ARSENICAL PESTICIDES, MAN, AND THE ENVIRONMENT

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Prepared for the Office of Pesticides Programs, Environmental
Protection Agency by:

Special Pesticide Review Group

O. Garth Fitzhugh, Ph.D., Chairman
William F. Durham, Ph.D., Vice-Chairman
Lamar B. Dale, Jr., Ph.D., Secretary
Homer E. Fairchild, Ph.D., Editor
Cipriano Cueto, Ph.D.
Joseph G. Cummings
Thomas E. DeVaney
George Robertson
Fred H. Tshirley, Ph.D.
Anne R. Yobs, M.D.
Clara H. Williams, Ph.D.

Special Working Group on Arsenic

James W. Akerman
S. C. Billings
Thomas D. Burkhalter, Ph.D.
Edward P. Carter
Thomas B. Gaines
Paul M. Ochs
Roger L. Pierpont
John A. Shaughnessy
James L. Skaptason
Joseph L. Svirbely, Ph.D.

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Mrs. Claudia Lewis

INTRODUCTION

Arsenic is a metalloid which has usefully served mankind beginning at least as early as 400 B.C. Hippocrates is reported to have recommended a paste of the sulfide for the treatment of ulcers (Buchanan, 1962). Arsenic was also one of the most common homicidal agents of the Middle Ages. It was so successful for this use that arsenic was soon suggested for the eradication of four-legged and six-legged pests. Roark (1935) noted that arsenical baits were recommended for ant control as early as 1669. Frost (1967) records the development of Paris green (copper acetoarsenite) in 1867 as the first pesticide to be used against the Colorado potato beetle.

Fowler's solution or 'ague drops' (1% potassium arsenite) and other inorganic arsenical preparations have been used for the treatment of anorexia, neuralgia, rheumatism, arthritis, tuberculosis, and skin diseases. Fowler's solution is still used in the treatment of myelogenous leukemia. However, in most of these disorders, arsenic has fallen into disrepute or has been replaced by specific therapy (Vallee, et al., 1960). Following Erlich's discovery of the chemotherapeutic action of arsenicals against trypanosomes in 1905, more than 8000 organic arsenicals were in use as chemotherapeutic agents by 1937. These agents, including arsphenamine, neoarsephenamine, and mapharsen were the most important therapeutic weapons against syphilis and trypanosomiasis until the introduction of the antibiotics about 1940. On the other hand, because of the great toxicity of some arsenicals to man, arsenic has been considered as synonymous with poison.

Arsenic is a ubiquitous element present in all soils, in amounts varying from less than 10 to 500 ppm. It is found in metal ores, chiefly in Canada, Saxony, and Sweden, combined with other minerals such as realgar (As_2S_3), orpiment (As_2S_2), and arsenolite (As_2O_3). Arsenic is not usually mined separately, but is recovered as a byproduct from the treatment of copper, lead, zinc, and gold ores. When ores or concentrates containing these metals are smelted, the arsenic which does not melt at atmospheric pressure, but sublimes at 218°C, is liberated from the flue dust and separated by filters or electrostatic precipitators as an oxide, chiefly as the trioxide (Brownine, 1969).

Arsenic has been detected and measured in practically every area of man's environment; in the earth's crust, the biosphere, soil, water vegetation, marine forms and food and cosmetics. Man in his technological advances, has added to his exposure through different industries, such as mining, and smelting of industrial ores, farming and vineyard activities where arsenical pesticides are used, the herbicidal use of arsenic, in the formulation of pesticides, and in medicated animal food production.

Although there is no evidence that there is biomagnification of arsenic in the food chain, marine life is capable of bioconcentration of arsenic. McBride and Wolfe have demonstrated that microorganisms in sediments that contain arsenic convert arsenic into the highly toxic dimethylarsine (Anonymous, 1971). Therefore, a pollution hazard exists for aquatic and terrestrial environments that have large amounts of arsenic introduced where anaerobic organisms are growing.

Beginning around 1900, the inorganic arsenicals were very extensively used as pesticides until they were, to a great extent, replaced as insecticides by the chlorinated hydrocarbons and organic phosphorous compounds following World War II. In fact, the amount of one arsenical insecticide, lead arsenate, used in the Wenatchee, Washington area in 1937 amount to slightly more than the total use of that compound in the United States in 1967 (Neal, et al., 1941; USDA, 1970).

The U.S. Department of Interior Minerals Yearbook for 1969 reported that arsenic was used principally for its toxic qualities in insecticides and herbicides. Lead arsenate, calcium arsenate, sodium arsenate, sodium arsenite, and arsenic-containing organic compounds were used in formulating pesticides. In 1968 the world production, excluding the United States, of arsenic trioxide was 66,000 tons, an increase from the production of 55,000 tons in 1962. Over 4 million pounds of lead arsenate and about 2 million pounds of calcium arsenate were produced in the United States in 1969.

Because of the limitations placed on the use of DDT and other organochlorine insecticides, there has been some recent increase in the use of arsenicals as insecticides.

Approximately one million gallons of arsenic acid at 1.5 quarts/acre are used annually in the cotton producing areas of Texas and Southwestern Oklahoma. This calculates to 2.5 to 3.0 million acres treated annually. In Texas, approximately 73% of the crop is machine stripped, 25% spindle picked, and 2% hand harvested.

It has recently been reported that arsenic build-up in soils after years of pesticidal use reached 1.8 to 830 ppm while untreated areas ranged from 0.5 to 14 ppm in areas tested in North America. In orchard areas of the United States where arsenic-containing pesticides have been in use for decades, the arsenic has accumulated in the soil to the point where the soil is toxic, shortening the life of trees and making it difficult for the profitable use of orchard lands for the forage crops that normally follow orchards in rotation (Mrak, 1969).

There have been reports of chronic arsenic intoxication from North Carolina (Keyman, et al., 1956) and from Texas (Micks, et al., 1956) in farmworkers using calcium and lead arsenates. Farner, et al., 1949) reported lead intoxication in a significant number of workers employed in apple orchards in Washington. There is considerable confusion in the literature concerning the role of arsenicals in the production of cancer. The earliest published claim of arsenic cancer was made by Paris in 1820 in which he reported occasional cases of cancer of the scrotum in copper smelters (Buchanan, 1962).

Other investigators have since reported an increased incidence of cancer both of the skin and internal organs, in persons exposed to excessive levels of arsenic. Attempt to demonstrate cancer in experimental animals exposed to arsenic generally have not met with success.

Because of the increasing incidence of cases of arsenic poisoning, arsenic insecticides were outlawed in Germany in 1942.

The Canadian Department of Agriculture has recently completed a reevaluation of arsenical pesticides as related to effectiveness, safety, and need. Their memorandum of November 30, 1971, indicates a reduction of approved arsenical pesticide uses in Canada by 1973. The following is a brief summary of the expected arsenical pesticide registrations or eliminations from use which will be followed by Canada for 1973:

(1) Ammonium methyl arsonate is eligible for registration to control crabgrass, chickweed, and witch grass in lawns.

(2) Disodium methyl arsonate is eligible for registration to control crabgrass in lawns.

(3) Monosodium acid methane arsonate is eligible for registration as a precommercial thinning agent for young conifer stands.

(4) Calcium arsenate is eligible for registration to control insects on blueberries and for control of Poa annua on golf courses.

(5) Lead arsenate is eligible for registration for control of apple maggot (apples), tent caterpillars (apple and pears), plum curculio (plums) and earthworms (bowling greens and golf greens).

(6) Sodium arsenite will not be eligible for registration as a herbicide.

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SUMMARY AND CONCLUSIONS

Arsenic is ubiquitous and occurs naturally in the environment. The arsenic levels currently found in the environment may or may not be an original deposition. Certain of these levels may be the result of industrialization and agricultural uses. The burning of fossil fuel and the smelting of ores release arsenic into the atmosphere from where it may be carried back to earth by rain. The pesticidal usage of arsenic in large dosage rates has produced local damage to soils resulting in the inability of the soil to sustain plant life (soil sterilization).

Certain forms of marine life contain high levels of arsenic and it appears that these forms are capable of bioconcentration of arsenic. However, biomagnification in the food chain does not seem to occur. Arsenic is apparently stored in the tissues in a pentavalent-organically bound form which, according to some experts, is unavailable to man. Pentavalent arsenic, both organic and inorganic, is less toxic than the trivalent forms of arsenic. In the terrestrial environment the arsenites will accumulate in mammalian and avian tissues. It may be concluded that trivalent arsenic presents a hazard to the environment.

Because of its phytotoxicity, the greatest threat of the unrestricted use of pentavalent arsenical pesticides is soil sterilization. This has occurred in the past when high use rates were employed in orchards and may occur again if heavy uses of arsenicals are resumed.

The Secretary's Commission on Pesticides and Their Relationship to Environmental Health recommended the use of arsenic be restricted to specific essential uses. The Special Pesticide Review Group agrees with this recommendation and concludes that a total ban need not be placed on the arsenical pesticides. Rather, that uses be retained where a definite need could be established; that the usage rates in these retained uses be reduced to the optimal effective rates; and that unnecessary uses and uses requiring excessively high dosage rates be abandoned.

The Group has solicited the aid of members of the Department of Agriculture in ascertaining which uses of arsenical pesticides are necessary in the production of food or fiber or in the preservation of the beauty of the landscape.

The Special Pesticide Review Group has placed an estimate on the social and economic impact caused by cancellation of certain uses of the arsenical pesticides. The Group did not evaluate the full range of economic and social consequences of cancellation. The conclusions and proposals given below are based upon the assumption that all registered uses of pesticides under consideration are economically and

socially desirable. The Group has suggested that registration be continued if effective alternates are not reasonably available and use patterns indicate a relatively low hazard to man or his environment. Cancellation is suggested for those uses with the greatest hazards or for those uses with lesser hazards if an acceptable alternate control method exists to accomplish the same results.

The arsenical pesticide uses with no acceptable registered alternates were found to be limited to few crops or specific use sites. However, there were needs currently considered essential for the arsenicals as insecticides, herbicides, desiccant and defoliant, plant regulator, fungicides and rodenticides. The general conclusions and proposals for continued use or cancellation of the arsenical pesticides are:

1. Lead arsenate insecticide uses on apples, apricots, cherries, peaches, pears, plums, prunes, nectarines, quinces and grapes should be retained subject to review by the Pesticide Regulation Division and phase out prior to the 1975-use season if satisfactory alternates exist.

2. All calcium arsenate insecticide uses except the following should be cancelled: dusts on selected fruits and vegetables; sprays for the fruitfly on blueberries; and baits on the soil to control armyworms, cutworms, slugs, snails, and sowbugs attacking fruit, vegetables, and ornamentals.

3. The currently registered insecticide uses for basic copper arsenate on vegetable crops should be cancelled.

4. Since there is no satisfactory substitute for arsenic in the preservative mixture for insecticidal or fungicidal action, registrations for ammonium arsenite, arsenic acid, arsenic pentoxide, arsenic trioxide, sodium pyroarsenate sodium arsenate, and Wolman salts should be retained for wood preservation.

5. The use of cacodylic acid for insect trapping in the forest should be restricted to U.S. Forest Service use only.

6. Sodium arsenite is too toxic for patterns of use involving storage in the home environment. The registered uses for control of subterranean termites and ants by the homeowner should be cancelled.

7. Sodium arsenite and potassium arsenite are essential in cattle dips at the Mexico-United States border to protect against introduction of the Texas fever tick. This application is restricted to use by the United States Department of Agriculture for quarantine purposes. The registered use should be retained until a satisfactory alternate tickicide is developed with a simple and efficient vat-side test.

8. The registered use of sodium arsenate should be retained for termites, wood destroying insects, and ant baits.

9. The registered uses of Paris green should be retained for control of mosquito larvae, drywood termites and in anti-fouling paints to control insects and other pests.

10. The registered use of cacodylic acid for weed control in citrus should be retained.

11. The registered uses of cacodylic acid, DSMA, and MSMA around ornamental trees and shrubs should be retained.

12. The following actions are suggested for registered arsenical herbicides on lawns and ornamental turf: arsenic acid should be cancelled; calcium arsenate should be limited to Poa annua control and restricted to optimal effective rates on golf courses and related recreational turf; the use of cacodylic acid should be retained; lead arsenate should be cancelled; DSMA, MSMA, and AMA should be retained in use; and sodium arsenite and arsenic trioxide should be cancelled.

13. The actions on herbicide uses of arsenic acid, cacodylic acid, DSMA and MSMA for non-crop, industrial sites, rights-of-way, driveways and sidewalks should be the same as in Item 12, above, for the respective pesticide.

14. The registered uses of cacodylic acid and MSMA for hardwood tree control should be retained.

15. The presently registered uses for sodium are arsenite and arsenic trioxide as semi-soil sterilants should be cancelled.

16. The currently registered uses of MSMA and DSMA alone or in combinations for cotton should be retained.

17. The registered use of arsenic acid as a desiccant and defoliant of cotton should be retained.

18. Lead arsenate regulator use should be retained on grapefruit intended for harvest in Florida subject to clearance of calcium arsentate for this use and review of status by the Pesticide Regulation Division prior to the 1975-use season.

19. The registered use of arsenic trioxide baits for rodent control should be restricted to pest control operators.

20. The registered fungicidal use of sodium arsenite for control of black measles, crown gall and dead arm on grapes should be retained.

21. The registered uses of basic copper arsenate for the control of early and late blight on tomatoes should be retained subject to review by the Pesticides Regulation Division of the status of satisfactory alternates prior to the 1975-use season.

22. Pressure treatment uses registered for the following arsenical fungicide wood preservatives should be retained: arsenic acid, sodium arsenate, arsenic pentoxide, sodium pyroarsenate; and disodium arsenate.

23. Injection treatment fungicidal uses registered for arsenic trioxide and sodium arsenate as wood preservatives should be retained.

