing characteristics in the soil as was shown by Dickens and Hiltbold (1967) for inorganic arsenates. Additionally, several authors have shown that cacodylic acid is degraded to inorganic arsenate. Thus, in the final analysis, the behavior and fate of inorganic arsenate is of prime importance, regardless of the source of the arsenic. Arsenic applications to crops by way of pesticides for insect control, weed control, and defoliation desiccation may result in arsenic accumulations in the soil that may ultimately build up to levels toxic to plants as well as to other biota (Woolson et al. 1970b).

Lunde (1969) reported residues of organic arsenic in fish caught in Norwegian ocean waters: 5.2 to 21.6 ppm for herring (Clupses harengus), 3.1 ppm for mackerel (Scomber scomber), and 7.9 ppm for capelin (Mallotus villosus).

The data regarding the behavior of cacodylic acid in soil and water, although limited, indicates that movement of cacodylic acid from treated land to water by leaching or surface runoff appears to be minimal or nil. The observations from the treatment of irrigation ditchbanks with cacodylic acid support this conclusion. Cacodylic acid residues in the soil do not appear to be persistent. Accumulation of phytotoxic residue levels of the unchanged parent compound in the soil therefore appears very unlikely.

In a study of 5 annual applications of cacodylic acid to a sandy clay loam by the Ansul Company (1973), no increase in the amount of arsenic in the

plow layer was observed. Reduction of organoarsenicals to volatile methylarsines and their subsequent environmental redistribution were given as a possible explantion for lack of arsenic buildup in this study.

However, gradual accumulation of arsenic-containing degradation products in soils appears to be possible, especially in areas of heavy use of organoarsenical pesticides. Cotton fields receiving multiple applications of cacodylic acid and two other arsenicals used as defoliants would be an example. Little information seems to be available on the possible magnitude and significance of such arsenic buildup.

Furthermore, several studies reported above indicate that following application of cacodylic acid (and other organoarsenical pesticides), substantial quantities of arsenic escape to the air in the form of volatile, biologically active degradation products.

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PART II. INITIAL SCIENTIFIC REVIEW

SUBPART D. PRODUCTION AND USE

CONTENTS

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This section contains data on the registration, and on the production and uses of cacodylic acid. The section summarizes rather than interprets data reviewed.

Registered Uses of Cacodylic Acid

Federally Registered Uses - Cacodylic acid, also known as dimethylarsinic acid, or hydroxydimethylarsine oxide, is a contact herbicide that will defoliate or desiccate a wide variety of plants. It is nonselective in its action and is useful for general postemergence weed control. It does not have any pre-emergence herbicidal activity. Upon contact with green vegetation, cacodylic acid is absorbed into plant cells, killing them. Cacodylic acid's only apparent translocation is apoplastic. Appropriate surfactants are either included in formulated products, or may be added to the spray tank if they are not already contained in the formulation. Small quantities of cacodylic acid are used for tree killing and bark beetle control purposes in forest management.

Two basic manufacturers produce cacodylic acid in the United States--The Ansul Company, Marinette, Wisconsin, and Vineland Chemical Company, Inc., Vineland, New Jersey. Each company markets several different herbicide formulations containing cacodylic acid as sodium salt or acid by itself or in combination with other herbicides. In addition, a specialty formulation of cacodylic acid for tree killing purposes is available through the TSI Company, Flanders, New Jersey. (See subsection on Formulations, p. 111.)

Registered cacodylic acid uses and application rates are listed as follows:

1. General weed control in noncrop areas such as drainage ditchbanks; rights-of-way; along sidewalks, driveways and fences; along railways, highways and other roads; around buildings, ornamentals, lumber yards, grain elevators, parking lots, etc.

   Rate: 2.5 to 5.0 lb acid equivalent per 100 gal of water, applied at a volume sufficient to cover the unwanted vegetation to just short of run-off. Reapply as required (no limitations).

2. Weed control as a "directed application" in nonbearing citrus orchards (orange, grapefruit, tangerine, lemon and lime orchards), to be applied in interspaces between, and around the base of trees.

   Rate: 3.75 to 5.0 lb acid equivalent per acre, to be mixed with water at the rate of 2.5 to 5.0 lb acid equivalent in 50 to 100 gal, and applied as a full-coverage spray to just short of run-off. Application should be repeated as required if regrowth occurs, but no more than 3 applications per year are permitted. This use is not permitted in Florida.

3. Lawn renovation by application of cacodylic acid to lawn mowed to about 1 in height, preferably on a warm, sunny day.

Rate: About 8.5 lb acid equivalent per acre, equal to 3 oz of acid equivalent per 1,000 sq ft, in 4 gal of water. This rate corresponds to 10 fluid ounces of a cacodylic acid formulation containing 2.5 lb acid equivalent per gallon in 4 gal of water per 1,000 sq ft.

If green areas remain, reapply after 5 days. When top growth is all brown, dead vegetation should be removed, and the lawn may be promptly re-established because the phytotoxic properties of cacodylic acid are quickly inactivated on contact with soil.

4. Defoliation of irrigated and dryland cotton by aerial or ground application, to be applied when 50% or more of the cotton bolls are open, and 7 to 10 days prior to anticipated picking.

   Rate: On dryland cotton, about 0.8 to 1.0 lb acid equivalent per acre. In airplane applications, 5 to 10 gal of water should be used, and 15 to 25 gal of water per acre for ground applications.

5. For general postemergent weed control in noncrop areas, a combination product is registered and recommended that contains MSMA and cacodylic acid at the ratio of 2.4 parts MSMA and 1 part cacodylic acid. This combination offers quick burn-down of vegetation in conjunction with the systemic effect necessary to control certain deep-rooted perennial grasses and weeds. Weeds against which this combination product is registered and recommended include puncture vine, wild mustard, wild oats, chickweed, sandburn, common ragweed, pigweed, crabgrass, lambs-quarter, common plantain, prostrate spurge, giant foxtail and yellow foxtail. It provides top-kill of certain perennial grasses such as Johnson grass, dallisgrass and nutsedge.

   Rate: 4.25 to 8.5 lb of combined active ingredients in 40 to 100 gal of water per acre. Reapply as required.

6. Crown kill of undesirable trees, including both conifers and hardwoods, through spaced-cut injection methods.

   Rate: About 1 ml of a formulation containing 50% cacodylic acid per cut per 2 in of tree diameter at breast height (DBH) for trees below 8 in DBH; 1 ml of 50% formulation per cut per 1 in DBH for trees 8 in DBH and larger.

   Rate: Recommended rates vary somewhat depending upon whether conifers or hardwoods are to be killed, and whether the treatment is made during the growing or the dormant season. (See Table 12, p. 105.)

7. Bark beetle control is used by professional foresters and entomologists only; cacodylic acid can also be employed to control Southern pine beetle (Dendroctonus frontalis), spruce beetle (Dendroctonus rufipennis), Engelmann spruce beetle (Dendroctonus obesus), mountain pine beetle (Dendroctonus ponderosae), Douglas-fir beetle (Dendroctonus pseudotsugae), round-headed pine beetle

(Dendroctonus adjunctus), Arizona 5-spined beetle (Ips lecontei), pine engraver beetle (Ips pini), and the California 5-spined beetle (Ips confusus). Suggested uses include: pre-flight treatment (trap tree technique), pre-harvest treatment (elimination of logging debris as brood material), pre-cutting treatment (in areas to be disturbed as, for instance, in trail building), and post-flight treatment (lethal trap technique).

Rate: For best results, a complete, trough-like frill has to be made around the entire tree within 18 in of the ground. One milliliter of a 50% cacodylic acid formulation per inch of tree circumference is to be applied evenly in the frill. Pre-flight treatment (for spruce beetle only) may be made in October, with treated trees to be felled 4 weeks after treatment, or in the spring, 4 to 8 weeks before peak bark beetle emergence, with treated trees to be felled 2 to 4 weeks after treatment. Pre-harvest and pre-cutting treatments involve treating 4 weeks prior to cutting the tree. Post-flight treatments should be made within 2 to 3 weeks after the tree is attacked. (For further details, refer to table 13, page 105.)

Specimen labels for 2 widely used weed control formulations of cacodylic acid, a cotton defoliant formulation and a forestry use formulation, are included in this report. The labels give a complete overview of these registrations, including the range of dosage rates, general and specific directions for use, use limitations, caution statements and other fetails relevant to commercial use.

1. Table 10: Cacodylic acid formulation containing: 22.73% sodium cacodylate; 3.88% cacodylic acid; 12.75% total elemental arsenic, all in water soluble form; 2.48 lb cacodylic acid equivalent per gallon. This product also contains a surfactant.

   Product name: Phytar 560 Herbicide
   Manufacturer: The Ansul Company, Marinette, Wisconsin
   EPA Registration No.: 6308-20

2. Table 11: Cacodylic acid formulation containing: 27.38% sodium cacodylate; 4.67% cacodylic acid; 15.41% total elemental arsenic, all in water soluble form; 3.1 lb cacodylic acid equivalent per gallon. This product also contains a surfactant.