24. Diffusion treatment fungicide uses registered for sodium arsenate as wood preservatives should be retained.

25. Brush, mop or swab treatment fungicide uses registered for ammonium arsenite, arsenic pentoxide, and sodium arsenate as wood preservatives should be retained.

26. The registered uses of 10, 10' -oxybisphenoxarsine for control of fungi attacking cotton fabric and vinyl films should be retained.

27. Following is a table giving the arsenical pesticide cancellations suggested in Chapter I according to crop or site of application:

Pesticide	Crop or Site of Application Suggested to be Cancelled
Lead Arsenate (Insecticide)	Asparagus (foliar application), tomatoes (foliar application), tobacco (foliar application), ornamentals (foliar application) and lawns and ornamental turf (soil and surface applications).
Calcium Arsenate (Insecticide Sprays)	Broccoli (foliar application), Brussels sprouts (foliar application), cabbage (foliar application), cauliflower (foliar application), celery (foliar application), cucumbers (foliar application), melons (foliar application), peppers (foliar application), squash (foliar application), tomatoes (foliar application), poultry houses (droppings under cages or wire floors for fly control) and lawns and ornamental turf (soil and surface applications).
Basic Copper Arsenate (Insecticide)	Brussel sprouts (foliar application), cabbage (foliar application), cauliflower (foliar application), kohlrabi (foliar application), and tomatoes (foliar application).
Sodium Arsenite (Insecticide)	Household and commercial (soil and bait applications).
Arsenic Acid (Herbicide)	Lawns and ornamental turf (soil application and non-crop industrial sites, rights-of-ways, driveways, and sidewalks (soil application).
Lead Arsenate (Herbicide)	Lawns and ornamental turf (soil application).
Sodium Arsenite (Herbicide)	Semi-soil sterilant (soil application), ornamental turf (soil application).
Arsenic Trioxide (Herbicide)	Ornamental turf (soil application), semi-soil sterilant.
Arsenic trioxide (Rodenticide)	Rodents (baits - homeowner use).
Sodium Arsenate (Fungicide)	Wood preservative (diffusion treatments).

Pesticide Uses of Arsenic as Related to Alternate Pesticides and Impact

Pesticidal compounds of arsenic have been used extensively for many years in the United States. One of the significant early uses of arsenic was in production of lead arsenate for control of the gypsy moth. Relatively large amounts of arsenical insecticides were used until the introduction of DDT. More recently, during the past ten years, arsenical desiccants and herbicides have been of increasing importance to the production of cotton in large areas of the United States. Rodents and plants diseases are also controlled with arsenical pesticides. Details on production and trends of use are given in Chapters II and IV.

I. A. Summary

This chapter presents the arsenical pesticide uses currently registered along with the registered alternate pesticides (substitutes) and the conclusions or impact of any proposed action. Following is an outline of the material presented:

1. Registered uses of arsenical pesticides for which there are no alternate registrations (tables 1 through 8);

2. Registered arsenical insecticide uses with registered alternates and suggestions for action (see I.B. 1. through I.B. 13.);

3. Registered arsenical herbicide uses with registered alternates and suggestions for action (see I.B. 14. through I.B. 20.);

4. Registered arsenical desiccant and defoliant uses with registered alternates and suggestions for action (see I.B. 21.);

5. Registered arsenical regulator use with suggestions for action (see I.B. 22.);

6. Registered arsenical rodenticides with alternates and suggestions for action (see I.C.); and,

7. Registered arsenical fungicides with alternates and suggestions for action (see I.D.).

Table 1. Lead Arsenate Insecticide Uses With No Registered Alternates

Crop	Pest	Use Rate
Apples	Applethorn Skeletonizer	2 lbs/100 gal.
(Foliar)	Case Bearers	2-3 lbs/100 gal.
	Syneta Bettle	3 lbs/100 gal.
Apricots		
(Foliar)	Syneta Beetle	5-6 lbs/100 gal.
Cherries		
(Foliar)	Apple Maggot	2-3 lbs/100 gal.
	Syneta Beetle	5-6 lbs/100 gal.
	Red-Humped Caterpillar	3-4 lbs/100 gal.
Peaches		
(Foliar)	Apple Maggot	1-1/2 - 2 lbs./100 gal.
	Cankerworm	1-1/2 - 2 lbs/100 gal.
	Syneta Beetle	5-6 lbs/100 gal.
Pears		
(Foliar)	Case Bearers	2-3 lbs/100 gal.
	Syneta Leaf Beetle	3 lbs/100 gal.
	Red-Humped Caterpillar	3-4 lbs/100 gal.
	Round-Headed Apple Tree Borer	3 lbs/100 gal.
	Pear Leafworm	2 lbs/100 gal.
Plums		
(Foliar)	Apple Maggot	1-1/2 - 2 lbs/100 gal.
	Cankerworm	1-1/2 - 2 lbs/100 gal.
Prunes		
(Foliar)	Cankerworms	2-4 lbs/100 gal.
Quince		
(Foliar)	Tent Caterpillar	2-3 lbs/100 gal.
	Red-Humped Caterpillar	3-4 lbs/100 gal.
	Syneta Beetle	5 lbs/100 gal.
	California Oak Moth	3-4 lbs/100 gal.
Grapes		
(Foliar)	Achnemon Sphinx Moth	3-4 lbs/100 gal.
	Grape Rootworm	3-4 lbs/100 gal.

Table 2. Calcium Arsenate Insecticide Uses With No Registered Alternates

Crop or Site	Pest	Use Rate
Cabbage (Foliar)	Colorado Potato Beetle	4 lbs/acre
Celery (Foliar)	Colorado Potato Beetle	1-1-3/4 lbs/acre

Baits used as soil treatments are used against armyworms, cutworms, slugs, snails and sowbugs. Used only in accordance with appropriate clearance and limitations on crops as specified.

Table 3. Cacodylic Acid Insecticide Uses With No Registered Alternates

Crop or Site	Pest	Use Rate
Forest application (U.S. Forest Service only)	Insect trapping – Englemen Spruce Beetle Mountain Pine Beetle Douglas Fir Beetle Round-headed Pine Beetle Arizona Five-Spined Beetle Pine Engraver Beetle California Five-Spined Beetle	1 ml/inch of the surface

Table 4. Sodium Arsenite and Potassium Arsenite Insecticide
Use With No Approved Alternate

Crop or Site	Pests	Use Rate
Livestock Quarantine – Cattle Dip	Ticks	0.25% solution as a dip

Table 5. Lead Arsenate Plant Regulator Use With No Registered Alternates

Crop	Action	Use Rate
Grapefruit	Plant Regulator to Reduce Acidity	1.7-5.4 lbs/acre

Table 6. Sodium Arsenite Fungicide Use With No Registered Alternates

Crop	Disease	Use Rate
Grapes	Black measles crown gall	3-9 lbs/acre

Table 7   Special Uses of Arsenic Compounds as Wood
Preservatives With <u>No</u> <u>Registered</u> <u>Alternates</u>

Uses	Compounds*	Special Remarks
Pressure treatments	Arsenic acid; arsenic pentoxide dihydrate; sodium arsenate; sodium hyroarsenate; arsenic pentoxide; disodium arsenate	Used in varying concentrations with other chemicals. Paintable and safer to handle than cresote or pentachlorophenol. Arsenic containing preservatives give up to 80 years life to treated wood. Loss of use considered a national disaster.
Injection treatments	Arsenic trioxide and sodium arsenate	Used in varying concentrations with other chemicals. No substitutes. Arsenic containing preservatives give up to 80 years life to treated wood. Loss of use considered a national <u>disaster</u>.
Diffusion treatments	Sodium arsenate	Used with other chemicals. No substitutes. Method of application seldom used. Effective but too time consuming. Impact of withdrawing this method of application would be <u>slight</u>.
Brush, Mop or Swob treatments	Ammonium arsenite; arsenic pentoxide; and sodium arsenite	Used in combination with other chemicals. No substitutes. Effective and necessary use. Impact of withdrawal of use would be great.

I. B. Summary of Registered Arsenical Insecticide and Herbicide Uses
and Substitutes

I. B. 1. Lead Arsenate Insecticide Uses

Fruit Crops

Crop or Site of Application	Insect Pest	Maximum or Usual Dosage Rate (Lbs. of Actual Insecticide Per 100 Gallons or Per Acre)	Lead Arsenate Limitations	Registered Alternates
Apples Foliage Application	Codling moth	2-3 lb. per 100 gals.	30 days Remove excess residues at time of harvest. Do not graze livestock on treated areas	Carbaryl Diazinon EPN Ethion Gardona Guthion Imidan Malathion Methoxychlor Methyl Parathion Parathion Trithion
	Plum Curculio	2-3 lb. per 100 gals.		BHC Carbaryl EPN Gardona Guthion Imidan Lindane Malathion Methoxychlor Methyl Parathion Parathion

Lead Arsenate Insecticide Uses

Fruit Crops (continued)

Crop or Site of Application	Insect Pest	Maximum or Usual Dosage Rate (Lbs. of Actual Insecticide Per 100 Gallons or Per Acre)	Lead Arsenate Limitations	Registered Alternates
Apples Foliage Application	Red-Banded Leafroller	2-3 lb. per 100 gals.		BHC Carbaryl Gardona Guthion Imidan Malathion Methyl Parathion Parathion
	Green Fruitworm	2-3 lb. per 100 gals.		Carbaryl Guthion
	Tent Caterpillar	2-3 lb. per 100 gals.		BHC Carbaryl Lindane Malathion
	Apple Maggot	2-3 lb. per 100 gals.		Carbaryl Diazinon Gardona Guthion Imidan Methoxychlor
	Cankerworm	2-3 lb. per 100 gals.		Methoxychlor
Apples Foliage Application	Applethorn Skeletonizer	2 lb. per 100 gals.		None
	Bagworm	3-4- lb. per 100 gals.		Carbaryl Malathion Parathion

Fruit Crops (continued)

Crop or Site of Application	Insect Pest	Maximum or Usual Dosage Rate (Lbs. of Actual Insecticide Per 100 Gallons or Per Acre)	Lead Arsenate Limitations	Registered Alternates
	Round Headed Apple Treeborer	3 lb. per 100 gals.		
	Fall Webworm	2 lb. per 100 gals.		Parathion Guthion
	Red Humped Caterpillar	3-4 lb. per 100 gals.		Malathion Parathion
	Eyespotted Bud Moth	3 lb. per 100 gals.		Guthion Parathion
	Case Bearers	2-3 lb. per 100 gals.		None
	Syneta Beetle	3 lb. per 100 gals.		None
Apricots Foliage Application			30 days Remove excess residues at time of harvest. Do not graze treated forage to livestock.	
	Syneta Beetle	5-6 lb. per 100 gals.		None
	Peach Twigborer	3-4 lb. per 100 gals.		Chlordane Diazinon Endosulfan Guthion Imidan

Fruit Crops (continued)

Crop or Site of Application	Insect Pest	Maximum or Usual Dosage Rate (Lbs. of Actual Insecticide Per 100 Gallons or Per Acre)	Lead Arsenate Limitations	Registered Alternates
	Leafroller	3-4 lb. per 100 gals.		Chlordane Guthion Imidan
Cherries Foliage Application	Plum Curculio	3-4 lb. per 100 gals.	30 days Remove residues at time of harvest. Do not graze treated forage by livestock.	Carbaryl EPN Guthion Lindane Methoxychlor Parathion
	Cherry Fruit Fly	2 lb. per 100 gals.		Carbaryl Diazinon Guthion Malathion Methoxychlor Parathion Rotenone
	Codling Moth	2-3 lb. per 100 gals.		Carbaryl
	Apple Maggot	2-3 lb. per 100 gals.		None
	Cankerworm	3-4 lb. per 100 gals.		Parathion
	Red-Banded Leafroller	2-3 lb. per 100 gals.		Carbaryl EPN
	Pear Slug	2-3 lb. per 100 gals.		Parathion

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Fruit Crop (continued)

Crop or Site of Application	Insect Pest	Maximum or Usual Dosage Rate (Lbs. of Actual Insecticide Per 100 Gallons or Per Acre)	Lead Arsenate Limitations	Registered Alternates
	Black Cherry Fruit Fly	2-3 lb. per 100 gals.		Diazinon Parathion
	Rose Chafer	2 lb. per 100 gals.		Methoxychlor
	Syneta Beetle	5-6 lb. per 100 gals.		None
	Tent Caterpillar	3-4 lb. per 100 gals.		Carbaryl Methoxychlor
	Red Humped Caterpillar	3-4 lb. per 100 gals.		None
	Cherry Slug	3-4 lb. per 100 gals.		Malathion Methoxychlor Parathion
Nectarines Foliage Application	Peach Twig Borer	3-4 lb. per 100 gals.	30 days. Remove excess residues at time of harvest. Do not graze livestock on treated areas.	Carbaryl Diazinon Imidan
	Leafroller	3-4 lb. per 100 gals.		Carbaryl Imidan
Peaches Foliage Application	Plum Curculio	1.5-2 lb. per 100 gals.	30 days. Remove excess residues at time of harvest. Do not graze livestock on treated areas.	EPN Guthion Imidan Lindane Methoxychlor Methyl Parathion Parathion Toxaphene

Fruit Crops (continued)

Crop or Site of Application	Insect Pest	Maximum or Usual Dosage Rate (Lbs. of Actual Insecticide Per 100 Gallons or Per Acre)	Lead Arsenate Limitations	Registered Alternates
	Peach Twig Borer	3-4 lb. per 100 gals.		Carbaryl Diazinon Guthion Imidan Rotenone
	Red-Banded Leafroller	3-4 lbs. per 100 gals.		Carbaryl Guthion Parathion
	Cherry Fruitfly	2 lb. per 100 gals.		Methoxychlor
	Codling Moth	1.5-2 lb. per 100 gals.		Carbaryl Chloroph- enamidine
	Apple Maggot	1.5-2 lb. per 100 gals.		None
	Cankerworm	1.5-2 lb. per 100 gals.		None
	Syneta Beetle	5-6 lb. per 100 gals.		None
Pears Foliage Application	Codling Moth	2-3 lb. per 100 gals.	30 days. Remove excess residues at time of harvest. Do not graze live- stock on treated areas.	Carbaryl Delnav Diazinon Ethion Guthion Imidan Malathion Methoxychlor Parathion Trithion

Lead Arsenate Insecticide Uses

Fruit Crops (continued)

Crop or Site of Application	Insect Pest	Maximum or Usual Dosage Rate (Lbs. of Actual Insecticide Per 100 Gallons or Per Acre)	Lead Arsenate Limitations	Registered Alternates
	Plum Curculio	2-3 lb. per 100 gals.		BHC Carbaryl Guthion Imidan Lindane Malathion Methoxychlor Parathion
	Red Banded Leafroller	2-3 lb. per 100 gals.		Carbaryl Guthion Imidan Malathion Parathion
	Fruit Tree Leafroller	4 lb. per 100 gal.		Guthion Parathion
	Apple Maggot	2-3 lb. per 100 gals.		Carbaryl Diazinon Guthion Methoxychlor
	Tent Caterpillar	2-3 lb. per 100 gals.		BHC Carbaryl Lindane
	Green Fruitworm	2-3 lb. per 100 gals.		Carbaryl Guthion
	Case Bearers	2-3 lb. per 100 gals.		None
	Syneta Leaf Beetle	3 lb. per 100 gals.		None

Fruit Crops (continued)

Crop or Site of Application	Insect Pest	Maximum or Usual Dosage Rate (Lbs. of Actual Insecticide Per 100 Gallons or Per Acre)	Lead Arsenate Limitations	Registered Alternates
	Red-Humped Caterpillar	3-4 lb. per 100 gals.		None
	Round Headed Apple Tree Borer	3 lb. per 100 gals.		None
	Pear Leafworm	2 lb. per 100 gals.		None
	Pear Slug	4 lb. per 100 gals.		Parathion
Plums - Foliage Application	Plum Curculio	1.0-2 lb. per 100 gals.	30 days. Remove excess residues at time of harvest. Do not graze livestock on treated areas.	Carbaryl Lindane Methoxychlor Methyl Parathion Parathion Toxaphene
	Cherry Fruit Fly	2 lb. per 100 gals.		Carbaryl Methoxychlor
	Apple Maggot	1.5-2 lb. per 100 gals.		None
	Codling Moth	1.5-2 lb. per 100 gals.		Carbaryl
	Cankerworm	1.5-2 lb. per 100 gals.		None

Lead Arsenate Insecticide Uses

Fruit Crops (continued)

Crop or Site of Application	Insect Pest	Maximum or Usual Dosage Rate (Lbs. of Actual Insecticide Per 100 Gallons or Per Acre)	Lead Arsenate Limitations	Registered Alternates
Plums Foliage Application	Red-Banded Leafroller	1.5-2 lb. per 100 gals.		Carbaryl Guthion
	Peach Twig Borer	3-4 lb. per 100 gals.		Carbaryl Diazinon Guthion
	Eye-spotted Bud Moth	3 lb. per 100 gals.		Carbaryl Guthion Methoxychlor Parathion
Prunes Foliage Application	Plum Curculio	2 lb. per 100 gals.	30 days. Remove excess residues at time of harvest. Do not graze live-stock on treated areas.	Carbaryl Guthion Imidan Lindane Methoxychlor Parathion
	Peach Twig Borer	3-4 lb. per 100 gals.		Carbaryl Diazinon Guthion Imidan
	Leaf Rollers	3-4 lb. per 100 gals.		Carbaryl Guthion Imidan
	Eye-Spotted Bud Moth	3 lb. per 100 gals.		Carbaryl Guthion Parathion
	Cherry Fruit Fly	2 lb. per 100 gals.		Carbaryl Methoxychlor

Crop or Site of Application	Insect Pest	Maximum or Usual Dosage Rate (Lbs. of Actual Insecticide Per 100 Gallons or Per Acre)	Lead Arsenate Limitations	Registered Alternates
	Cankerworms	2-4 lb. per 100 gals.		None
	Syneta Beetle	5-6 lb. per 100 gals.		Carbaryl
Quince Foliage Application	Codling Moth	2-3 lb. per 100 gals.	30 days. Remove excess residues at time of harvest. Do not graze livestock on treated areas.	Delnav Guthion Malathion Methoxychlor Trithion
	Plum Curculio	2-3 lb. per 100 gals.		Guthion Malathion Methoxychlor Parathion
	Cankerworm	2-3 lb. per 100 gals.		Methoxychlor
	Red-Banded Leafroller	2-3 lb. per 100 gals.		Guthion
	Tent Caterpillar	2-3 lb. per 100 gals.		
	Apple Maggot	2-3 lb. per 100 gals.		Guthion Methoxychlor
	Fruitworms	2-3 lb. per 100 gals.		Guthion
	Red-Humped Caterpillar	3-4 lb. per 100 gals.		None

Lead Arsenate Insecticide Uses

Fruit Crops (continued)

Crop or Site of Application	Insect Pest	Maximum or Usual Dosage Rate (Lbs. of Actual Insecticide Per 100 Gallons or Per Acre)	Lead Arsenate Limitations	Registered Alternates
	Syneta Beetle	5 lb. per 100 gals.		None
	California Oak Moth	3-4 lb. per 100 gals.		None
Grapes Foliage Application	Achnemon Sphinx Moth	3-4 lb. per 100 gals.	Do not apply after edible parts start to form.	None
	Grape Rootworm	3-4 lb. per 100 gals.		None
	Grape Leaffolder	3-4 lb. per 100 gals.		Carbaryl Diazinon
	Grape Leafroller	3 lb. per 100 gals.		Guthion

Lead Arsenate Insecticide Uses

Vegetable Crops

Crop or Site of Application	Insect Pest	Maximum or Usual Dosage Rate	Lead Arsenate Limitations	Registered Alternates
Asparagus Foliage Application	Asparagus Beetle	3 lb. per acre	Do not apply during cutting season.	Carbaryl Malathion Parathion Rotenone
Tomatoes Foliage Application	Tomato Fruitworm	4-6 lb. per acre	Remove excess residues at time of harvest.	Calcium Arsenate Carbaryl EPN Methoxychlor Methomyl Naled

Lead Arsenate Insecticide Uses

Vegetable Crops (continued)

Crop or Site of Application	Insect Pest	Maximum or Usual Dosage Rate (Lbs. of Actual Insecticide Per 100 Gallons or Per Acre)	Lead Arsenate Limitations	Registered Alternates
	Hornworm	3 lb. per acre		Calcium Arsenate Copper Arsenate Carbaryl Chlordane Naled Parathion Rotenone
	Colorado Potato Beetle	3 lb. per acre		Calcium Arsenate Carbaryl Di-Syston Endosulfan Methoxychlor Parathion Phosphamidon
	Flea Beetle	4 lb. per acre		Calcium Arsenate Copper Arsenate Carbaryl Disyston Endosulfan Methyl Parathion Naled Parathion Rotenone
	Grasshoppers	10 lb. per acre		Carbaryl* Parathion

*Bait Application

Vegetable Crops (continued)

Crop or Site of Application	Insect Pest	Maximum or Usual Dosage Rate (Lbs. of Actual Insecticide Per 100 Gallons or Per Acre)	Lead Arsenate Limitations	Registered Alternates
	Armyworms	4-6 lbs. per acre		Calcium Arsenate BHC Carbaryl* Chlordane* Diazinon Heptachlor Lindane Methyl Parathion Parathion Toxaphene Trichlorofon*

*Bait Application

Lead Arsenate Insecticide Uses

Field Crops

Tobacco Foliage Application	Hornworms	4-6 lb. per acre		Carbaryl Guthion Bacillus Thuringiensis

Lead Arsenate Insecticide Uses

Ornamentals

Ornamentals Foliage Application	California Oak Moth	3-4 lbs. per 100 gals.		Bacillus Thuringiensis
	Bagworms	3 lbs. per 100 gals.		Calcium Arsenate Chlordane Diazinon Dylox Malathion Toxaphene Trithion

Lead Arsenate Insecticide Uses

Ornamentals (continued)

Crop or Site of Application	Insect Pest	Maximum or Usual Dosage Rate (Lbs. of Actual Insecticide Per 100 Gallons or Per Acre)	Lead Arsenate Limitations	Registered Alternates
	Cankerworms	3 lb. per 100 gals.		Calcium Arsenate Methoxychlor Toxaphene
	Pine Sawfly	3 lb. per 100 gals.		Malathion
	Japanese Beetle	3-6 lb. per 100 gals.		Carbaryl Chlordane Methoxychlor
	Catalpa Sphinx	3-6 lb. per 100 gals.		Toxaphene
	Walnut Caterpillar	4 lb. per 100 gals.		Carbaryl Toxaphene
	Fall Webworm	4 lb. per 100 gals.		Diazinon Methoxychlor
	Eastern Tent Caterpillar	4 lb. per 100 gals.		Carbaryl Diazinon Dibrom
	Forest Tent Caterpillar	4 lb. per 100 gals.		Malathion Methoxychlor Toxaphene
	Gypsy Moth	4-6 lb. per 100 gals.		Carbaryl Dylox Gardona Methoxychlor
	Tussock Moth	4-6 lb. per 100 gals.		Methoxychlor

Ornamentals (continued)

Crop or Site of Application	Insect Pest	Maximum or Usual Dosage Rate (Lbs. of Actual Insecticide Per 100 Gallons or Per Acre)	Lead Arsenate Limitations	Registered Alternates
	Elm Leaf Beetle	4 lb. per 100 gals.		Carbaryl Methoxychlor Toxaphene
	Codling Moth	2.0-3.0 lb. per 100 gals.		Guthion Malathion Methoxychlor

Lead Arsenate Insecticide Uses

Lawns and Ornamental Turf

Lawns and Ornamental Turf Soil and Surface Applications		Calcium Arsenate	Carbaryl	Chlordane	Diazinon	Heptachlor	Toxaphene
				REGISTERED ALTERNATES			
Armyworms	80		X	X	X	X	X
Asiatic Garden Beetle	430	X		X		X	
Cutworm	80	X	X	X	X	X	
Earthworm	220	X	X				
Japanese Beetle	430	X		X		X	X
Sod Webworm	80	X	X	X	X	X	
White Grub	220	X		X		X	

I.B.1.a. Conclusions

Lead arsenate has been considered of increasing importance during the
past several years for certain fruit insect control spray schedules.
Reasons given for considering the return to lead arsenate as an insecticide
in integrated control programs have been:

1. Being a stomach poison, the lead arsenate does not kill beneficial
   invertebrate parasites and predators in the orchards as do many
   modern organic pesticides;

2. Need for use of a miticide is greatly reduced on fruit crops
   treated with arsenical pesticides; and

3. If chlorinated hydrocarbon pesticides are severely restricted
   or cancelled certain important fruit pests may not have a
   satisfactory control agent.

All insecticidal uses of lead arsenate are recognized as presenting a hazard to
man and his environment. However, because of need in the integrated spray programs,
the registered uses of lead arsenate on selected fruit crops should be continued
subject to review and phase out prior to the 1975 use-season if satisfactory
alternates are developed. The following crop uses should be retained: apples,
apricots, cherries, nectarines, peaches, pears, plums, prunes, quinces and grapes.
All other uses of lead arsenate as an insecticide should be cancelled since
acceptable alternate pesticides are available.

I.B.2. Calcium Arsenate Insecticide Uses

Crop or Site of Application	Insect Pest	Maximum or Usual Dosage Rate (Lbs. of Actual Insecticide Per 100 Gallons or Per Acre)	Calcium Arsenate Limitations	Registered Substitutes
Berry Crops				
Blueberries Foliage Application	Fruitfly	2 lbs. per 100 gals.	14 days (processed fruit) 30 days (fresh fruit)	Carbaryl Diazinon Guthion Malathion Parathion Rotenone
Vegetable Crops				
Broccoli Foliage Application	Cabbage worms	3-4 lbs. per acre	Do not apply after edible parts start to form	Carbaryl Chlordane Endosulfan Guthion

Vegetable Crops (continued)

Crop or Site of Application	Insect Pest	Maximum or Usual Dosage Rate (Lbs. of Actual Insecticide Per 100 Gallons or Per Acre)	Calcium Arsenate Limitations	Registered Alternates
	Imported Cabbage Worm	4 lb. per acre		Basic copper-arsenate Carbaryl Chlordane Diazinon Endosulfan Guthion Lindane Malathion Methomyl Methyl Parathion Naled Parathion Perthane Toxaphene Rotenone
Cabbage Foliage Application	Cabbage Worm	3-4 lb. per acre	Do not apply after edible parts start to form.	Carbaryl Chlordane Endosulfan Guthion Lindane Malathion Methoxychlor Methyl Parathion Naled Parathion Rotenone
	Cabbage Looper	4 lb. per acre		Endosulfan Guthion Malathion Methomyl Methyl Parathion Naled

Calcium Arsenate Insecticide Uses

Vegetable Crops (continued)

Crop or Site of Application	Insect Pest	Maximum or Usual Dosage Rate (Lbs. of Actual Insecticide Per 100 Gallons or Per Acre)	Calcium Arsenate Limitations	Registered Alternates
	Cabbage Looper cont.			Parathion Perthane Rotenone
	Imported Cabbage Worm	4 lbs. per acre		Basic copper arsenate Carbaryl Endosulfan Guthion Malathion Methomyl Methyl Parathion Naled Parathion Perthane Rotenone
	Diamond Back Moth	4 lbs. per acre		Basic copper arsenate Endosulfan Guthion Malathion Methomyl Methoxychlor Naled Parathion Rotenone
	Fruitworm	4 lbs. per acre		Malathion Methomyl
	Tomato Hornworm	4 lbs. per acre		Malathion