   Product name: Bolls-eye Cotton Defoliant
   Manufacturer: The Ansul Company, Marinette, Wisconsin
   EPA Registration No.: 6308-91-AA

3. Table 12: Cacodylic acid formulation containing: 50.0% cacodylic acid; 27.1% total elemental arsenic, all in water soluble form; 6.0 lb cacodylic acid equivalent per gallon. This product also contains a surfactant.

Product name: Silvisar 510 Tree Killer
Manufacturer: TSI Company, Flanders, New Jersey
EPA Registration No.: 28301-2

4. Table 13: Directions for the use of cacodylic acid for bark beetle control (by professional foresters and entomologists only).

5. Table 14: Cacodylic acid and MSMA formulation containing: 26.02% MSMA; 10.47% sodium cacodylate; 1.80% cacodylic acid; 17.92% total elemental arsenic, all in water soluble form; 3.0 lb MSMA and 1.25 lb cacodylic acid equivalent per gallon. This product also contains a surfactant.

Product name: Broadside Herbicide
Manufacturer: The Ansul Company, Marinette, Wisconsin

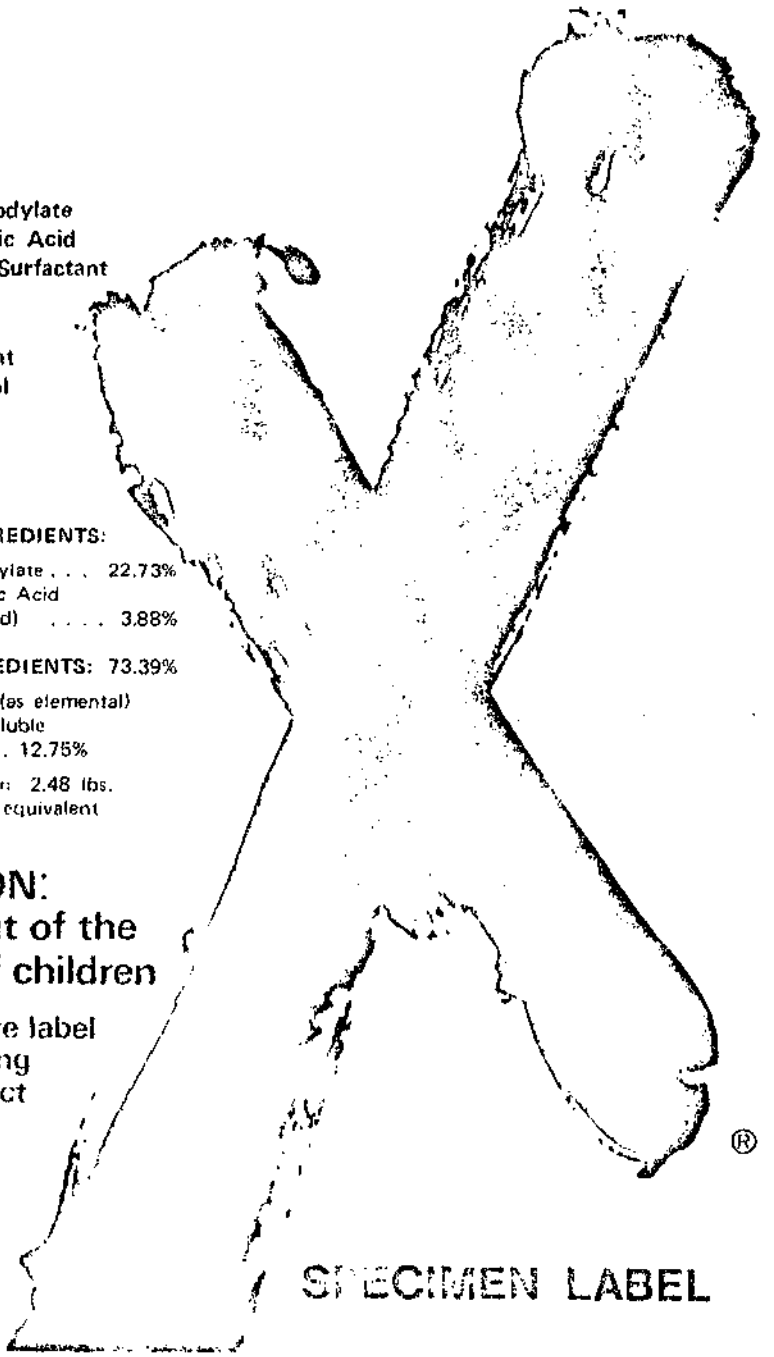
State Regulations - Toxicity studies indicate that cacodylic acid is not highly toxic to mammals. Some states that regulate the use of pesticides have placed special restrictions on pesticides which are highly toxic or otherwise hazardous to human and/or environmental health. For instance, in California, 42 specific pesticides have been designated as "injurious or restricted materials." The use of pesticides in this category is subject to special restrictions under regulations administered by the California State Department of Agriculture.

The California list of "injurious materials" includes "certain arsenic compounds," which include inorganic trivalent arsenicals and inorganic pentavalent aresnates, but not organic pentavalent arsenates, such as cacodylic acid. Therefore, cacodylic acid is not subject to special restrictions in California or, as far as is known, in any other state.

Table 10. CACODYLIC ACID (2.48 LB ACID EQUIVALENT PER GALLON) HERBICIDE SPECIMEN LABEL

Phytar® 560

Herbicide



Sodium Cacodylate and Cacodylic Acid Liquid Plus Surfactant

For General Post-Emergent Weed Control

ACTIVE INGREDIENTS:

Sodium Cacodylate . . . 22.73%
Dimethylarsinic Acid (Cacodylic Acid) 3.88%

INERT INGREDIENTS: 73.39%

Total Arsenic (as elemental) all in water soluble form 12.75%

Product contain: 2.48 lbs. cacodylic acid equivalent per gallon.

CAUTION:
Keep out of the reach of children

Read entire label before using this product

®

SPECIMEN LABEL

CAUTION: Keep Out of the Reach of Children

CAUTION. Harmful if swallowed. Avoid contact with skin. Avoid breathing spray mist. Wash hands after using. Avoid storage near feed or food products. Keep children and domestic animals off treated areas until this material has been washed into the soil.

Do not contaminate waters used for domestic consumption, or by animals, wildlife and aquatic life, or for irrigation purposes. Do not graze treated areas to livestock.

ANTIDOTE: If taken internally, induce vomiting and call physician at once.

READ ENTIRE LABEL BEFORE USING THIS PRODUCT.

WARRANTY – CONDITION OF SALE: DIRECTIONS FOR USE of this product are based on field use and tests believed reliable and should be followed carefully. It is however impossible to eliminate all risks associated with use of this product. Because such factors as weather conditions, foreign material and manner of use for application are all beyond the control of The Ansul Company or the Seller of this product, such things as crop injury, ineffectiveness or other unintended consequences may result. ALL SUCH RISKS ARE ASSUMED BY THE BUYER.

Ansul warrants that this product conforms to the chemical description on the label and is reasonably fit for the purposes referred to in the directions for use as modified by the above. Ansul makes no other warranties, express or implied, including FITNESS or MERCHANTABILITY. In no case shall Ansul or the Seller be liable for consequential, special or indirect damages resulting from the use or handling of this product. The foregoing is a condition of sale by The Ansul Company and is accepted as such by the Buyer.

GENERAL INFORMATION: PHYTAR 560 Herbicide is useful for general post-emergent weed control. It is non-selective in its action. Its phytotoxic properties are quickly inactivated on contact with soil. It contains a surfactant. **It is unnecessary to add any other surfactant to the spray solution.** Best results are obtained on young actively growing weeds. It produces top-kill only, so repeat applications are required for season long weed control of perennials.

MIXING INSTRUCTIONS: PHYTAR 560 Herbicide is completely water soluble. Any spray equipment that gives good coverage may be used. Fill the spray tank about half full with water and add the required amount of herbicide with agitation. Finish filling the tank with water and apply. After use, clean equipment thoroughly by flushing with water. Do not store spray solution in tank for a prolonged period. Although PHYTAR 560 Herbicide is only moderately corrosive, do not use in galvanized or aluminum equipment.

CONTAINER DISPOSAL: Do not reuse empty container. Wash thoroughly with water and detergent, crush if possible, and discard in a safe place.

DIRECTIONS FOR USE:

NON-CROP: PHYTAR 560 Herbicide is useful for general weed control on drainage ditchbanks and rights-of-way, along sidewalks, driveways and fences, around buildings and ornamentals, and on similar non-crop areas. Mix 1 to 2 gallons of PHYTAR 560 Herbicide in 100 gallons of water. Spray unwanted vegetation to just short of run-off. If regrowth occurs reapply as required.

Do not allow spray to come in contact with foliage, green bark, grafted unions, or scuffed, damaged or broken bark when spraying around trees and ornamentals.

AGRICULTURAL PLANTINGS - CITRUS (Except Florida): PHYTAR 560 Herbicide is useful as a directed application in non-bearing citrus orchards such as orange, grapefruit, tangerine, lemon and lime orchards. It should be applied at the rate of 1½ to 2 gallons per acre.