Vegetable Crops (continued)

Crop or Site of Application	Insect Pest	Maximum or Usual Dosage Rate (Lbs. of Actual Insecticide Per 100 Gallons or Per Acre)	Calcium Arsenate Limitations	Registered Alternates
	Flea Beetle	3-4 lb. per acre		Carbaryl Chlordane Diazinon Di-Syston Endosulfan Methoxychlor Methyl Parathion Parathion
	Colorado Potato Beetle	4 lbs. per acre		None
Cauliflower Foliage Application	Cabbageworm & Imported Cabbageworm	3-4 lb. per acre	Do not apply after edible parts start to form.	Basic copper arsenate Carbaryl Chlordane Endosulfan Guthion Malathion Methomyl Methoxychlor Methyl Parathion Parathion Phosphamidon Rotenone Toxaphene
	Cabbage Looper	3-4 lb. per acre		Basic copper arsenate Chlordane Endosulfan Guthion Malathion Methomyl Methyl Parathion

Calcium Arsenate Insecticide Uses

Vegetable Crops (continued)

Crop or Site of Application	Insect Pest	Maximum or Usual Dosage Rate (Lbs. of Actual Insecticide Per 100 Gallons or Per Acre)	Calcium Arsenate Limitations	Registered
	Cabbage Looper cont.			Parathion Perthane Rotenone
	Flea Beetles	3-4 lb. per acre		Carbaryl Chlordane Endosulfan Si-Syston Methoxychlor Methyl Parathion Parathion Rotenone
Celery Foliage Application	Colorado Potato Beetle	1-1.75 lb. per acre	Do not apply after bunch begins to form or after plants are half grown	None
	Flea Beetles	1-1.75 lb. per acre		Methoxychlor Methyl Parathion
	Leaf Hoopers	1-1.75 lb. per acre		Methoxychlor Methyl Parathion Parathion
	Celery Leaf Tier	4.0-5.5 lb. per acre		Methoxychlor Parathion
	Tarnished Plant Bug	4.0-5.5 lb. per acre		Methoxychlor Parathion

Calcium Arsenate Insecticide Uses

Vegetable Crops (continued)

Crop or Site of Application	Insect Pest	Maximum or Usual Dosage Rate (Lbs. of Actual Insecticide Per 100 Gallons or Per Acre)	Calcium Arsenate Limitations	Registered Alternates
Cucumbers Foliage Application	Striped Cucumber Beetle	1-1.75 lb. per acre	Remove excess residues at harvest	Carbaryl Guthion Malathion Methoxychlor Parathion Rotenone
	Squashvine Borer			Methoxychlor Parathion Rotenone
Melons Foliage Application	Striped Cucumber Beetle	1-1.75 lb. per acre	No time limitation	Carbaryl Guthion Methoxychlor Parathion Rotenone
	Squash Bug	4.0-5.5 lb. per acre		Carbaryl
	Squash Vine Borer	4.0-5.5 lb. per acre		Guthion Methoxychlor Parathion
Peppers Foliage Application	Imported Cabbageworm, Cabbage Looper, Diamond back Moth	4 lb. per acre	Remove excess residues at harvest	Methyl Parathion
	Fruitworm	4 lb. per acre		Carbaryl
	Tomato Hornworm	4 lb. per acre		Carbaryl Endosulfan

Calcium Arsenate Insecticide Uses

Vegetable Crops (continued)

Crop or Site of Application	Insect Pest	Maximum or Usual Dosage Rate (Lbs. of Actual Insecticide Per 100 Gallons or Per Acre)	Calcium Arsenate Limitations	Registered Alternates
	Colorado Potato Beetle	4 lb. per acre		Carbaryl Methoxychlor Toxaphene
	Flea Beetles	4 lb. per acre		Carbaryl Endosulfan Methoxychlor Methyl Parathion Parathion Toxaphene
Squash Foliage Application	Striped Cucumber Beetles	1-1.75 lb. per acre	Remove excess residues at harvest	Carbaryl Methoxychlor Parathion Rotenone
Tomatoes Foliage Application	Imported Cabbage Worm	4 lb. per acre	Remove excess residues at harvest	Methyl Parathion
	Cabbage Looper	4 lb. per acre		Methomyl Methyl Parathion
	Diamond Back Moth	4 lb. per acre		
	Tomato Fruitworm	1-1.75 lb. per acre		Lead Arsenate Carbaryl EPN Methomyl Methoxychlor Naled

Vegetable Crops (continued)

Crop or Site of Application	Insect Pest	Maximum or Usual Dosage Rate (Lbs. of Actual Insecticide Per 100 Gallons or Per Acre)	Calcium Arsenate Limitations	Registered Alternates
	Hornworm	3 lb. per acre		Lead Arsenate Copper Arsenate Carbaryl Chlordane Naled Parathion Rotenone
	Budworm	3.5-7 lb. per acre		
	Colorado Potato Beetle	1-1.75 lb. per acre		Lead Arsenate Carbaryl Di-Syston Endosulfan Methoxychlor Parathion Phosphamidon
	Flea Beetle	3 lb. per acre		Lead Arsenate Copper Arsenate Carbaryl Di-Syston Endosulfan Methyl Parathion Naled Parathion Rotenone
	Leafhoppers	1-1.75 lb. per acre		Carbaryl Di-Syston Methyl Parathion Parathion

Calcium Arsenate Insecticide Uses

Poultry Houses

Crop or Site of Application	Insect Pest	Maximum or Usual Dosage Rate (Lbs. of Actual Insecticide Per 100 Gallons or Per Acre)	Calcium Arsenate Limitations	Registered Alternates
Poultry Houses for application to droppings under birds in cages or on wire floors	Housefly and Soldier fly larvae	1.7 lb. per 100 sq. ft. of poultry droppings	Apply to surface of droppings under birds in cages or on wire floor for control of fly larvae.	Kepone Dicapthon Zython

Calcium Arsenate Insecticide Uses

Special Applications--Baits

Calcium Arsenate baits limited to soil treatments are acceptable for use against armyworms, cutworms, slugs, snails and sowbugs. This type application may be used only in accordance with appropriate "Summary clearance and limitations on crops so specified.

Calcium Arsenate Insecticide Uses

Lawns and Ornamental Turf

Crop or Site of Application		Carbaryl	Chlordane	Diazinon	Heptachlor	Lead Arsenate	Toxaphene
Lawns and Ornamental Turf							
Soil and Surface Applications							
Asiatic Garden Beetle*	430		X		X	X	
Cutworms*	430	X	X	X	X	X	
Earwigs*	430	X	X	X	X		
Earthworms*	430		X				

Lawns and Ornamental Turf   (continued)

Crop or Site
of Application

Lawns and Ornamental Turf Soil and Surface Applications		Carbaryl	Chlordane	Diazinon	Heptachlor	Lead Arsenate	Toxaphene
Japanese Beetles*	430		X		X	X	X
Sod Webworms*	430	X	X	X	X	X	
White Grubs*	430		X		X	X	

*Incidental claims - Use of 430 lbs. per acre primarily registered for crabgrass control.

I.B.2.a.   Conclusions

Calcium arsenate dusts and baits have been used extensively for pest control in many crops and ornamentals. Dust applications of the calcium arsenate are effective when used at rates up to 10 pounds of actual per acre in conformity with registrations and tolerances. The bait treatments are used as soil applications for armyworms, cutworms, slugs, snails and sowbugs. Baits of calcium arsenate are registered on a number of crops at rates of 15 pounds of actual per acre. The baits are effective when used in conformity with current registrations and tolerance clearances. Reasons given for retention of calcium arsenate for vegetable and selected fruit control programs have been:

1. Calcium arsenate does not seriously affect beneficial invertebrate parasites and predators in vegetable crops as do many modern organic pesticides; and

2. Need to use a miticide is greatly reduced on vegetables treated with calcium arsenate.

The currently registered uses of calcium arsenate for dusts on vegetables, baits, and for fruitfly on blueberries will be continued. The following uses should be retained:

Type of Application	Crops or Uses
Dusts	Blueberries, Broccoli, Brussels Sprouts, Cabbage, Cauliflower, Celery, Cucumbers, Melons, Peppers, Squash, Tomatoes.
Baits on Soil	General Use.
Sprays	Blueberries

All other uses of calcium arsenate as an insecticide should be cancelled since these uses present a hazard to man and his environment and acceptable alternate pesticides are available.

I. B. 3. Basic Copper Arsenate Insecticide Uses

Vegetable Crops

Crop or Site of Application	Insect Pest	Maximum or Usual Dosage Rate (Lbs. of Actual Insecticide Per 100 Gallons or Per Acre)	Basic Copper Arsenate Limitations	Registered Alternates
Brussels Sprouts Foliage Applications	Cabbage Looper	8 lbs. per acre	Do not apply after edible parts start to form.	Calcium Arsenate Chlordane Endosulfan Guthion Malathion Methomyl Methyl Parathion Naled Parathion Perthane Rotenone
	Imported Cabbageworm	8 lbs. per acre		Calcium Arsenate Carbaryl Chlordane Diazinon Endosulfan Guthion Lindane Malathion Methomyl Methyl Parathion Naled Parathion Perthane Rotenone Toxaphene
Cabbage Foliage Application	Imported Cabbageworm	8 lbs. per acre	Do not apply after edible parts start to form.	Calcium Arsenate Carbaryl Endosulfan Guthion

Vegetable Crops (continued)

Crop or Site of Application	Insect Pest	Maximum or Usual Dosage Rate (Lbs. of Actual Insecticide Per 100 Gallons or Per Acre)	Basic Copper Arsenate Limitations	Registered Alternates
	Imported Cabbageworm cont.			Malathion Methomyl Methyl Parathion Naled Parathion Perthane Rotenone
	Diamond Back Moth	8 lbs. per acre		Calcium Arsenate Endosulfan Guthion Malathion Methomyl Methoxychlor Naled Parathion Rotenone
Cauliflower Foliage Application	Cabbage Worm	8 lbs. per acre	Do not apply after curd starts to form.	Calcium Arsenate Carbaryl Chlordane Endosulfan Guthion Malathion Methomyl Methoxychlor Methyl Parathion Parathion Perthane Phosphamidon Rotenone Toxaphene

Basic Copper Arsenate Insecticide Uses

Vegetable Crops (continued)

Crop or Site of Application	Insect Pest	Maximum or Usual Dosage Rate (Lbs. of Actual Insecticide Per 100 Gallons or Per Acre)	Basic Copper Arsenate Limitations	Registered Alternates
	Imported Cabbageworm	8 lbs. per acre		Calcium Arsenate Carbaryl Chlordane Diazinon Endosulfan Guthion Malathion Methomyl Methoxychlor Methyl Parathion Parathion Perthane Phosphamidon Rotenone Toxaphene
	Cabbage Looper	8 lb. per acre		Calcium Arsenate Chlordane Endosulfan Guthion Malathion Methomyl Methyl Parathion Parathion Perthane Rotenone

Vegetable Crops (continued)

Crop or Site of Application	Insect Pest	Maximum or Usual Dosage Rate (Lbs. of Actual Insecticide Per 100 Gallons or Per Acre)	Basic Copper Arsenate Limitations	Registered Alternates
Kohlrabi Foliage Application	Cabbage Looper	8 lbs. per acre	Do not apply after edible parts start to form.	Chlordane Carbaryl Lindane Methyl Parathion Naled Parathion Rotenone
	Imported Cabbageworm	8 lbs. per acre		Chlordane Carbaryl Lindane Methyl Parathion Parathion
Tomatoes Foliage Application	Flea Beetles	15 lbs. per acre	No time limit.	Lead Arsenate Calcium Arsenate Carbaryl Di-Syston Endosulfan Methyl Parathion Naled Parathion Rotenone
	Hornworms	15 lbs. per acre		Lead Arsenate Calcium Arsenate Carbaryl Chlordane Naled Parathion Rotenone

I.B.3.a. Conclusions

The registered uses for basic copper arsenate as an insecticide should be cancelle
These uses present a hazard to man and his environment. Acceptable alternate
pesticides are available.

I.B. 4. Ammonium Arsenite Insecticide Uses

Wood Preservative

Crop or Site of Application	Insect Pest	Maximum or Usual Formulation Ingredient	Registered Alternates
Wood Preservative	Wood Destroying Insects	7.7%*	Creosote Pentachlorophenol

*Pressurized with other ingredients

I.B.4.a. Conclusions

The registered use for ammonium arsenite as a wood preservative (insecticide
and fungicide) should be retained. For more details, see I.B.9.a. and I.D.,
Industrial Wood Preservatives.

I.B. 5. Arsenic Acid Insecticide Uses

Wood Preservative

Crop or Site of Application	Insect Pest	Maximum or Usual Formulation Ingredient	Registered Alternates
Wood Preservative	Wood Destroying Insects	42.0%*	Creosote Pentachlorophenol

*Pressurized with other ingredients

I. B. 5.a. Conclusions

The registered use of arsenic acid for wood destroying insects should be retained. For more details see I.B.9.a. and I.D., Industrial Wood Preservatives.

I.B. 6. Arsenic Pentoxide Insecticide Uses

Wood Preservative

Crop or Site of Application	Insect Pest	Maximum or Usual Formulation Ingredient	Registered Alternates
Wood Preservative	Wood Destroying Insects	4.08-34.0%*	Creosote Pentachlorophenol

*Pressurized with other ingredients

I.B.6.a. Conclusions

The registered use of arsenic pentoxide for wood destroying insects should be retained. For more details see I.B.9.a. and I.D., Industrial Wood Preservatives.