Mix 1 to 2 gallons of PHYTAR 560 Herbicide in 50 to 100 gallons of water. Apply as a directed spray in interspaces and around base of trees. Spray unwanted vegetation to just short of run-off. If regrowth occurs, reapply as required, however, **do not exceed 3 applications per year.**

Do not allow spray solution to contact leaves, stems or bark. Use a shield, if necessary, for nursery plantings or young trees. **Do not apply around trees from which fruit will be harvested within one year of treatment.**

LAWN RENOVATION: Mow lawn to about 1 inch high before treatment. Mix 10 fluid ounces of PHYTAR 560 Herbicide in 4 gallons of water and apply to 1,000 sq. ft. Spray foliage thoroughly, preferably on a warm sunny day, foliage will usually turn brown in about five days. Bermudagrass and other deep-rooted perennials, or partially sprayed foliage, may require a second treatment. Reapply five days later if green areas remain.

When foliage is all brown, matted areas should be raked to remove dead vegetation. The lawn may then be re-established according to local practice.

Keep children and pets off treated areas until after first rain or sprinkling following treatment. Do not track from treated to untreated areas.

PHYTAR 560 Herbicide is manufactured by The Ansul Company, Marinette, Wisconsin 54143.

U.S. Patents 3,173,937 and 3,056,668 and others pending.

Net Contents 5 Gallons

EPA Reg. No. 6308-20

Form No. C-7384

THE ANSUL COMPANY,
MARINETTE, WISCONSIN

Table 11. CACODYLIC ACID (3.1 LB ACID EQUIVALENT PER GALLON) COTTON DEFOLIANT SPECIMEN LABEL

Bolls-eye™

Cotton Defoliant

Sodium Cacodylate and Cacodylic Acid Liquid Plus Surfactant

For Use As A Defoliant For Irrigated and Dryland Cotton

ACTIVE INGREDIENTS:

Sodium Cacodylate . . . 27.38%
Dimethylarsinic Acid (Cacodylic Acid) 4.67%

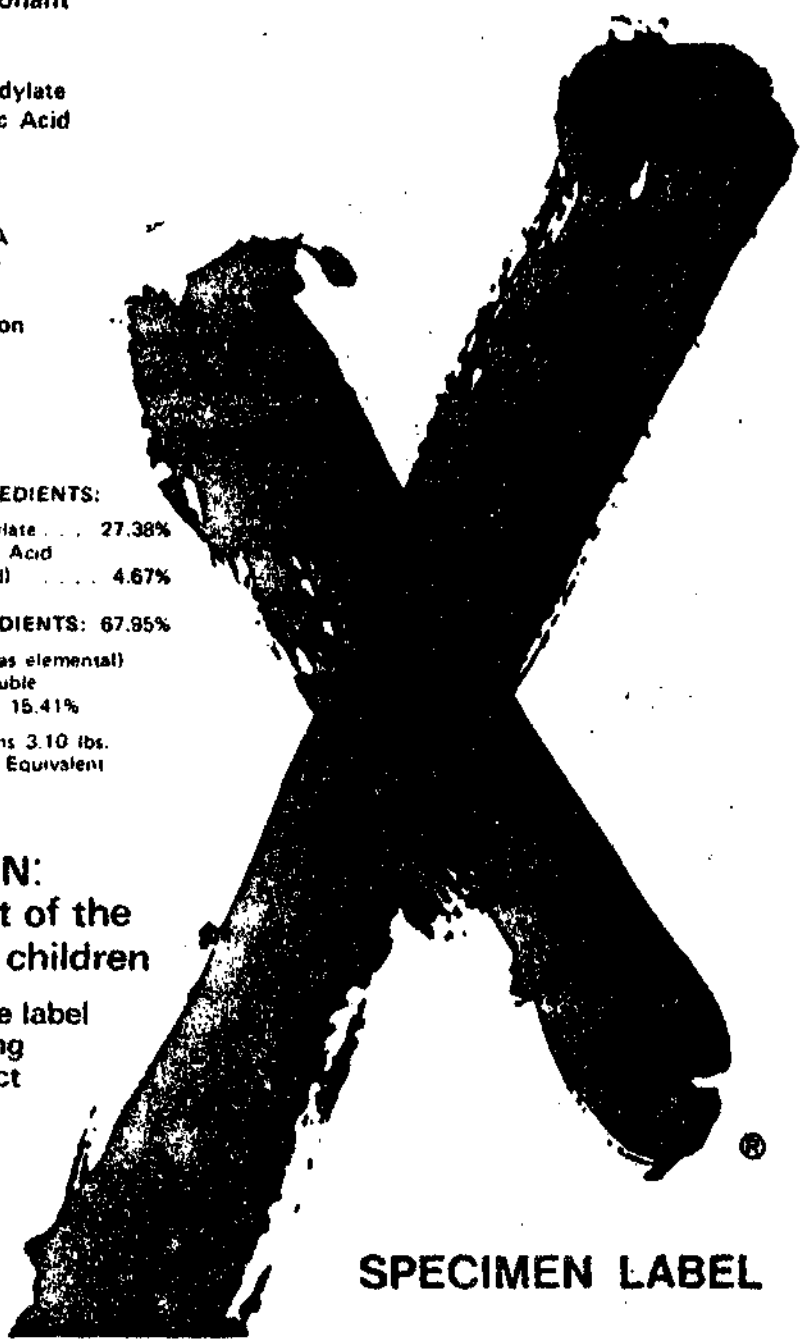
INERT INGREDIENTS: 67.95%

Total Arsenic (as elemental) all in water soluble form 15.41%

Product Contains 3.10 lbs. Cacodylic Acid Equivalent Per Gallon.

CAUTION:
Keep out of the reach of children

Read entire label before using this product



®

SPECIMEN LABEL

CAUTION: Keep Out of the Reach of Children

CAUTION: Harmful if swallowed. Avoid contact with skin. Avoid breathing spray mist. Wash hands after using. Avoid storage near feed or food products. Keep children and domestic animals off treated areas until this material has been washed into the soil.

ANTIDOTE: If taken internally, induce vomiting and call physician at once.

READ ENTIRE LABEL BEFORE USING THIS PRODUCT.

PATENT NOTICE: The price of this product includes the royalty of 10 cents per pound (for a license to use the contents hereof under the claims of U.S. Patent No. 3,378,364). A license under the said patent is available to anyone who wishes to practice the patented method with materials obtained from other sources.

WARRANTY -- CONDITION OF SALE: DIRECTIONS FOR USE of this product are based on field use and tests believed reliable and should be followed carefully. It is however impossible to eliminate all risks associated with use of this product. Because such factors as weather conditions, foreign material and manner of use for application are all beyond the control of The Ansul Company or the Seller of this product, such things as crop injury, ineffectiveness or other unintended consequences may result. ALL SUCH RISKS ARE ASSUMED BY THE BUYER.

Ansul warrants that this product conforms to the chemical description on the label and is reasonably fit for the purposes referred to in the directions for use as modified by the above. Ansul makes no other warranties, express or implied, including FITNESS or MERCHANTABILITY. In no case shall Ansul or the Seller be liable for consequential, special or indirect damages resulting from the use or handling of this product. The foregoing is a condition of sale by The Ansul Company and is accepted as such by the Buyer.

GENERAL INFORMATION: BOLLS-EYE Cotton Defoliant is used as a harvest aid for the defoliation of cotton. Its phytotoxic properties are quickly inactivated on contact with the soil. It is a combination of a defoliating agent and surfactant. It is desirable to add additional surfactant when using ground application equipment (see use directions), none need be added for aerial application.

CARE OF EQUIPMENT: Although BOLLS-EYE Cotton Defoliant is only moderately corrosive, do not apply with any applicator that is lined with zinc, tin, or aluminum.

MIXING INSTRUCTIONS: BOLLS-EYE Cotton Defoliant is completely water soluble. Fill the spray equipment reservoir about half full with water and add the required amount of defoliant with agitation. Finish filling the reservoir with water and apply. After use, clean equipment thoroughly by flushing with water. Do not store spray solution in tank for a prolonged period.

CONTAINER DISPOSAL: Do not reuse empty container. Wash thoroughly with water and detergent, crush if possible and discard in a safe place.

Do not contaminate waters used for domestic consumption, or by animals, wildlife and aquatic life, or for irrigation purposes. Do not feed treated foliage to livestock or graze treated areas.

DIRECTIONS FOR USE: BOLLS-EYE Cotton Defoliant is useful as a harvest aid for the defoliation of irrigated and dryland cotton with aerial or ground application equipment. For the most effective defoliation, good coverage of all leaves is essential.

Nozzles must be arranged to provide thorough coverage of the foliage. If applied by airplane, use 5 to 10 gallons of water per acre. This range will generally provide adequate coverage. If applied by ground equipment, a spray volume of 15 to 25 gallons of water per acre is preferred. With ground application equipment and at spray volumes of 15 to 25 gallons per acre, add 1/3 to 2/3 pints of a suitable surfactant.

DEFOLIATION OF DRYLAND COTTON: Apply 2 to 2.5 pints of BOLLS-EYE Cotton Defoliant per acre when 50% or more of the bolls are open and 7 to 10 days prior to anticipated picking.

DEFOLIATION OF IRRIGATED COTTON: Apply 2.5 to 3 pints of BOLLS-EYE Cotton Defoliant per acre when 50% or more of the bolls are open and 7 to 10 days prior to anticipated picking.

BOLLS-EYE Cotton Defoliant is manufactured by The Ansul Company, Marinette, Wisconsin 54143.