I.B.7. Arsenic Trioxide Insecticide Uses

Wood Preservative

Crop or Site of Application	Insect Pest	Maximum or Usual Formulation Ingredient	Registered Alternates
Wood Preservative	Wood Destroying Insects	37.0%*	Creosote Pentachlorophenol

Wood Preservative (continued)

Crop or Site of Application	Insect Pest	Maximum or Usual Formulation Ingredient	Registered Alternates
Antifouling Paint	Insect and Invertebrate Pests	1.5%*	Metallic copper compounds Tri-N-Butyltin Flouride Tri-N-Butyltin Oxide Tri-N-Butyltin Resinate

*Pressurized with other ingredients

I.B.7.a. Conclusions

The combination of arsenic trioxide or Paris green with copper compounds in anti-fouling paints enhances the anti-fouling activity which cannot be achieved with copper compounds alone. The organic tin compounds are also toxic and on a cost basis less effective than the arsenicals. The quantities used and the dispersal achieved in a body of water can have no general effect on the ecosystem and the arsenic content of sea water. The registered uses of arsenic trioxide as a wood preservative and in antifouling paint should be retained. For more details, see I.B.9.a. and I.D. Industrial Wood Preservatives.

I.B.8. Sodium Pyroarsenate Insecticide Uses

Wood Preservative

Crop or Site of Application	Insect Pest	Maximum or Usual Formulation Ingredient	Registered Alternates
Wood Preservative	Wood Destroying Insects	6.2%*	Creosote Pentachlorophenol

*Pressurized with other ingredients.

I.B.8.a. Conclusions .

The registered use of sodium pyroarsenate for wood destroying insects should
be retained. For more details, see I.B.9.a.

I.B.9. Wolman Salts Insecticide Uses

Wood Preservative

Crop or Site of Application	Insect Pest	Maximum or Usual Formulation Ingredient	Registered Alternates
Wood Preservative	Wood Destroying Insects	6.2-26.9%*	Creosote Pentachlorophenol

*Pressurized with other ingredients.

I.B.9.a. Conclusions

Arsenic is a standard ingredient in water soluble preservatives which are
used to pressure impregnate wood products. In pressurized treatments
the chemicals are contained in an enclosed system which is recycled and
do not contaminate the environment. Two common mixtures contain salts of
copper, chromium and arsenic. Another is a fluoro-chrome-arsenic-
phenol mixture. The purpose of treating the wood with these preservatives
is to protect it against decay and insect attack.

Arsenic exhibits both fungicidal and insecticidal properties. It is an
important ingredient of the preservative mixture. Arsenic plays an important
role in the fixation of the chemicals in wood. The chemicals undergo reactions
with the wood and are converted to insoluble compounds. The arsenic is fixed
to the wood and does not leach out.

There is no satisfactory substitute for arsenic in the preservative mixture.
For these uses, we should retain the registrations for arsenic acid, ammonium
arsenite, arsenic pentoxide, arsenic trioxide, sodium pyroarsenate, sodium
arsenate, and Wolman salts.

I. B. 10. Cacodylic Acid Insecticide Uses

Forest Application

Crop or Site of Application	Insect Pest	Maximum or Usual Dosage Rate	Limitations	Registered Alternates
Forest Application By U.S. Forest Service only	Insect Trapping			
	Engleman Spruce Beetle	1 ML per inch of tree surface		None
	Mountain Pine Beetle			
	Douglas Fir Beetle			
	Round Headed Pine Beetle			
	Arizona Five-Spined Beetle			
	Pine Engraver Beetle			
	California Five-Spined Beetle			

I. B. 10. a. Conclusions

The registration of cacodylic acid for forest application (trapping insects) should be retained for the U.S. Forest Service.

I.B.11. Sodium Arsenite and Potassium Arsenite Insecticide Uses

Soil, Household and Commercial

Crop or Site of Application	Insect Pest	Maximum or Usual* Dosage Rate	Sodium Arsenite Limitations	Registered Alternates
Soil	Subterranean Termites	9% Solution		Chlordane Heptachlor Pentachloro phenol
Household and Commercial (Bait Application)	Ants	2.0%		Kepone

*Formulation Ingredient

Sodium Arsenite and Potassium Arsenite Insecticide Uses

Livestock

USDA Livestock Quarantine (Cattle Dip)	Ticks	0.25% Solution		None

*Formulation Ingredient

I.B.11.a. Conclusions

Sodium arsenite is too toxic for patterns of use involving storage in the home environment. The registered uses for control of subterranean termites and ants by the homeowner should be cancelled.

The essential program of guarding the United States - Mexico border against introduction of the Texas cattle fever tick is based on the use of sodium arsenite and potassium arsenite in dip tanks. This use is restricted to the United States Department of Agriculture. There is no safe and effective alternate pesticide which has a simple and efficient vat-side test for determining pesticide concentration. The risk of re-introduction of this tick into the United States would be great without availability of the arsenical dip or until an alternate tickicide is developed. . .

I. B. 12. Sodium Arsenate Insecticide Uses

Soil, Structures, Wood Preservative, Household and Commercial

Crop or Site of Application	Insect Pest	Maximum or Usual** Dosage Rate (Lbs. of Actual Insecticide Per 100 Gallons or Per Acre)	Registered Alternates
Structural	Drywood Termites	43% Dust	Hydrogen Cyanide Methyl Bromide Sulfuryl Flouride
Soil	Subterranean Termites	2% Solution	Chlordane Heptachlor Pentachlorophenol
Wood Preservative	Termites and Wood Destroying Insects	14.0-43.5%*	Creosote Pentachlorophenol
Household and Commercial (Bait Application)	Ants	0.7-3.0%	Kepone

*Pressurized with other ingredients.

**Formulation Ingredient

I.B.12.a. Conclusions

The package for the household bait should not exceed one fluid ounce containing 2.5 percent sodium arsenate or any combination of concentration and package size that contains no more than 0.75 gram of sodium arsenate. The use of sodium arsenate should be retained for structural and soil applications by pest control operators only to control drywood and subterranean termites. The use of sodium arsenate as a wood preservative should be retained. For more details, see I.B.9. and I.D., Industrial Wood Preservatives (fungicide).

I. B. 13. Paris Green Insecticide Uses

Aquatic, Structures, and Antifouling Paint

Crop or Site of Application	Insect Pest	Maximum or Usual Dosage Rate (Lbs. of Actual Insecticide Per 100 Gallons or Per Acre)	Lead Arsenate Limitations	Registered Alternates
Aquatic Areas	Mosquito Larvae	0.6-15 lbs. per acre		Abate BHC Coal Tar Neutral Oils Cresylic Acid Malathion Methoxychlor
Structures	Dry Wood Termites	100% Dust		Hydrogen Cyanide Methyl Bromide Sulfuryl Fluoride
Antifouling Paint	(Insect and Invertebrate Pests)	16-26.5%		Metallic Copper Compounds
	Gribbles			Tri-N-Butyltin Fluoride
	Teredos			Tri-N-Butylin Oxide
	Shipworms			Tri-N-Butyltin Resinate

I.B.13.a. Conclusions

Paris green has been used in a large volume (957,144 pounds of 5% granules
Florida in 1970) in several Southeastern states during tthe past 15 years.
While several insecticides are available for use as a larvicide, oil is
the only known substance that can be used in place of Paris green without
risking loss of control due to resistance.' Oils, which may be substituted
in the spring, have to be abandoned when the vegetation prevents adequate
penetration. In addition to the resistance problem, the synthetic organic
pesticides are generally more hazardous to fish and wildlife than Paris green.

Personnel of the West Florida Arthropod Research Laboratory have conducted research on the disappearance of arsenic from soil and water. Mr. C.B. Rathburn in an article entitled "The Arsenic Content in Soil Following Repeated Applications of Granular Paris Green" (Mosquito News 26, 537-539, 1966) states that from data obtained there appears to be no evidence of an accumulation of arsenic in soil following repeated (8) applications of granular Paris green to the water surface as a larvicide.

The registered uses of Paris green should be retained for control of mosquito larvae, drywood termites and in antifouling paints to control insect and invertebrate pests.

For use in antifouling paint see I.B.7.a.

I.B.14. Herbicide--Citrus

Arsenical	Action	Usual Dosage Rate (Lbs. of Actual Per Acre)	Limitations	Registered Alternates
Cacodylic Acid	Weed Control	2-5	Nonbearing citrus only. Do not exceed 3 applications per year. Do not harvest fruit from treated trees within one year	Bromacil Dalapon Dichlobenil DNBP Diphenamid Diuron Eptam Paraquat Monuron-TCA

I.B.14.a. Conclusions

The registered use of cacodylic acid for weed control in citrus should be retained. Cacodylic acid is essential for the control of emerged johnsongrass.

I.B.15.a. Herbicide--Around Ornamental Trees and Shrubs

Arsenical	Action	Usual Dosage Rate (Lbs. of Actual Per Acre)	Arsenic Limitations	Registered Alternates
Cacodylic Acid	Weed Control	10-20	Do not graze.. Do not contaminate water.	Atrazine Benefin Betasan CDEC Dacthal
DSMA	"	5-15	Do not contaminate water.	Dichlobenil IPC Norea Paraquat
MSMA	"	2-5	Do not treat newly seeded lawns.	Simazine Silvex Treflan

I.B.15.a. Conclusions

The registered uses of cacodylic acid, DSMA and MSMA around ornamental trees
and shrubs should be retained.

These materials are essential for control of emerged johnsongrass

I.B.16. Herbicides--Lawns and Ornamental Turf

Arsenical	Action	Usual Dosage Rate (Lbs. of Actual Per Acre)	Arsenic Limitations	Registered Substitutes
Arsenic Acid	Weed Control	10-40	Do not water for 3 days after treatment.	Atrazine Benefin Betasan Dalapon
Calcium Arsenate (tricalcium arsenate)	"	80-600	Do not apply to newly seeded lawns. Do not allow children or pets on lawn before it dries.	Dicamba Dichlobenil Petroleum o Siduron Simazine Silvex Treflan
Cacodylic	"	10-20	Do not graze. Do not contaminate water.	2,4-D
Lead Arsenate	"	70-200	Keep children and pets off treated area.	
DSMA	"	5-15	Do not contaminate water.	
MSMA	"	2-5	Do not treat newly seeded lawns	
AMA	"	1-3	Do not use on newly seeded lawns.	
Arsenic Trioxide (Arsenous oxide)	"	200-400		
Sodium Arsenite	"	1-8		

I.B.16.a. Conclusions

The following actions are suggested for the registered arsenical herbicides
for lawns and ornamental turf:

1. Arsenic acid is too toxic for this use and should be cancelled;

2. Calcium arsenate use limited to Poa annua control and restricted
    to optimal effective rates on golf courses and related recreational
    turf;

3. Cacodylic acid use should be retained, especially for control of
    emerged johnsongrass;

4. Lead arsenate should be cancelled to reduce the amount of lead
    introduced into the home environment.

5. DSMA, MSMA and AMA should be retained, especially for control
    of emerged johnsongrass;

6. Arsenic trioxide and sodium arsenite are too toxic for this use
    and should be cancelled.

I.B.17. Herbicides--Non-Crop, Industrial Sites, Rights-of-Way
         Driveways and Sidewalks

Arsenical	Action	Usual Dosage Rate (Lbs. of Actual Per Acre)	Arsenic Limitations	Registered Alternates
Arsenic Acid	Weed Control	10-40	Spray to runoff. Do not graze treated areas. Do not contaminate water.	Amitrole Ammonium sulfamate Atrazine Bromacil
Cacodylic Acid	"	2-5 lbs/100 gal. H_2O		Dicamba Diphenamid Diuron
DSMA	"	2-5 lbs/100 gal. H_2O		DNBP Eptam Fenac Linuron

Arsenical	Action	Usual Dosage Rate (Lbs. of Actual Per Acre)	Arsenic Limitations	Registered Alternates
MSMA	Weed Control	2-5 lbs/100 gal. H_2O		Monuron Paraquat Petroleum oil Simazine Silvex 2,4-D 2,4,5-T

I. B. 17. a. Conclusions

The actions on arsenic acid, cacodylic acid, DSMA and MSMA should be the same as given for I.B.16.a.

I. B. 18. Herbicides--Hardwood Tree Control

Arsenical	Action	Usual Dosage Rate (Lbs. of Actual Per Acre)	Arsenic Limitations	Registered Alternates
Cacodylic Acid	Tree Injection	1 ml/cut		Dicamba 2,4-D 2,4,5-T
MSMA		1-2ml/cut		Picloram

I.B.18.a. Conclusions

This method of application minimizes environmental contamination. The registered uses of cacodylic acid and MSMA for hardwood tree control should be retained.

I. B. 19.--Herbicides Semi-Soil Sterilant

Arsenical	Action	Usual Dosage Rate (Lbs. of Actual Per Acre)	Arsenic Limitations	Registered Alternates
Sodium Arsenite (Arsenic Trioxide)	Weed Control	To 50 lbs/A.	Bare ground application and must be enclosed.	Bromacil Sodium Borate-Chlorate Combinations Ammonium Sulfamate
Sodium Arsenite (Arsenic Trioxide)	"	50 or more lbs/A.	Must be covered by pavement.	Same

I. B. 19.a. Conclusions

The registered uses for sodium arsenite and arsenic trioxide as a semi-soil sterilants are too hazardous and should be cancelled. Safer alternates are available and should be substituted.

I.B. 20. Herbicides--Cotton

Arsenical	Action	Usual Dosage Rate (Lbs. of Actual Per Acre)	Lead-Arsenic Limitations	Registered Alternates
MSMA	Post emergence weed control	1-2	Do not graze or feed forage to livestock. Do not apply after first bloom.	Betasan Dacthal Diuron Eptam Monuron Norea Treflan
DSMA	"	2-3		

NOTE: Large favorable response requesting use after Federal Register Notice.