Net Contents 5 Gallons EPA Reg. No. 6308-91-AA

Form No. C-7374

THE ANSUL COMPANY,
MARINETTE, WISCONSIN

Table 12. CACODYLIC ACID (6.0 LB ACID EQUIVALENT PER GALLON) TREE KILLER SPECIMEN LABEL

Silvisar® 510

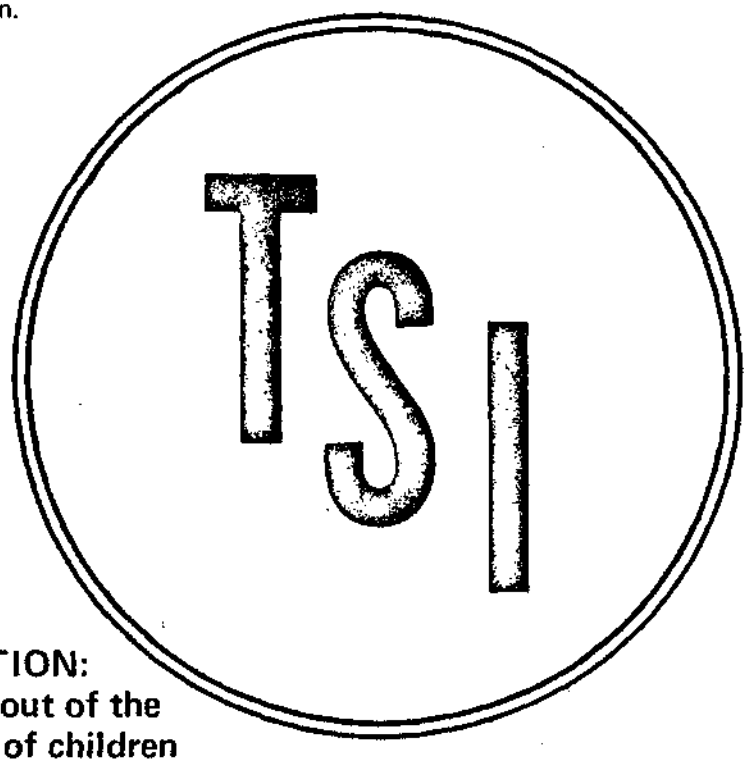
Tree Killer

For General Forestry Use

ACTIVE INGREDIENTS:
Dimethylarsinic Acid
(Cacodylic Acid) 50.0%

INERT INGREDIENTS: . . . 50.0%
Total Arsenic (as elemental)
all in water soluble
form 27.1%

Product contains 6.0 lbs.
dimethylarsinic acid equivalent
per gallon.



CAUTION:
Keep out of the reach of children

Read entire label
before using
this product

SPECIMEN LABEL

CAUTION: Keep Out of the Reach of Children

CAUTION: Harmful if swallowed. Avoid contact with skin. Wash thoroughly after using. Store in a safe place away from feed and food products.
ANTIDOTE: If taken internally, induce vomiting and call physician at once.
READ ENTIRE LABEL BEFORE USING THIS PRODUCT.
WARRANTY – CONDITION OF SALE: DIRECTIONS FOR USE of this product are based on field use and tests believed reliable and should be followed carefully. It is, however, impossible to eliminate all risks associated with use of this product. Because such factors as weather conditions, foreign material and manner of use for application are all beyond the control of TSI Company or the Seller of this product, such things as crop injury, ineffectiveness or other unintended consequences may result. ALL SUCH RISKS ARE ASSUMED BY THE BUYER.
TSI Company warrants that this product conforms to the chemical description on the label and is reasonably fit for the purposes referred to in the directions for use as modified by the above. TSI makes no other warranties, express or implied, including FITNESS or MERCHANTABILITY. In no case shall TSI or the Seller be liable for consequential, special or indirect damages resulting from the use or handling of this product. The foregoing is a condition of sale by TSI Company and is accepted as such by the Buyer.
GENERAL INFORMATION: SILVISAR 510 Tree Killer is designed for crown kill of undesirable trees, including both conifers and hardwoods, through spaced-cut injection methods. It shows negligible translocation through root grafts and has no residual phytotoxic action in the soil.
CARE OF EQUIPMENT: SILVISAR 510 Tree Killer is entirely soluble in water. Although SILVISAR 510 Tree Killer is only moderately corrosive, do not apply with any applicator that is lined with zinc, tin, or aluminum. Rinse all injection equipment thoroughly after use, and dispose of liquid wastes in a pit in non-crop lands located away from water supplies.
CONTAINER DISPOSAL: Do not reuse empty container. Wash thoroughly with water and detergent, crush if possible, and discard in a safe place.
DIRECTIONS FOR USE:
SPACED-CUT INJECTION WITH TSI "HYPO-HATCHET" INJECTOR: The TSI HYPO-HATCHET Injector cuts and injects in one operation. When a tree is struck with the injector, a pre-set amount of SILVISAR 510 Tree Killer is injected automatically into the sap stream of the tree immediately after impact. The injector works by inertia and is calibrated to inject at least one milliliter of chemical per stroke. The cuts should be evenly spaced around the trunk to give proper distribution into the sapwood. For detailed instructions on how to use the TSI HYPO-HATCHET Injector, refer to the Operation Manual.
CONIFERS AND HARDWOODS (Growing Season) – For trees below 8 inches diameter at breast height (DBH), make one cut per 2 inches of DBH (4½" spacing between cut edges) at waist height or below. For trees 8 inches DBH and larger, make one cut per 1 inch DBH (1½" spacing between cut edges).
CONIFERS (Dormant season) – Make one cut per 1 inch of DBH (1½" spacing between cut edges) at waist height or below.
HARDWOODS (Dormant season) – Make a complete frill at waist height or below.
SPACED-CUT APPLICATION: Although spaced-cut application is facilitated by use of the TSI HYPO-HATCHET Injector, a hatchet or similar cutting tool can be used. The number of cuts per tree depends upon the size of the cuts and the volume to be injected, but in any case, should be sufficient to hold the silvicide without running down the trunk. The cuts should be evenly spaced around the trunk to give proper distribution into the sapwood. Apply SILVISAR 510 Tree Killer with a pump-type oil can, plastic squeeze bottle, or other suitable dispenser; however, do not apply with any applicator that is lined with zinc, tin, or aluminum.
CONIFERS AND HARDWOODS (Growing season) – For trees below 8 inches diameter breast height (DBH), apply 1 milliliter of SILVISAR 510 Tree Killer per cut per 2 inches of DBH (6" spacing between cut centerlines) at waist height or below. For trees 8 inches DBH and larger, use 1 to 2 milliliters per cut per 1 inch DBH (3" spacing between cut centerlines).
CONIFERS (Dormant season) – Apply 1 milliliter of SILVISAR 510 Tree Killer per cut per 1 inch of DBH (3" spacing between cut centerlines).
HARDWOODS (Dormant season) – Apply 1 milliliter of SILVISAR 510 Tree Killer per cut in a complete frill at waist height or below.

SILVISAR 510 Tree Killer is manufactured by TSI Company, Flanders, New Jersey 07836.

SILVISAR, HYPO-HATCHET are registered trademarks U.S. Patent 3,173,937 and others pending.

Net Contents Gallons EPA Reg. No. 28301-2

TSI

TSI COMPANY
FLANDERS, NEW JERSEY, U.S.A.

Table 13. CACODYLIC ACID - DIRECTIONS FOR BARK BEETLE CONTROL

Silvisar® 510

SILVISAR 510 TREE KILLER FOR USE IN BARK BEETLE CONTROL FOR USE BY PROFESSIONAL FORESTERS AND ENTOMOLOGISTS ONLY

SILVISAR 510 Tree Killer can be used to control Southern pine beetle (*Dendroctonus frontalis*), Spruce beetle (*D. rufipennis*), Englemann spruce beetle (*D. obesus*), Mountain pine beetle (*D. ponderosae*), Douglas-fir beetle (*D. pseudtsugae*), round headed pine beetle (*D. adjunctus*), Arizona five-spined beetle (*Ips. lecontei*), pine engraver beetle (*Ips. pini*), and the California five-spined beetle (*Ips. confusus*) in treated trees. The treatment of trap trees intended for harvest or cutting can serve as an aid in the control of these pests in a forestry management program in the states of Virginia, Georgia, Louisiana, Texas, Oregon, Utah, Idaho, Wyoming and in the Rocky Mountains of South Dakota, Colorado, Arizona and New Mexico.

SUGGESTED USES

1) Pre-flight treatment (trap tree technique).
2) Pre-harvest treatment (elimination of logging debris as brood material).
3) Pre-cutting treatment (in areas to be disturbed, e.g., trail building).
4) Post-flight treatment (lethal trap technique).

DIRECTIONS FOR USE IN CONIFERS:

Make a complete, trough-like frill around the entire tree within 18 inches of the ground. Apply 1 milliliter (approximately 1/30 of an ounce) evenly in the frill for each inch of tree circumference.

1) **Pre-Flight Treatment** (for spruce beetle only)--
   Fall Treatment -- Treat in October and fell 4 weeks after treating. Use half strength (diluted with equal amount of water) or full strength SILVISAR 510 Tree Killer.
   Spring Treatment -- Treat 4-8 weeks before peak beetle emergence and fell 2-4 weeks after treating. Use half strength (diluted with equal amount of water) of SILVISAR 510 Tree Killer.
2) **Pre-Harvest and Pre-Cutting Treatments** (for all beetle species mentioned above)--Treat with full strength SILVISAR 510 Tree Killer at least 4 weeks before cutting the tree. Allow a minimum of 4 weeks between treating and felling.
3) **Post-Flight Treatment** (for all beetle species mentioned above)--Treat with full strength SILVISAR 510 within 2-3 weeks after the tree is attacked.

Form No. 73173 Litho in U.S.A.

Source: TSI Company, Flanders, New Jersey

Table 14. CACODYLIC ACID (1.25 LB ACID EQUIVALENT PLUS MSMA 3.0 LB PER GALLON) HERBICIDE SPECIMEN LABEL

Broadside®

Herbicide

MSMA Sodium Cacodylate
Liquid Plus Surfactant

For General
Post-Emergent
Weed Control

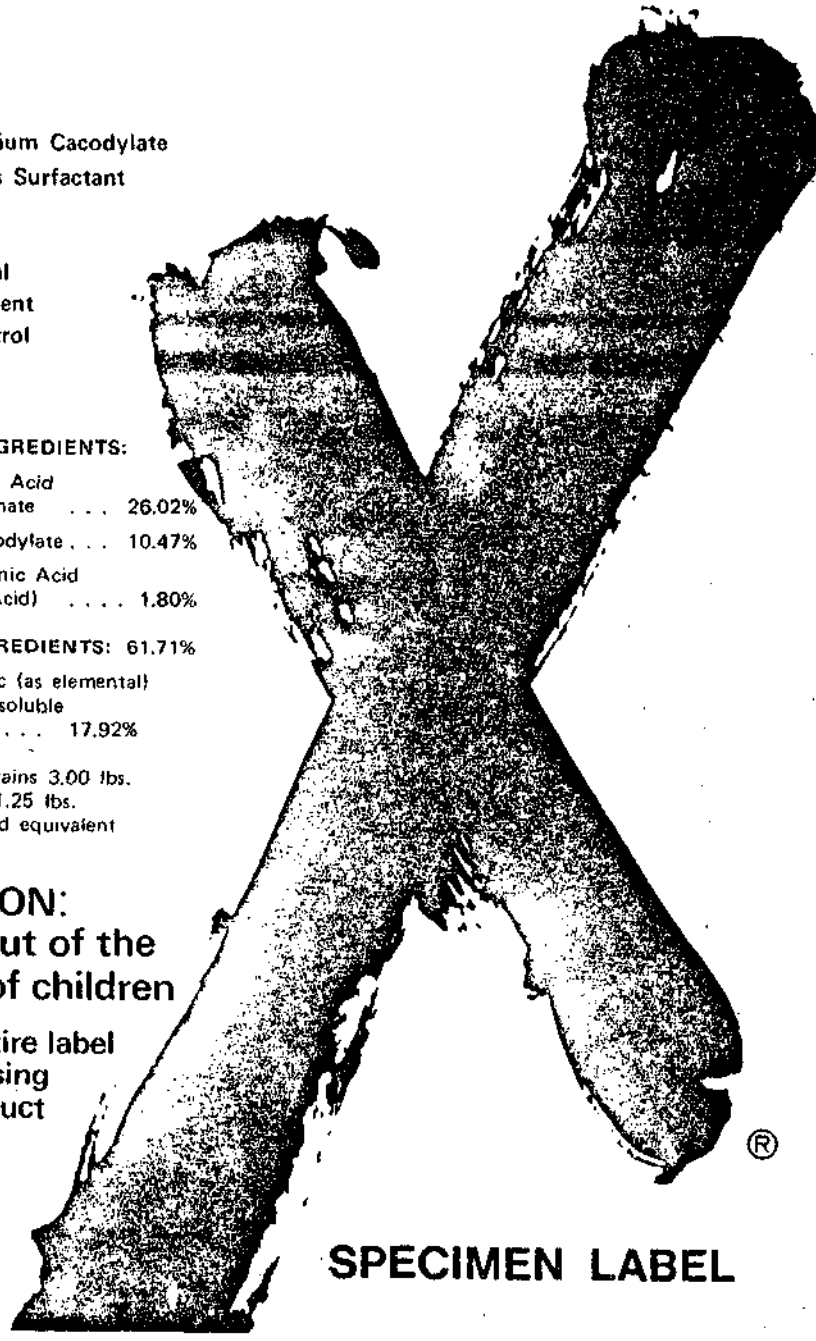
ACTIVE INGREDIENTS:

Monosodium Acid Methanearsonate . . .	26.02%
Sodium Cacodylate . . .	10.47%
Dimethylarsinic Acid (Cacodylic Acid)	1.80%
INERT INGREDIENTS:	61.71%
Total Arsenic (as elemental) all in water soluble form	17.92%

Product contains 3.00 lbs. MSMA and 1.25 lbs. cacodylic acid equivalent per gallon.

CAUTION:
Keep out of the reach of children

Read entire label before using this product



®

SPECIMEN LABEL

CAUTION: Keep Out of the Reach of Children

CAUTION: Harmful if swallowed. Avoid contact with skin. Avoid breathing spray mist. Wash hands after using. Avoid storage near feed or food products. Keep children and domestic animals off treated areas until this material has been washed into the soil.

ANTIDOTE: If taken internally, induce vomiting and call physician at once.

READ ENTIRE LABEL BEFORE USING THIS PRODUCT.

WARRANTY – CONDITION OF SALE: DIRECTIONS FOR USE of this product are based on field use and tests believed reliable and should be followed carefully. It is however impossible to eliminate all risks associated with use of this product. Because such factors as weather conditions, foreign material and manner of use for application are all beyond the control of The Ansul Company or the Seller of this product, such things as crop injury, ineffectiveness or other unintended consequences may result. ALL SUCH RISKS ARE ASSUMED BY THE BUYER.

Ansul warrants that this product conforms to the chemical description on the label and is reasonably fit for the purposes referred to in the directions for use as modified by the above. Ansul makes no other warranties, express or implied, including FITNESS or MERCHANTABILITY. In no case shall Ansul or the Seller be liable for consequential, special or indirect damages resulting from the use or handling of this product. The foregoing is a condition of sale by The Ansul Company and is accepted as such by the Buyer

GENERAL INFORMATION: BROADSIDE Herbicide is a special formulation of herbicides in combination with a surface-active (wetting) agent, for general post-emergent weed control. It is unnecessary to add any other surfactant to the spray solution. This product is effective on both broadleaf weeds and grasses. The phytotoxic properties of these materials are quickly inactivated on contact with the soil. Best results are obtained on young actively growing weeds at air temperatures above 70° F.

MIXING INSTRUCTIONS: BROADSIDE Herbicide is completely water soluble. Fill the spray equipment reservoir about half full with water and add the required amount of herbicide with agitation. Finish filling the reservoir with water and apply. After use, clean equipment thoroughly by flushing with water. Do not store spray solution in tank for a prolonged period.

CONTAINER DISPOSAL: Do not reuse empty container. Perforate, crush and bury in a safe place. Drums may be returned to a drum reconditioner.

DIRECTIONS FOR USE:

BROADSIDE Herbicide is a post-emergent herbicide useful for controlling broadleaf weeds and grasses, such as puncture vine, wild mustard, wild oats, chickweed, sandbur, common ragweed, pigweed, crabgrass, lambsquarter, common plantain, prostrate spurge, giant foxtail and yellow foxtail; and to top-kill certain perennials such as johnsongrass, dallisgrass and nutsedge.

BROADSIDE Herbicide is useful for general weed control on drainage ditchbanks, rights-of-way, fence rows, and storage yards; along highways, utility lines and pipe lines; around power plants and buildings, and on similar non-crop areas.

Use BROADSIDE Herbicide at the rate of 1 to 2 gallons per acre in sufficient water to get full coverage. Ground application normally requires 40 to 100 gallons of spray solution per acre. Any spray equipment that gives good coverage may be used. If regrowth occurs, reapply as required.

Bindweed (Morningglory) control: Use 1½ to 2 gallons BROADSIDE Herbicide in 50 to 100 gallons of water per acre. Make first application at first bloom, wetting foliage just short of run-off. Repeat application as needed for top-kill, but limit to three applications per year.

Do not contaminate waters used for domestic consumption, or by animals, wildlife and aquatic life, or for irrigation purposes. Avoid spray contact with foliage on fruit or food crops and ornamentals. Do not pasture livestock on treated areas.

BROADSIDE Herbicide is manufactured by The Ansul Company, Marinette, Wisconsin 54143.

BROADSIDE, ANSUL are registered trademarks of The Ansul Company.

Net Contents 5 gallons Patent Pending EPA Reg. No. 6308-65

Form No. C-72136

THE ANSUL COMPANY,
MARINETTE, WISCONSIN

Production and Domestic Supply

Volume of Production - The Tariff Commission (TC) annual reports for the 1970 to 1973 period list only one basic producer of cacodylic acid in the United States--The Ansul Company, Marinette, Wisconsin. However, cacodylic acid has also been produced by Vineland Chemical Company, Vineland, New Jersey. The TC reports do not carry the production and sales volumes of cacodylic acid individually. Cacodylic acid is included in the category "Pesticides and Related Products, Acyclic." The reported production volume of total active ingredient (AI) for this composite group was 43,004,000 lb in 1970, 25,780,000 lb in 1971, 48,883,000 lb in 1972, and 68,841,000 lb in 1973.