T. B.20.a. Conclusions

These materials are essential in combination or alone in post-emergence weed control programs of cotton to minimize loss of crop due to emerged johnsongrass and other hard to control weeds. MSMA or DSMA are used on 4,000,000 acres of cotton for control of weeds. It has been estimated that up to 12,000,000 pounds of these materials are used annually on cotton in the United States.

Inability to use MSMA and DSMA in cotton would result in losses of about $60,000,000 per year. It would also require heavy use of other replacement herbicides and hand labor.

Registered uses of DSMA and MSMA do not increase the content of arsenic in cotton seed. Danger to workers in cotton production, to wildlife and to farm animals is minimal. There has been concern expressed by investigators that the increasing use of these materials could lead to residual amounts of arsenic in the soil. More than 5 ppm available arsenic in the soil may be hazardous to field crops.

The registered uses of MSMA and DSMA for weed control in cotton should be retained.

I.B. 21. Desiccant and Defoliant--Cotton

Arsenical	Action	Usual Dosage Rate (Lbs. of Actual Per Acre)	Arsenic Limitations	Registered alternates
Arsenic Acid	Harvest aid (desiccant and defoliant)	2-4.4	Apply 7-10 days before harvest.	Sodium borate Sodium chlorat Ammonia Ammonium nitrat Neo-decanoic acid Def Folex

NOTE: Large favorable response requesting use after Federal Register Notice.

I.B. 21.a. Conclusions

Approximately 900,000 gallons of arsenic acid are used each year as a
preharvest desiccant of cotton. An effective desiccant is essential for
economical production of cotton on about 2,000,000 acres of land in
Texas and Oklahoma. In these two states, where the arsenic acid is needed,
the cotton is harvested by mechanical strippers which are used on special
varieties of cotton after defoliation. No economically satisfactory
desiccant, other than arsenic acid, has been developed in the specific
areas of Texas and Oklahoma. Inability to use the arsenic acid as a desiccant -
defoliant would cause an estimated loss of $163,000,000 in the two states.

The hazard of using arsenic acid as a desiccant on cotton has been recognized.
However, the United States Department of Agriculture is not aware of serious
injury to people exposed during the cotton production and processing procedures.
There has been concern expressed by investigators that increased use of arsenic
acid could lead to residual amounts of arsenic in the soil.

The registered use of arsenic acid as a desiccant and defoliant of cotton
should be retained.

I.B. 22. Regulator--Grapefruit

Arsenical	Action	Usual Dosage Rate (Lbs. of Actual Per Acre)	Arsenic Limitations	Registered Alternates
Lead Arsenate	Plant regulator - Reduce acidity	1.7-5.4	Do not use on other citrus. Do not apply within 3 days of harvest	None

I.B.22.a. Conclusions

Arsenic is needed as a regulator of grapefruit intended for harvest in Florida.
Lead arsenate has been registered for the use (reduce acidity) at rates of
1.7 to 5.4 pounds of actual per acre. It is not intended for use on other
citrus or within 3 days of harvest. Successful marketing of Florida grapefruit
would not be possible without arsenic to reduce natural acidity.

Lead arsenate has had a long history of successful use on Florida grapefruit.
In the central part of the state where approximately 75 percent of the Marsh
Seedless grapefruit, 60 percent of the Red and Pink grapefruit, and 85 percent
of the seedy grapefruit are produced, arsenic is used on 90 percent of the
acreage. It is estimated that this use represents a total of approximately
60,000 acres of Florida grapefruit.

Residues from the use of lead arsenate as described above on mature washed fruit are less than 0.5 ppm arsenic and seldom over 0.5 ppm lead on the whole-fruit basis. Arsenic residues in the edible portion ranged from 0.003 ppm down to 0.0003 ppm.

Failure to have arsenic available for use would delay picking, packing and processing. It is not feasible to extend the season into June and July because Florida grapefruit is such that satisfactory quality in most groves is impossible to maintain to such late dates. This would create a serious marketing problem for most of the Florida grapefruit.

Although there is no other registered arsenical for this use, it is believed that calcium arsenate can be substituted. This would eliminate the potential hazards which the use of lead creates. Calcium arsenate should be registered for this use. The use of lead arsenate should be retained subject to review of the status of calcium arsenate as a replacement prior to the 1975 use-season.

I.C. Summary of Registered Arsenical Rodenticides Uses and Registered Substitutes

Arsenical	Rodent	Concentration Used	Registered Substitutes
Arsenic Trioxide	Rats	1.5 - 3% Baits	Red Squill Zinc Phosphide
	House Mice	1.5 - 3% Baits	Zinc Phosphide Strychnine
	Moles	1.5% Baits	Strychnine Calcium Cyanide

I.C.1. Conclusions

Zinc phosphide is an acceptable substitute for arsenic trioxide for house mice. The registered uses of arsenic trioxide should be retained for rodent control by pest control operators only.

I.D. Summary of Registered Arsenical Fungicide Uses and Registered Non-Arsenical
Substitutes

I.D.1. Agricultural Food Crops

Arsenical	Crop or Site of Application	Plant Disease	Maximum or Usual Dosage Rate (lbs. of Actual Fungicide Per 100 gals. or per acre)	Registered Substitutes
Sodium Arsenite	Grapes	Black Measles Crown Gall and Dead Arm	3-9 lbs per acre in dormant season	None
Basic Copper Arsenate	Tomatoes	Early and Late Blight	13.65 lbs actual/ acre. 7 to 10 day intervals	Captan, various copper compounds, various dithio-carbamates, ethylenebis dithiocarbamates. Dichlone Dyrene Difolatan

I.D.1.a. Conclusions

Sodium Arsenite on Grapes:

This use is confined to western areas, principally in the San Joaquin Valley
of California where it is the only fungicide which effectively controls the
diseases for which it is registered. On some farms it is necessary to apply
annually, on others it may be used once every two or three years. In
California 30,000 acres require treatment annually. Annual losses in
California without treatment have been estimated for 1.5 to 5.0 percent with
an average of 3.0 percent. Losses in individual vineyard range from 1.0 to
40.0 percent of the fruit. Infected fruit have no economic value. The
California crop is valued at $165,000,000 with an average loss without
treatment at $7,000,000. Note that the University of California is presently
engaged (with EPA) in a cooperative monitoring study.

The California Pesticide Use Report lists 534 applications of a total of
90,000 pounds of Sodium arsenite on grapes in 1970.

The registered uses of sodium arsenite as a dormant application for black
measles, dead arm and crown gall control on grapes should be retained.

Basic Copper Arsenate on Tomatoes:

The currently registered uses of basic copper arsenate for early and late
blight on tomatoes should be retained subject to review and phase out prior to
the 1975 use season if satisfactory alternates exist.

I.D. 2. Industrial Uses as Wood Preservatives

Pressure Treatments

Arsenical Pesticides and other Compounds	Special Comments	Registered Substitutes*
14% arsenic acid, 34% chromic acid and 9% copper oxide	Used as 1 to 5% aqueous solutions	None
42% arsenic acid, 27% chromic acid and 15% copper oxide	Used as 1 to 5% aqueous solutions	"
35% arsenic acid, 36.5% sodium arsenate, and 28.1% sodium dichromate	Used only by importer in his plant	"
30.5% arsenic pentoxide dihydrate, 6.2% sodium hypoarsenate, 31.5% sodium dichromate and 26.8% copper sulfate	Used as 1 to 5% aqueous solutions	"

I.D.2. (cont'd)

Arsenical Pesticides and other Compounds	Special Comments	Registered Substitutes*
34% pentoxide, 26.5% chromic acid, and 14.5% cupric oxide	Used as 1 to 5 % aqueous solution	None
26.9% arsenic pentoxide, 42.6% sodium dichromate, and 25.5% copper sulfate	Used as a 1 to 5% aqueous solution	None
23.8% arsenic pentoxide, 33.35% chromic acid, and 12.95% copper oxide	Used as to 1 to 5% aqueous solution	None
17% arsenic pentoxide, 23.75% chromic acid, and 9.25% cupric oxide	Used as a 1 to 5% aqueous solution	None
10% arsenic pentoxide, 53% potassium dichromate, and 32% copper sulfate	Used as a 1 to 5% aqueous solution	None
23.8% disodium arsenate, 34.2% sodium chromate, 27.5% sodium fluoride, and 9.5% technical sodium pentachlorophenate	Used as 0.5 to 5% aqueous solutions	None
23.8% sodium arsenate, 35.6% sodium chromate, 23.8% sodium fluoride, and 11.8% pentachlorophenol	Used as 0.5 to 5% aqueous solutions	None
6.0% sodium arsenate, 33.3% sodium fluoride, 32% sodium dichromate, and 4.3% 2,4-dinitrophenol	Used as 1.5 to 3% solution	None

*Creosote, pentachlorophenol and etc. are oil-borne products which can be substituted only in limited use for the above pressure treatments.

I.D.2. (cont'd)

Injection Treatments

Arsenical Pesticides and Other Compounds	Special Comments	Registered Substitute**
20% arsenic trioxide, 51% sodium fluoride and 21.5% 2,4-dinitrophenol	Injected as an aqueous paste	None
11.59% arsenic trioxide, 26.04% sodium fluoride, 16.23% 2,4-dinitrophenol, and 5% pentachlorophenol	a ready-to-use liquid for injection	"
4.8% sodium arsenate and 10.9% sodium fluoride	Dilute 1 gallon of concentrate with 1.5 gals. of water and inject 1 gallon of diluted solution/cubic foot of wood or until refusal	"

**Creosote, pentachlorophenol and etc. are oil-borne products which can be substituted only in limited use for the above injection treatments.

Diffusion Treatments

6% sodium arsenate, 33% sodium fluoride, 32% sodium dichromate, and 4.3% dinitrophenol	Use on green mine timbers. Method of application seldom used. Effective but time consuming	None

Brush, Mop or Swab Treatments

7.7% ammonium arsenite and 4.3% metallic copper in a copper-ammonium complex	Brush or spray to surfaces of chemonite (R) pressure treated wood with new exposures due to cutting, notching or dapping	None
4.08% arsenic pentoxide, 3.8% chromic acid, and 1.74% cupric oxide	A ready-to-use solution for brush, mop or pressure treating of wood.	None
25% sodium arsenate, 32.98% sodium fluoride, 32% sodium dichromate, and 6.3% 2,4-dinitrophenol	Apply solutions of 1.14 to 1.6 specific gravity to green timbers and posts. Cover air tight and allow to stand 30 days or longer to allow diffusion of ingredients into timbers	None

I.D.2. (cont'd)

Arsenical Pesticides and Other Compounds	Special Comments	Registered Substitute
5.04% sodium arsenate, 7% potassium dichromate, 6.86% sodium fluoride, and 1.23% 2,4-dinitrophenol	Apply to mine timbers	None
1.4% sodium arsenate, 2.1% sodium chromate, 1.4% sodium fluoride, 1.4% pyridine and 0.7% 2,4-dinitrophenol	Apply to exposed surfaces when cutting, dapping or notching pressure-treated wood.	"

I.D. 2.a. Conclusions

Pressure treatments for wood preservatives:

The arsenic containing wood preservatives are "permanent" and treated woods have a useful life of up to 80 years in products such as poles, ties, bridge members and other heavy members. Properly treated railroad ties are replaced for mechanical failure before failure of the preservatives.

A total of 260.3 million cubic feet of wood products were treated by the United States wood-preserving industry in 1970. It has been estimated that 291,449,000 board feet of lumber and timber, 7,680,000 square feet of plywood, 715,000 cubic feet of miscellaneous materials, 431,000 posts and 27,000 cross ties were treated with arsenic compound products in 1970 in the United States. Failure to maintain long service life would result in astronomical replacement costs. In some areas failure to adequarely provide treated wood would require a switch to other, more expensive and less desirable building materials, and in the case of poles and ties, to relatively less safe substitutes. Certain types of wood products intended for particular uses have substitute materials available, particularly creosote. No substitute for the arsenic preservatives are available, for other types of wood where color, paintability, presence of certain fungi or other factors are involved. These data and comments are also applicable to injection treatments. It is concluded that the pressure treatments of all the arsenic compounds should be retained.

Injection treatments for wood preservatives:

For more details see the "Conclusions" for pressure treatments. The injection treatments of the arsenic compounds should be retained.

Diffusion treatments for wood preservatives:

Diffusion treatments are more effective than brush or spray applications of the same type of products and less effective than pressure treatments of the same products. These treatments are needed especially in Alaska where simplicity of equipment and a small capital investment are necessary to maintain an industry. The double diffusion treatments should be retained for industrial application only.

Brush, Mop or swab treatments for wood preservatives:

Products designed for application by brush, mop or swab are used as a
follow-up after cutting, notching or dapping of pressure or injection
treated wood. They are applied "on the job" by the construction contractor's
personnel to insure maximum protection of the wood to be placed under
extreme exposure conditions. These treatments are a valuable adjunct and
"insurance policy" for extended useful life of sills, foundation timbers,
bridges and other structures. The volume of such use is very small, less
than 1.0 percent of the total use of commercial wood preservatives, and it
does not represent a hazard to man and his environment.

The brush, mop and swab treatments should be retained.

I.D.3. Other Industrial Uses

Arsenical Pesticide	Use	Special Comments	Registered Substitutes
10,10'-oxybisphenoxarsine	Cotton fabric coated with thermo-plastic system protects against fungi	Apply by padding to retain 400 to 1000 ppm.	3,4'5-tribromo-salicylanilide
10,10'-oxybisphenoxarsine	Vinyl films (shower curtains, wall coverings, and similar items.	Use at 300-500 ppm by weight. Not to be used on clothing or other material for which pro-longed contact with skin is recommended	Bistributyltin oxide; bistributyl tin oxide in combination with dialkyl dimethyl ammonium chloride, salicylic acid and isopropanol. Captan; 2,4-dichloro-6-(0-chloroanilino)-S-triazine; tributyl tin linoleate; phenylmercuric hydroxide; 3,4', 5-tribromosalicyl-anilide; zinc 2-pyridimethiol 1-oxide

I D.3.a. Conclusions

Textiles - cotton fabric coated with thermoplastic systems:

10,10'-oxybisphenoxarsine is more effective than the substitute chemical
and possibly less subject to leaching. Impact of withdrawal of this use for
arsenic would be severe, particularly on boat fabrics in tropical and semi-
tropical locations. This is the principle use described above.