Compared to other pesticides in this category, the production and sales volume of cacodylic acid is so small that TC data is not useful in estimating volumes. However, based on an independent survey of pesticide and trade sources, Midwest Research Institute (MRI) estimated the 1973/1974 domestic production volume as between 1.4 and 1.8 million lb acid equivalent per year.

Imports - Based on an absence of data in TC reports on benzenoid and non-benzenoid chemicals (TC Publication 601) and Department of Agriculture reviews on pesticides, it appears that cacodylic acid has not been imported into the United States, at least in significant quantities, in recent years.

Exports - Cacodylic acid is not specifically listed in Bureau of Census commodity descriptions on pesticide exports. The 1972 report lists a composite export total of formulated herbicides as 38,867,237 lb. Based on other sources, MRI estimated that the export volume of cacodylic acid in 1972 was small, probably not amounting to more than 100,000 to 200,000 lb of acid equivalent.

Domestic Supply - Based on information presented in preceding subsections, MRI estimated that domestic consumption of cacodylic acid in 1973 was 1.3 to 1.7 million lb acid equivalent.

Formulations - Cacodylic acid is available to users in the United States in several different concentrations and formulations. All of these are liquid concentrates containing the active ingredient in water-soluble form, water as the principal solvent, and varying amounts of surfactant(s). The most widely used cacodylic acid formulations intended for foliar application (for weed control or for defoliation) all contain at least some surfactant. One formulation (Table 11) recommends adding additional surfactant to the spray tank for use with higher volumes of dilute spray.

Cadodylic acid formulations are offered by several suppliers under different tradenames or lines of tradenames, including Phytar ®, Bolls-eye ™ and Broadside ® (Ansul); Rad-E-Cate ® and Chex-Mate ® (Vineland); and Silvisar ® (TSI Company, previously Ansul).

In the past, Ansul marketed cacodylic acid-containing herbicides under the names, Ansar® 138 or Phytar® 138. These products are no longer marketed, and the names are obsolete. One leading cacodylic acid formulation, Ansul's Phytar® 560, containing 2.48 lb of cacodylic acid equivalent per gallon is characterized in Table 10.

A very similar product, also containing about 2.5 lb acid equivalent per gallon, is offered by Vineland under the name Rad-E-Cate®. Another Vineland cacodylic acid formulation contains 3.1 lb of acid equivalent per gallon; it is identified as Rad-E-Cate® 35.

Ansul's cacodylic acid cotton defoliant contains 3.1 lb of acid equivalent per gallon. (See Table 11.)

TSI's cacodylic acid tree killer formulation contains 50% of cacodylic acid, equivalent to 6.0 lb of acid equivalent per gallon. (See Table 12.)

At least two cacodylic acid-MSMA combination formulations are currently marketed. One of these, Ansul's Broadside®, contains 3.00 lb MSMA and 1.25 lb cacodylic acid equivalent per gallon. (See Table 14.) A very similar formulation, containing 26% MSMA, 10.5% sodium cacodylate and 1.8% cacodylic acid, is offered by Vineland under the name Chex-Mate®.

All currently available cacodylic acid formulations are corrosive, the degree of corrosiveness depending largely upon the concentration of cacodylic acid in the formulation. Most labels recommend against using these products in application equipment lined with zinc, tin or aluminum. All equipment should be thoroughly rinsed after use, and spray solutions should not be stored in spray tanks for prolonged periods.

There are no dry powder or granular formulations of cacodylic acid commercially available.

Use Patterns of Cacodylic Acid in the United States

General - Cacodylic acid is an organic arsenical herbicide deriving from pentavalent arsenic. Cacodylic acid is used for general, postemergent weed control in noncrop areas and in nonbearing citrus orchards (this use not permitted in Florida), as a cotton defoliant, and as a tree killing agent in forest management practices. The registration of cacodylic acid as a cotton defoliant was obtained only recently and it is believed to be the fastest growing use of cacodylic acid at the present time.

For general weed control and for cotton defoliation, cacodylic acid formulations are used as foliar sprays, diluted in water. Application is generally made by ground equipment, except in cotton defoliation where application by air is the preferred method of treatment.

When used as a tree killer, the product is to be applied through spaced-cut injections, at the rate of about 0.7 g AI/cut. This rate is obtained by using about 1 ml of a formulation containing 5 lb of cacodylic acid per gallon per cut. Trees below 8 in diameter at breast height (DBH) require one cut per 2 in of DBH, trees 8 in DBH and larger require one cut per 1 in DBH. These rates are applicable to conifers and hardwoods during the growing season. Treatment of smaller conifers (up to 8 in DBH) during the dormant season requires twice that rate, for example, about 0.7 g of cacodylic acid active ingredient per cut per in DBH.

Applying these rates, 1 gal of cacodylic acid formulation containing 50% AI will kill approximately 2,000 trees 4 in DBH in size during the growing season or 1,000 such trees during the dormant season or 500 trees 8 in DBH in size in either season.

In this use, the cacodylic acid formulation can be applied with pump-type oil cans, plastic squeeze bottles or other suitable dispensers to cuts made by hatchets or similar cutting tools. A tool combining both functions, i.e., cutting and injecting the herbicide, is the Hypo-Hatchet® injector that cuts and injects in one operation. When a tree is struck with the injector, a preset amount of the cacodylic acid tree killer formulation is automatically injected into the sap stream of the tree immediately after impact. The injector is connected by tube to a herbicide dispensing bottle attached to the operator's belt. The herbicide is fed to the injector automatically (inertia principle). The usefulness of this tool is not limited to cacodylic acid; it works with any water-soluble herbicide suitable for the killing of trees.

Cacodylic acid for tree killing purposes is used primarily on northern hardwood species in the Pacific Northwest. It is not as effective on southern hardwoods which prevail in other parts of the United States and represent the largest part of the silvicide market.

Cacodylic Acid Uses by Functions and Areas - Table 15 presents an estimate of the quantities of cacodylic acid used in the United States in 1973 by functions, in terms of percentage of total U.S. use, and in terms of quantities of active ingredient (as acid equivalent), assuming two different levels of use, i.e., 1.4 million lb (Case A), and 1.6 million lb (Case B). RvR Consultants estimated that the total U.S. use of cacodylic acid in 1973 ranged between 1.3 and 1.7 million lb of acid equivalent. Based on the available information, the use volumes assumed in Case A and Case B, respectively, appear to be plausible. Time and resources available for this task did not permit further refinement of these estimates, nor retrospective expansion.

According to Table 15, nonselective weed control and cotton defoliation account for the primary domestic use of cacodylic acid in 1973. MRI estimated that weed control makes up about 50%, and cotton defoliation about 40% of the total. Forest management uses amount to about 20,000 lb AI, about 1% of the total consumption. All others combined, including lawn usage, make up the balance, an estimated 5%, amounting to 70,000 to 80,000 lb of acid equivalent.

Table 15. ESTIMATED USES OF CACODYLIC ACID IN THE UNITED STATES BY MAJOR FUNCTIONS AND AREAS OF USE, 1973

Function	Estimated share of total use	Estimated use, lb of AE[a/]		Primary area of use
		Case A[b/]	Case B[c/]	
Nonselective weed control[d/]	52%	725,000	830,000	Western and southern states
Cotton defoliation	42%	585,000	670,000	Cotton states
Forest management	1%	20,000	20,000	Northwest
All other uses[e/]	5%	70,000	80,000	All areas
Total United States use	100%	1,400,000	1,600,000	

a/ AE = acid equivalent.
b/ Case A: Assuming total U.S. use = 1,400,000 lb AE.
c/ Case B: Assuming total U.S. use = 1,600,000 lb AE.
d/ Including directed application in nonbearing citrus orchards.
e/ Including lawn renovation, and all other (including nonregistered) uses.
Source: RvR Consultants, Shawnee Mission, Kansas.

Information from the field indicates that the total volume of use of cacodylic acid in the United States is on the increase, and that cotton defoliation represents the most rapidly growing use.

Cacodylic Acid Uses in California - California keeps detailed records of pesticide uses by crops and commodities which are published quarterly and summarized annually. Table 16 presents the recorded uses of cacodylic acid in California by crops and other use categories for the 1970 to 1973 period. A total of 112,366 lb of cacodylic acid were used in California in 1970; the total dropped to 23,230 lb in 1971, then increased again to 35,414 lb in 1972 and to 153,335 lb in 1973.

The California pesticide use report for 1970 lists cacodylic acid as Ansar ® 138, while there are no entries under cacodylic acid or sodium cacodylate. The 23,230 lb reportedly used in 1971 are identified as cacodylic acid; there are no entries under Ansar ®, or under sodium cacodylate. In the 1972 and 1973 reports, uses of cacodylic acid and sodium cacodylate in California are reported separately; they have been totaled for each of these 2 years in Table 16 and detailed individually in Tables 17 through 20.