The use of 10,10'oxybisphenoxarsine in textiles should be retained.

Vinyl films (shower curtains, wall coverings and other similar items):

10,10'oxybisphenoxarsine is more effective and less subject to leaching than
the substitute compounds. It is estimated that this arsenical compound is
used in 90 percent of all flexible polyvinyl chloride films produced to
control all commercially important fungal organisms associated with surface
growth and vinyl degradation. Millions of pounds of vinyl film formulations
were treated with 10,10'-oxybisphenoxarsine in 1970. This represents tens
of millions of dollars in protected vinyl films and coatings.

Use of 10,10'oxybisphenoxarsine in vinyl films should be retained.

Arsenic is one of the elements for which a review of its distribution
and significance in the environment has been found essential. Such a
review would not be complete without a summarization of pertinent facts
for arsenic from the analytical viewpoint.

II.A. General Chemistry -- Arsenic (As) has the atomic number 33 and an
atomic weight of 74.92. In the periodic table of the elements, arsenic
is midway between germanium and selenium in atomic mass. Arsenic, as a
member of Group V of the periodic table has physiochemical properties
similar to phosphorus. Arsenates strongly resemble phosphates in
solubility and crystal form. Arsenic also forms trihalides analogous
to those of phosphorus. (Vallee, et al., 1960).

The important compounds of arsenic are classified into three groups:
(a) Inorganic arsenicals: white arsenic (arsenic trioxide), arsenate
salts, and arsenite salts; (b) organic arsenicals: These compounds
include the mono and disodium salts of methanearsonic acid, and cacodylic
(dimethylarsenic) acid; and (c) gaseous arsenic, that is, arsine, or
hydrogen arsenite.

In the native state, arsenic usually exists as a sulfide ore--orpiment
(As_2S_3), realgar (As_2S_2), or arsenopyrite (FeAsS). Arsenic sulfides
are usually found with metal sulfides, silver, lead, copper, nickel,
antimony, and cobalt, as well as iron. Arsenic trioxide (also called
arsen(i)ous acid, arsen(i)ous oxide, or white arsenic) is a byproduct
of the smelting of copper and lead ores. Most arsenical pesticides are
prepared from arsenic trioxide, although lead arsenate is not.

To prepare lead arsenate, litharge (lead oxide) is the starting material.
Litharge plus acetic acid yields acetate, which reacts with sodium
arsenate to form lead arsenate. Lead arsenate has been used as an
insecticide in the United States since 1892 (Mrak, 1969).

Briefly, other common arsenic pesticides are prepared as follows: (1)
Sodium arsenite is the reaction product of arsenic trioxide plus sodium
hydroxide; (2) Oxidation of sodium arsenite by nitric acid or hydrogen
peroxide yields sodium arsenate; (3) DSMA is manufactured by methylation
of sodium arsenite with methylchloride; and, (4) MSMA is produced by
treatment of DSMA with hydrochloric acid.

II. B. Analytical Methods - There are a number of official AOAC methods for analyses of arsenic in pesticide formulations, foods, drugs, animal feeds, and mineral waters. The methods are nonspecific with regard to parent pesticides (Anonymous, 1970a and Anonymous, 1971).

In addition to the officially adopted methods, methods based on atomic absorption and activation analysis have been applied. The extreme sensitivity attainable by the latter method is somewhat nullified by the endogenous arsenic or background found in most soils, crops, marine organisms, and animal tissues. Discussion of methods for the individual substrates are given below.

II.B.1. Analysis of Formulations - The hydrazine sulfate distillation procedure (AOAC Method 6.004) is said to be suitable for analysis of Paris green, lead arsenate, calcium arsenate, zinc arsenite, and Bordeaux mixtures. Nitrates do not interfere with success of the method.

If the formulation contains sulfides, sulfites, thiousulfates, and large quantities of organic matter, the method of choice would be the iodimetric titration (AOAC Method 6.007) following nitric-sulfuric acid digestion. However, iron, copper, chromium, tin, antimony, and manganese interfere with the titration.

Inorganic arsenates and arsenites in formulations may be determined by an ion exchange method (AOAC Method 6.009).

II. B. 2. Analysis of Food Crops - Residues of arsenic in food crops may be determined by the official molybdenum blue method (AOAC 25.014) or the official silver diethyldithiocarbamate method (AOAC 25.016). These methods have to some extent supplanted the traditional Gutziet method for measuring evolved arsine. The estimated sensitivities in food products are about 0.1 ppm for the molybdenum blue method and 0.01 ppm for the silver diethyldithiocarbamate method (expressed as As_2O_3). Atomic absorption procedures for analysis of arsenic in foods appears promising.

II.B.3. Analysis of Biologicals - Residues of arsenic in biological materials may be analyzed by the AOAC silverdiethyldithiocarbamate method, following digestion to remove organic material. Neutron activation methods have also been used.

II.B.   Analysis of Water - Water is generally analyzed by modifications of the above methods. However, the usual procedure is the silver diethyldithiocarbamate method.

II. B. 5. – Analysis of Soils -- Several of the various analytical techniques mentioned above could probably be adapted to soils. At the present time, the methods of choice for arsenic in soils would be the official AOAC colorimetric procedures (AOAC 25.014 or AOAC 26.006). Successful application of these methods to soils were reported by Baker, et al (1969).

Application of an atomic absorption procedure to arsenic analyses of soils was reported by Stevens, et al (1970).

II. C. Arsenic in Soil –

II. C. 1. Buildup in Soil – Arsenic is one of the common constituents of all native soil. Vinogradov (1959) found the average arsenic content of soils from various countries to be above five parts per million (ppm). Other investigators report varying concentrations of arsenic in untreated soil in North America; Greaves (1913) found about 4 ppm; Olson et al. (1940) report 7.1 to 18.4 ppm; Jones and Hatch (1945) determined 2.7 to 6.1 ppm; and Bishop and Chisholm (1962) found 3.7 to 7.9 ppm arsenic in soil.

Another important use is arsenic acid applied as a dessicant to cotton. Only one application per year is made, at a rate of about 2.3 pounds per acre of arsenic equivalent. Pennwalt Corporation (Culver, 1971) reports that after 5–10 years dessication use, the concentration in the upper 0.24 inches of soil is 4.6-8.1 ppm arsenic. This is not much higher than the report figures for untreated soil.

II. C. 2. Fate of Arsenic in Soil – Arsenic residues are relatively stable when fixed in the soil. Fixation of arsenic in soil is related to soil textures and colloidal content. Heavy soils fix large amounts of arsenic, rendering it unavailable to plants (Rosenfels and Crafts 1939). Iron and Aluminum cations in the soil chemically absorb (tightly bind), and thus detoxify inorganic arsenate (Anonymous, 1969). Where the iron and aluminum content of soil is low, arsenic moves downward through the soil profile and becomes fixed as it encounters iron and aluminum ions. This causes arsenic distribution through a large soil cross section, but removal from the soil by leaching is said to be insignificant (Jacobs, et al., 1970).

Arsenites are fixed more rapidly in soil than are arsenates. The appearance of sillica suggests an exchange of SiO_3 for $HAsO_4$ (Wiklander and Frederickson, 1946). Keaton and Kardos (1940) as well as Quastell and Scholefield (1953) independently concluded that the more toxic arsenites are oxidized to arsenates on contact with ferric oxide (also found by Schroeder and Balassa 1966). Von Endt et al. (1968), say that organic arsenicals such as MSMA degrade to inorganic arsenates in the soil. Thereafter, their behavior is that of inorganic arsenates.

II. D. Uptake by Plants – Plants grown in virgin (untreated) soil commonly contain 1.7 to 6.1 ppm arsenic (Olson, et al., 1940). Residues in plants are related loosely to the amounts of arsenic in the soil whether natural or added, but are modified by variables including plant species, geographic regions, and soil type.

Arsenic residues in vegetables have not occurred in significant amounts even when grown in soils treated with up to 1000 pounds of lead arsenate per acre. The amount of arsenic uptake varied between plant species and increased with the amount in the soil, but residues were generally low. Residues in plants growing in soil treated with 1000 pounds of lead arsenate per acre ranged from a trace to 0.8 ppm (McLean, et al., 1944).

Olsen, et al. (1940), concluded that there is no relation between the arsenic content of soil and the arsenic content of plants.

When arsenic compounds are applied to soil, residues accumulate under certain conditions. Unlike some organic pesticides which eventually are degraded in soils the repeated application of arsenicals leads to build up of the arsenic content of soils (Woolson et al; unpublished). A soil monitoring project of the USDA (Stevens, et al., 1970) analyzed soil from areas having various histories of arsenical use. The results may be summarized:

Crop History	No. of Samples	Arsenic Content ppm As
Cotton, vegetables	20	1.50 - 54.1
Orchards	30	1.27 - 220.0
Small grain and root crops	16	1.38 - 26.6

In the lower Rio Grande Valley of Texas, 75.0 lbs/acre of arsenic in the form of calcium arsenate was applied to a field during the period 1956 - 1965. Arsenic soil residues were 11.7 ppm in April 1965, and 10.22 ppm in October 1966. In Dade County, Florida, 73.0 lbs/acre of arsenic in the form of calcium arsenate was applied during the 1955 - 1966 period. This led to 50.92 ppm arsenic in the soil when analyzed in March 1968. Soils in five orchards in Adams County, Pennsylvania, were analyzed. The results are:

Orchard No.	Period	Arsenic Applied lbs/acre As Lead Arsenate	Elemental As Content (ppm)
1	1955-1965	40	47-130
2	"	110	93-220
3	"	110	56-113
4	"	95	18-42
5	"	110	54-118

Woolson, et al. (unpublished) claim that these high concentrations may not be harmful for crops and livestock. If the soil contains iron and aluminum, these elements combine with the arsenate ion to "fix" the arsenic as insoluble compounds.

Additional studies report the concentration of arsenic in treated soils as 138 ppm (Gile, 1936); 2-109 ppm (Greaves, 1934); 53-152 ppm (Jones and Hatch, 1945); and 10-124 ppm (Bishop and Chisholm, 1962). It should be noted that the foregoing figures are for arsenic when large quantities (up to 3600 pounds of lead arsenate) have been applied to the soil.

Additional studies confirm that arsenic uptake from soil by plants depends on the species, organ, soil type, and concentration in soil (Jones and Hatch, 1945; Taylorson, 1966; Stewart and Smith, 1922; Vandecaveye, et al., 1936; and Von Endt, et al., 1968).

II. E. Production - The use and production figures of arsenical pesticides are described in detail under "Trends of Use" in Chapter IV.

CHAPTER 2

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FATE AND IMPLICATIONS FOR ARSENIC IN THE ECOSYSTEM

One of the most crucial considerations in this review of arsenic is consideration of its fate and eventual effect upon all forms of life which make up the environment. Following is a summary primarily of fish and wildlife and other associated organisms as influenced by the presence of arsenic.

III. A. Toxicity to Fish and Wildlife - The chemical and biological characteristics of arsenic compounds vary greatly. Therefore, in this review, they must be seen as related but finally considered as individual compounds. The toxicity of arsenicals decrease as the three valence states (-3, +3, and +5) increase. Another important classification, as far as toxicity is concerned, is that of the organic and inorganic arsenic compounds. Arsenic refers to inorganic arsenicals and arsonic and arsinic denote organic arsenicals. The methyl-arsenic bond in organic arsenical compound lowers the acute toxicity much below that which is normally associated with inorganic compounds. See Table 1 for relative comparison of acute toxicities for arsenic compounds.

Following is a review of the available toxicity data for the different arsenicals to mammals, birds, fish and other aquatic organisms.

III. A. 1. Sodium Arsenite

III. A. 1.a. Mammals and Birds - The acute oral LD_{50} for sodium arsenite to rats is 10-50 mg/kg (House, et al., 1967), and for the mouse, 51 mg/kg Meliere, 1959). The acute oral toxicity for 3-4 month old mallard hens was 323 mg/kg accompanied with acute symptoms of ataxia, high carriage and tetanic seizures (Tucker and Crabtree, 1970). Mallards tolerated 8 mg/day for a period in which the total dose reached 973 mg/kg (USDI, 1963).

TABLE 1. Relative Toxicity of Arsenicals.

Classification	Arsenical	LD_{50} (rat)
Inorganic	arsine	3 [1] (mouse)
	sodium arsenite	10 [1]
	calcium arsenate	20 [2]
	lead arsenate	100 [2]
	arsenic acid	48-100 [3]
Organic	DSMA	1000 [3]
	cacodylic acid	1350 [3]
	MSMA	1800 [4]
	triethanolamine methanearsonate	14,000 [4]
	methanearsonic acid	1400 [5]

[1] The Merck Index of Chemicals and Drugs; Merck and Co., Inc. 1960.

[2] MSMA-DMA Weed Control; Vineland Chemical Company.

[3] FCH Farm Chemicals Handbook; The Meister Publishing Co., Willoughby, Ohio. 1970.

[4] Frear, D.E.H., Pesticide Index; College Science Publishers, State College, Pa. 1969.

[5] Unpublished data. Ansul Chemical Company. 1963.