Of the 112,366 lb of cacodylic acid used in California in 1970 according to the state report, 90,365 lb, or about 80% of the reported total, were used for nonagricultural purposes. The reports for 1972 and 1973 reflect the increasing use of cacodylic acid as a cotton defoliant, small uses on a number of other crops and substantially increasing uses along highways and other roads, by governmental agencies and for nonagricultural purposes.

It appears, however, that the California statistics reflect only use patterns, but not the total quantities of cacodylic acid actually used in the state.

In California, cacodylic acid is not subject to the special restrictions and reporting requirements imposed on the sale and use of pesticides designated as "restricted or injurious materials." For this reason, the percentage of all cacodylic acid uses reported to the California State Department of Agriculture and included in its statistics is not as high as in the case of restricted pesticides.

Tables 17 through 20 present the uses of cacodylic acid and sodium cacodylate in California in detail by crops and other uses, number of applications, pounds of active ingredient and number of acres treated for 1972 and 1973, the 2 most recent years for which such data is available. These tables expand and provide further insight into the cacodylic acid uses in California in 1972 and 1973 presented in summary form in Table 16.

At the present time, no other state in the Union records or publishes pesticide use data in comparable detail. Limitations of time and resources available for this task did not permit development of estimates on the uses of cacodylic acid by states or regions, crops, and other uses beyond the data provided in Tables 15 through 20.

Table 16. CACODYLIC ACID[a/] USES IN CALIFORNIA BY MAJOR CROPS AND OTHER USES, 1970 TO 1973

Crop/use	Year			
	1973	1972	1971	1970
	(Pounds of active ingredient)			
Cotton	89,449	11,014	7	--
Other crops[b/]	2,370	208	96	5,908
State highways and county roads	18,418	6,216	5,506	16,093
Other uses[c/]	43,098	17,976	17,621	90,365
Totals, all uses	153,335	35,414	23,230	112,366

a/ Referred to as Ansar ® 138 in 1970 including sodium cacodylate in 1972 and 1973.

b/ Including alfalfa, almonds, beans, citrus, grapes, lettuce, sugarbeets, tomatoes and fallow (open ground).

c/ Including Federal, state county and city agencies; park departments; school districts; reclamation, irrigation, flood control, water, water resource and vector control districts; the University of California; and uses on industrial, residential, turf and other nonagricultural areas.

Source: California Department of Agriculture, Pesticide use reports for 1970, 1971, 1972 and 1973.

Table 17. USE OF CACODYLIC ACID IN CALIFORNIA IN 1972 BY CROPS AND OTHER USES, APPLICATIONS, QUANTITIES, AND ACRES TREATED

Commodity	Applications	Pounds	Acres
Almond	4	108.09	435.00
City agency		563.63	
Cotton	190	2,558.16	26,107.00
County agricultural commissioner		4,060.15	
County or city parks		150.24	
County road		234.09	
Federal agency		331.13	
Fallow (open ground)	1	16.48	70.00
Flood control		2,306.02	
Industrial areas	5	2.46	3.25
Irrigation district		1,035.89	
Nonagricultural areas	62	484.94	1,719.24
Orange	8	18.42	140.00
Other agencies		1,029.52	
Recreational areas	1	0.49	1.00
Residential control		674.39	
School district		825.15	
State highway		4,455.91	
Structural control		10.41	
Sugarbeet	1	8.24	35.00
University of California		180.18	
Vector control		17.04	
Water areas	17	65.78	155.25
Water resources		1,738.19	
Total	289	20,875.00	28,665.74

Source: California Department of Agriculture, Pesticide Use Report 1972 (1972).

Table 18. USE OF SODIUM CACODYLATE IN CALIFORNIA IN 1972 BY CROPS AND OTHER USES, APPLICATIONS, QUANTITIES, AND ACRES TREATED

Commodity	Applications	Pounds	Acres
City agency		29.94	
Cotton	180	8,456.09	25,304.00
County agricultural commissioner		569.88	
County or city parks		7.61	
Fallow (open ground)	1	58.24	70.00
Industrial areas	2	1.66	.75
Irrigation district		1,057.85	
Nonagricultural areas	24	956.84	958.58
Other agencies		376.32	
Residential control		65.70	
School district		3.52	
State highway		1,525.85	
University of California		72.38	
Vector control		20.80	
Water areas	10	184.37	121.00
Water resources		1,152.31	
Total	217	14,539.36	26,454.33

Source: California Department of Agriculture, Pesticide Use Report 1972 (1972).

Table 19. USE OF CACODYLIC ACID IN CALIFORNIA IN 1973 BY CROPS AND OTHER USES, APPLICATIONS, QUANTITIES, AND ACRES TREATED

Commodity	Applications	Pounds	Acres
Beans, dry edible	1	3.53	15.00
City agency		615.18	
Conifer	6	65.38	25.00
Cotton	1,258	19,501.36	149,541.50
County agricultural commissioner		3,273.46	
County or city parks		614.47	
County road		231.11	
Federal agency		2,493.08	
Fallow (open ground)	8	83.92	280.25
Flood control		1,623.72	
Industrial areas	6	7.26	10.62
Irrigation district		670.24	
Lemon	1	3.76	32.00
Lettuce/head	1	18.32	120.00
Nonagricultural areas	43	240.71	667.21
Nonagricultural areas[a/]	4	1.15	4
Orange	60	430.85	1,470.00
Other agencies		1,522.47	
Pomegranate	1	1.41	3.00
Reclamation district		3.28	
Residential control		900.21	
School district		894.32	
State highway		7,136.34	
Turf	4	11.88	26.00
University of California		125.87	
Vector control		60.26	
Water areas	4	33.82	95.74
Water resources		808.28	
Total	1,397	41,375.64	152,286.32

a/ Miscellaneous units

Source: California Department of Agriculture, Pesticide Use Report 1973 (1973).

Table 20. USE OF SODIUM CACODYLATE IN CALIFORNIA IN 1973 BY CROPS AND OTHER USES, APPLICATIONS, QUANTITIES, AND ACRES TREATED

Commodity	Applications	Pounds	Acres
Beans, dry edible	1	12.48	15.00
City agency		1,008.63	
Cotton	1,258	69,948.17	149,541.50
County agricultural commissioner		2,635.99	
County or city parks		584.95	
County road		8.88	
Federal agency		8,110.93	
Fallow (open ground)	5	208.00	250.00
Flood control		3,778.40	
Industrial areas	1	1.66	2.00
Irrigation district		2,333.75	
Lemon	1	13.31	32.00
Lettuce/head	1	65.71	120.00
Nonagricultural areas	33	668.35	645.57
Nonagricultural areas[a/]	4	4.14	4
Orange	60	1,523.46	1,470.00
Other agencies		4,601.15	
Pomegranate	1	4.99	3.00
Reclamation district		11.64	
Residential control		1,757.05	
School district		1,175.77	
State highway		11,042.25	
Turf	4	42.15	26.00
University of California		108.67	
Vector control		212.98	
Water areas	4	119.57	95.74
Water resources		1,975.71	
Total	1,373	111,958.74	152,200.81

a/ Miscellaneous units.

Source: California Department of Agriculture, Pesticide Use Report 1973 (1973).

References

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PART III. EFFICACY AND PERFORMANCE REVIEW

CONTENTS

This section contains a general assessment of the efficacy of cacodylic acid. Studies on the production of cacodylic acid in the United States, as well as an analysis of its use patterns at the regional level and by major crop, were conducted as part of the Scientific Review (Part II) of this report. This section summarizes rather than interprets data reviewed.

Introduction

Efficacy tests are intended to determine a product's ability to actually control a specified target pest or produce a specified plant action. Data on actual usefulness is also evaluated since the effectiveness and usefulness of a given herbicide can differ. A herbicide can be effective in controlling a target weed species, but some adverse effect such as the death of desirable plants would negate its usefulness.

The following criteria were used to review efficacy tests: types of crops involved, target pests and population level, quantitative and qualitative changes in yields, and rates and time of application in accordance with conditions on the product's label. Data on higher dosages than recommended was also reviewed to allow an estimate of the margin of safety between effective pesticide levels and those which injure the crop. Some of these factors are crop; variety; geographical location of the test; year of the test; methods of application; numbers of sampling replicates; climatic conditions prior to treatment, at treatment, and right after treatment; edaphic (soil) factors; and many others. Statistical validity of tests was also considered.

This review presents a range of the potential benefits to be derived from the use of cacodylic acid for weed control of specific pests in a specific crop area.

Cacodylic acid is a broad spectrum herbicide used for postemergent weed control. It is nonselective and produces top kill only; repeat applications are required for seasonal weed control. It is often applied for control of weeds along drainage ditchbanks and rights-of-way. It is also used for weed control in nonbearing citrus orchards. Cacodylic acid is used as a harvest aid for the defoliation of dryland and irrigated cotton with aerial or ground application equipment. It is applied when 50% of the bolls are open and 7 to 10 days prior to anticipated picking. Conifer and hardwood trees are controlled by use of cacodylic acid which kills the crown when applied to the tree. It is used by professional foresters and entomologists to control several species of tree beetles.

An extensive literature review produced little information on the efficacy of cacodylic acid used on cotton, citrus or specific grasses. Some references reported the efficacy of mixtures of cacodylic acid and other herbicide combinations.

Efficacy of Pest Control

Weed Control - The results of efficacy tests on specific weed varieties show mixed results. Sckerl et al. (1966) evaluated several herbicides for control of Johnson grass, other grasses and broadleaf weeds along a highway right-of-way in Arkansas. Cacodylic acid was applied at the rate of 3 lb/acre 4 times during the 1964 growing season when the Johnson grass was approximately 12 inches in height. The results showed that the cacodylic acid treated plots had only slightly fewer weeds and grasses than an untreated check plot. The authors concluded that the treated plots were not significantly different from the untreated check.

Arnold and Aitken (1973) evaluated several herbicides for control of bahiagrass in Florida pecan orchards. Since most of these orchards are sodded and require mowing, growers are becoming interested in chemical grass control. Tests were conducted at Quincy, Florida, in 1972. Cacodylic acid was applied at a rate of 8.0 lb/acre in August. The results showed that it gave good initial knockdown, but failed to provide total control. The ratings (on the basis: 1 = no control; 10 = complete control) declined from 8.6, 2 weeks after application to 3.0, 15 weeks after application. Similar results occurred when an application of a mixture of 4.5 lb monosodium methylarsenate and 2.0 lb cacodylic acid were applied.

Lange et al. (1969) evaluated several herbicides for weed control in non-bearing citrus orchards containing Troyer citrange, trifoliate orange, Cleopatra mandarin and Citrus macrophylla liners (seedlings) in selected California counties between 1964 and 1968. The weeds included bindweed and a variety of annual weeds. Cacodylic acid applications were made at 4 and 16 lb/acre. At both of these rates, 100% control was evident 1 month after application. No other applications were made since the cacodylic acid was the most toxic herbicide to the Troyer citrange liners. The growth of the liners as measured by visual rating was about the same as the weeded check when cacodylic acid was applied at the 4 lb/acre rate but was much slower at the 16 lb/acre rate.

Cacodylic acid is often mixed with other herbicides. Bowmer and McCully (1969) conducted a 2-yr study on Texas roadsides for control of weeds with selected herbicide mixtures. Cacodylic acid mixed with another herbicide was comparable to other herbicide mixtures in initial control and superior to most in residual control. Treatments in June gave up to 75% control in October and up to 68% control in the following May. Treatments with the cacodylic acid mixtures resulted in superior total vegetation control.

Hardwood Tree Control - Cacodylic acid is used as a tool in forest management to thin trees. Single tree injection with the herbicide has been shown to be effective in controlling undesirable hardwoods. Smith (1965) injected several species of trees with cacodylic acid and reported 100% kill of the crowns of quaking aspen, red maple and paper birch, 3 weeks after injection. Tests on Jack pine resulted in 100% crown kill 2 months after injection.

Peevy (1969) evaluated several herbicides for control of blackjack oak and mockernut hickory. Dosage rates of cacodylic acid were varied from 2 to 4 ml from a solution containing 5.7 lb AI/gal. The acid was very effective against the oak, causing from 96 to 100% kill of top growth. Hickory was difficult to control. The results varied from 14 to 41% kill of the top growth.

Wiant and Walker (1969) evaluated cacodylic acid for precommercial thinning of loblolly pines. Tests were conducted in the Stephen F. Austin Experimental Forest near Nacogdoches, Texas, in 1969. Although 96% of the trees showed some crown kill after 3 weeks, the proportion of trees that were completely dead 2 yr later varied from 0 to 35%. The rate of kill increased with dosage of the herbicide.

Wiant and Walker (1969) also evaluated 30% cacodylic acid for control of white oak, post oak, southern red oak, blackgum, sweetgum and hickory. The average kill rate after 2 yr varied with the method of application and rate of herbicide. Kill rates as high as 89% of the crown and 72% of the roots were achieved. Blackgum and hickory were the most kill-resistant of the species tested.

The authors concluded that cacodylic acid in adequate dosages may be used to thin pines. Better hardwood kills are obtained when cacodylic acid silvicides are applied in frills rather than in bore holes.

Application of the herbicide has been difficult--particularly in assuring the proper injection into the tree. The development of the Hypo-Hatchet® has allowed foresters to inject the proper amount of herbicide automatically and to increase the speed of injection.

Hold and Voeller (1972) injected post oak trees in Oklahoma with 5.7 lb AI/gal cacodylic acid using the Hypo-Hatchet®. The authors concluded that cacodylic acid did not give good control and recovery was quite pronounced after two growing seasons. The percent defoliation declined from a mean of 61%, 7 months after application, to 56% after 22 months.

Somewhat better results were obtained by the authors on post oak and hickory during tests in Arkansas. Cacodylic acid gave extremely good initial control with the post oak, but the oaks consistently recovered as the season progressed. Good initial results were also observed on the hickory, but recovery was much faster. The authors also concluded that the degree of control with the Hypo-Hatchet® is the same as with tubular injectors; however, it is 2 to 3 times more efficient due to lower labor costs.

Voeller and Holt (1973) conducted further tests in 1971 and 1972 in Arkansas. Cacodylic acid gave good initial control, but by the following year profuse sprouting had developed. Tests on eastern red cedar showed poor control.

Tree Insect Control - Cacodylic acid has been evaluated for control of various insects that attack trees. Among these are bark beetles, spruce beetles, the Arizona 5-spined engraver, the round-headed pine beetle and the southern pine beetle.

Chansler and Pierce (1966) evaluated cacodylic acid for control of 5 types of bark beetles in New Mexico forests. The results showed that in trees injected with cacodylic acid (1) nearly all parent adults died before completing egg galleries, (2) some eggs failed to hatch, and (3) high brood mortality occured. The reduction in beetles ranged from 84 to 99%.

Stelzer (1970) evaluated cacodylic acid for control of the Arizona 5-spined engraver in green ponderosa pines located in the Prescott National Forest in Arizona. The Arizona 5-spined engraver readily attacked ponderosa pine trees that had been poisoned with a fast-acting herbicide containing cacodylic acid. The density of live brood, however, was reduced about 70% in trees treated from April to July, as compared with the density in untreated trees felled during the same period.

Trees poisoned from late July through August attracted more attacks than those poisoned at any other time of the year. Trees felled about 1 month after being poisoned in July were more effective as toxic trap trees than poisoned trees left standing; the density of attack and mortality of the brood and parent adults were appreciably greater in the felled trees. The treated trees evidently dried out rapidly, trapping the adults and preventing brood development.

Ninety percent of the August-treated trees were attacked within 1 month after treatment. This period coincided with the major flight of the beetle. Attack densities and subsequent mortality were extremely high--brood mortality was 100% and adult mortality about 60% in galleries situated on the upper bole. During the fall, the lower bole of the trees attracted mass attacks by adults that constructed hibernation-type galleries, but beetle mortality averaged 96%.

The round-headed pine beetle periodically causes significant mortality of pole-sized ponderosa pine in the Southwest. Buffam and Flake (1971) reported that these insects infested 100,000 acres in the Lincoln National Forest in 1969 killing up to 44 trees per acre in some areas. The authors achieved 100% reduction of the round-headed pine beetles when the trees were frilled with a hand hatchet and injected with cacodylic acid. Beetle mortality in power saw-frilled trees was significantly less than in hatchet-frilled trees.

Copony and Morris (1971) baited loblolly pine trees with Frontalure attractant to attract the southern pine beetle to cacodylic acid trap trees. All trap trees were poisoned with 1.2 ml of cacodylic acid applied to a shallow frill of overlapping ax cuts.

The Frontalure-cacodylic acid treatments appeared almost totally successful in controlling the spring populations of the southern pine beetle during epidemic conditions, where all trees within 15 ft of a baited trap tree were treated with cacodylic acid. The authors concluded that if treatments had been made earlier in the spring (2 to 4 weeks before beetle emergence), the results might have been more successful. Baited trap trees would then have been available for the earliest emerging beetles, and the trap trees would have had more time to accept the cacodylic acid poison, thus creating conditions less favorable to beetle development.

However, the Forest Service does not recommend the use of cacodylic acid combined with the pheromone, Frontalure. Some doubts exist as to whether cacodylic acid is translocated in the southern pine to provide control of the southern pine beetle. Consequently, it is more customary to control the southern pine beetle with the older method of salvaging attacked trees combined with piling and burning refuse.

The spruce beetle is the most serious pest of the Englemann spruce in the United States. Buffam and Yasinski (1971) used a hand ax to frill trees in the Carson National Forest in New Mexico. Cacodylic acid was applied to the trough and the trees felled 30 days after treatment. The authors reported that the method was successful in eliminating the hazard of spruce beetle buildup. Only 20 live larvae were found in all samples taken from 45 felled trees.

Frye and Wygant (1971) also evaluated cacodylic acid for treatment of the spruce beetle in Englemann spruce. The results showed that mortality rates of 98% were achieved.

Buffam (1971) added cacodylic acid to Englemann spruce trees in an effort to produce lethal traps for the spruce beetle and found that trees treated in mid-June and felled 2 weeks later had approximately the same number of attacks as check trees. However, only a few live spruce beetle larvae and pupae were found in samples from trees treated at this time whereas significant numbers were found in samples from check trees.

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