III. A. 1.b. Fish and Other Aquatic Organisms - Several investigators have determined the acute LC_{50} of sodium arsenite for various species of fish:

Fish Species	Exposure (hr)	LC_{50}
Rainbow Trout	24	100 [1]
Bluegill	24	58 [1]
Spottail Minnow	24	45 [2]
Lake Emerald Shiner	24	13.5 [3]
Channel Catfish	24	27.6 [4]
Rainbow Trout	48	36.5 [5]
Chum Salmon Fry	48	8.4 [6]
Channel Catfish	48,72	15 [4]

[1] Cope, O.B. 1965. Sports Fisheries Investigation. pp. 51-63. In Pesticide Wildlife Studies, U.S. Fish * Widl. Serv. Circ. 226.

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[5] FWPCA. 1968. Water quality criteria. Report of the National Tech. Adm. Comm. to Secr. of the Interior. Fed. Water Pollution Control Adm. U.S.D.I. 234 pp.

[6] Alderice, D.F. and J.R. Breh. 1957. Toxicity of Sodium arsenite to young chum salmon. Progress Report Pacific Coast Station Fisheries Res. Board, Canada. No. 108, 27.

Cope (1966) stated that sodium arsenite at 4 ppm caused kidney and liver damage to bluegills. Johnson (1965) indicated that sodium arsenite applied at 5 ppm in ponds had no effect on rainbow or brook trout populations. Sodium arsenite at 4 ppm had no effect on phytoplankton, but produced significant reductions in zooplankton (Cowell, 1965). Zischkale (1952) determined minimum lethal dosages (ppm) of sodium arsenite to produce a kill of 25 percent or better of the following fish food organisms: Daphnia, 3.0; Eucypris, 6.0; Hyallella, 2.5; Culex, Ades, Anopheles, 6.0; and Chironomus, 10.0. Walker (1962) reported that dosages of sodium arsenite from 2.5 to 20 ppm caused a 50 percent reduction in phantom midges, water bugs, and snails. Springer (1957) listed 1.9-3.0 ppm as the toxic level for midges and mayflies. McKee and Wolf (1963) stated that fish food organisms are susceptible at concentrations as low as 1.0 mg/liter.

III.A. 2. Sodium Arsenate

III. A. 2.a. Mammals and Birds - The acute oral LD_{50} for the rat is 112 mg/kg and by interperitoneal injection, 21 mg/kg (Merck, 1960). No adverse effects have noted for birds.

III. A. 2.b. Fish and Other Aquatic Organisms - Sodium arsenate is not highly toxic to fish or to other aquatic organisms. The lethal concentration of sodium arsenate for minnows is 234 ppm as arsenic.

III. A. 3. Copper Acetarsenite, Paris Green

III. A. 3.a. Mammals and Birds - The acute oral LD_{50} for the rat is 22 mg/kg (FCH, 1970). The lethal value for hares is 30 mg/kg (Chappellier and Rancort, 1936). Paris green when applied at 4 pounds/acre had no adverse effect on muskrats feeding on treated vegetation (Stearns, et al., 1947). The LC_{50} for mallards was 5000 ppm; for pheasants, 1000 to 1100 ppm; for bobwhite, 500 to 600 ppm; and for coturnix, 1200 to 1400 ppm when fed a diet for five days followed by a three day observation period (Heath, et al., 1970). The acute lethal value for gray partridge is approximately 30 mg/kg (Chappellier and Rancort, 1936).

III. A. 3.b. Fish and Other Aquatic Organisms - Paris green had no apparent effect on oysters, shrimp and fish at application of rates 100 pounds per acre.[7] Minute quantities of Paris green appear to have no effect upon top minnows or other fish (Barber, 1941), but excessive dosages may have ill effects on fish (Hackett, 1925). McCormick (1940) found arsenic in the bodies of Gambusia and catfish, but there were no evidence of fish mortality.

III. A. 4. Cacodylic Acid

7/ Unpublished data. Gulf Breeze, 1965.

III. A. 4. a. Mammals and birds - The LD_{50} for the rat was 1280-1400 mg/kg when fed orally (House et al., 1967). Acute toxicity data are available for birds.

III. A. 4. b. Fish and other aquatic organisms - Oliver (1966) exposed mosquito fish, largemouth bass, and taillight shiners to concentrations of 100 ppm for 72 hr with all fish surviving. Some mortality was observed when concentrations reached 631 ppm at 72 hr. Cacodylic acid at 40 ppm in water for 48 hr. had no noticeable effect on shell growth of oysters. Pink shrimp exposed to 40 ppm in water for 48 hr. showed no effect (USDI, 1966) and dragon fly nymphs exposed to 1000 ppm of cacodylic acid in water for 72 hr. showed no noticeable effects (Oliver et al., 1966).

III. A. 5 Monosodium methanearsonate, MSMA

III. A. 5. a. Mammals and birds - The acute oral LD_{50} for MSMA to albino rats is 1800 mg/kg (Barrier, 1970). No acute toxicity data are available for birds.

III. A. 5. b. Fish and other aquatic organisms - The acute LC_{50} for bluegills after 24 and 48 hr. exposure in water was greater than 2000 ppm. MSMA at 1 ppm had no effect on killifish or pink shrimp after 24 and 48 hr. exposure. There was no effect on shell growth in oysters with 96 hr exposure to 1 ppm MSMA in water.

III. A. 6. Disodium methanearsonate, DSMA.

III. A. 6. a. Mammals and birds - The acute oral LD_{50} for DSMA to rats is approximately 1000 mg/kg (FCH, 1970). No acute toxicity data are available for birds.

III. A. 6. b. Fish and other aquatic organisms - DSMA toxicity data for fish, shrimp, and oyster are approximately the same as MSMA.[8]

III. A. 7. Lead arsenate

III. A. 7. a. Mammals - The acute oral LD_{50} for lead arsenate to rats has been reported to be 800 mg/kg (Merck, 1960). Lead arsenate was found to have an acute oral LD_{50} of 192 mg/kg to sheep (St John et al., 1940). Metcalf et al. (1962) have reported the acute oral LD_{50} for rabbits to be 125 mg/kg.

III. A. 7. b. Fish

A concentration of 25 mg lead arsenate/liter of water has killed trout within 24 hours and a concentration of 17.1 mg lead arsenate/liter of stabilized tap water did not harm minnows during a 1 hour exposure (McKee and Wolf, 1963).

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[8] Unpublished data, Ansul Chemical Company.

III. A. 8.   Comparative Toxicity of Trivalent and Pentavalent Arsenic -

Two forms of arsenic exist in the environment, trivalent (arsenite) and
pentavalent (arsenate). Pentavalent arsenic as arsenate is relatively
nontoxic in normal concentrations, but trivalent arsenic (arsenite) is
toxic and is the principal form produced commercially. Schroeder and
Balassa (1966) compiled comparative toxicological data for sodium arsenite
and sodium arsenate (Table 2).

Table 2

Relative Toxicity of Sodium Arsenite and Sodium Arsenate to Selected Organisms

Item	Arsenite (ppm As)	Arsenate (ppm As)
Bacteria	290	10,000
Algae	---	1,000
Yeast	---	300
Daphnia magna	5.2	12.5
Flatworms	40	361
Minnows	20	250
Minnows	17.8	234
Minnows	11.6	60
Rat, acute oral LD_{50}	11.2	112

Several important factors to keep in mind when examining the implications
of arsenic in the environment are: the greatly increased toxicity of the
trivalent (arsenite) compared to pentavalent (arsenate); the widespread
distribution of arsenic in nature, and the misconception that all arsenic
compounds are highly poisonous.

III. B.   Residues in Fish and Wildlife from Environmental Exposure

It has been indicated that all living things contain arsenic with the
marine invertebrates and other aquatic organisms having the largest
amounts. Very limited work has apparently been done on the determination
of arsenic in wild animals and birds. Schroeder and Balassa (1966) trapped
several wild animals and analyzed them for arsenic in specific tissues.
Laboratory mice and rats, fed a diet of naturally occurring arsenic of
0.053 μg/g and water containing 0.51 μg/liter, were also included in the
investigation.

The data in Table 3 demonstrates the presence of arsenic in most of the wild animal tissues analyzed. The laboratory animals had small amounts of arsenic in most tissues, but a large quantity in the spleen.

Table 3

Natural Levels of Arsenic in Animals

Tissue	µg/g As	Tissue	µg/g As
Kidney		Lungs	
mice, lab	1.30	mice, lab	0.11
rats, lab	0.0	mice, lab	1.53
mice, wild	0.0	fox, cross, wild	0.69
fox, cross, wild	0.39		
		Spleen	
		mice, lab	5.60
Liver			
mice, lab	0.0		
rat, lab	0.49	Tumor	
rat, lab	0.0	mouse, lab	0.93
rat, lab	0.52		
mice, wild	0.74	Brain	
woodchuck	0.52	rats	0.0
		rat	0.31
Heart			
mice, lab	0.0		
mice, wild	1.10		
fox, cross, wild	0.25		

Coulson et al. (1935) investigated the arsenic residue in rats fed 17.9 ppm natural arsenic in shrimp (assumed to be pentavalent). He found that the pentavalent was only slightly (0.7 percent) retained in the tissue, whereas, the dose of sodium arsenite accumulated up to 18 percent of the amount given. Overby and Frost (1962) recovered in the excreta only one-half of the arsenite fed to rats, but virtually all the pentavalent form of arsenic. Chickens fed livers of pigs that had been given arsenite showed accumulation in muscle, whereas, those given arsenilic acid (an organic arsenical) had none (Overby and Staube, 1965). Schreiber and Brouwer (1964) demonstrated that pentavalent arsenic was much more readily excreted than trivalent arsenic. Peoples (1964) fed cows arsenate (1.25 mg/kg) without finding increases of arsenic in milk, indicating the existence of some mammary barrier and rapid elimination. However, the rat accumulates arsenates by binding it to hemoglobin and depositing it in the spleen, liver, kidney and heart to a much greater extent than cows, hamsters, guinea pigs and rabbits.

Experimental results indicate that there is a homeostatic mechanism for excretion of arsenates. As a general rule, pentavalent compounds are excreted by the intestines, some of them in the bile. This serves as a possible explanation as to why sodium arsenate and cacodylate are relatively nontoxic (Schroeder and Balassa, 1966). Frost (1967) indicated that arsenite has a

preference for kidney, liver, hair, nails and skin. Arsenite accumulates in tissues upon continued exposure up to a balance or to toxic levels, depending upon the dose and the degree of toxicity of the arsenical and is reflected in the levels of arsenic in vital tissues.

Ehman (1967), concluded that organic pentavalent arsenicals, even though having relatively low mammalian toxicity, are definitely toxic when in sufficient quantities or are potentially toxic in small quantities through possible breakdown to other arsenicals.

III. B. 1.   Teratogenic Studies

Ferm, et al. (1971) stated, after investigating the teratogenic profile of sodium arsenite in the golden hamster, that it is possible that either cumulative or accidental peak exposure of human or other animal populations to arsenic might have profound effects on reproduction mechanisms. Such effects might include lowered reproductive rates, or detectable increases in incidences of specific embryonic malformations. Several investigators (Boutwell, 1963; Ferm, et al., 1971; and Ferm and Carpenter, 1968) have examined the possible teratogenic effects caused by arsenic.

III. B. 2. Documented Arsenical Poisonings

Arsenical poisonings to both domestic and wild animals are well documented (Booth, 1964; Boyce and Verme, 1954; Clough, 1927; Cook, 1953; Glover, 1952; Hatch and Funnell, 1969; Jones, 1958; Motham and Coup, 1968; Peoples, 1964; Schreiber and Brouwer, 1964; Sutherland, et al., 1964; Towers, 1949; and Weaver, 1962). Many of these poisonings have resulted from the uses of sodium arsenite to debark trees, destroy trees and stumps, preserve wood, and as a herbicide, dessicant, or insecticide. Because of the extreme toxicity of this compound, many of the former uses of sodium arsenite have been cancelled.

III.   B.3. Natural Arsenic Residue Levels in Marine or Aquatic Animals and Fish

Arsenic is widely distributed in biologically significant quantities in sea water (2-5ppb). Table 5 presents arsenic residue levels for a number of marine animals and fish. Assuming the arsenic concentration of sea water as 5 ppb (2-5 ppb average), the corresponding concentration factors for various fish and other aquatic organisms has been calculated (Table 5). The assumed concentration factors illustrate the accumulative capabilities of organisms and it is readily apparent that arsenic in the form present in these animals has a relatively low toxicity. Vinogradov (1953) reported the following accumulations of arsenic in marine animals: sponges (8-24 ppm), molluscs (1-68 ppm), coelenterates (16 ppm), echinoderms (0.37-1.5 ppm), crustacea (10-79 ppm) and fish (0.2-15 ppm by wet weight and 2-25 ppm by dry weight). The whole fat, muscle fat, intestinal fat and liver fat of the marine fish contained 1.8-30.4 ppm arsenic with the highest level in the liver. McKee and Wolf (1963) indicate the arsenic trioxide concentrations in water that will kill food organisms and fish are lower than the concentrations of arsenic actually found in marine invertebrates and fish. Sodium arsenate at 100 times those concentrations exhibits little or no toxic effects to such organisms.

TABLE 5

Natural levels of arsenic in fish and other aquatic organisms

Species	mg/kg[*]	Conc. factor
Haddock[1]	2.17	430
Kingfish[1]	8.86	1770
Oyster, fresh[1]	2.9	580
Oyster, frozen[1]	2.7	---
Scallops, fresh[1]	1.67	330
Shrimp, fresh, frozen[1]	1.50	300
Shrimp shells[1]	15.3	3060
Clams, fresh frozen[1]	2.52	500
Conch, fresh[1]	3.1	620
Conch, dried, whole[1]	5.63	---
Escallops[2]	44	8800
Mussels[2]	80	16,000
Cockles[2]	26	5200
Whelks[2]	24	4800
Lobsters[2]	37	7400
Prawns[2]	72	12,400
Crabs[2]	46	9200
Plaice[2]	10	2000
Soles[2]	7	1400
Dabs[2]	4	800

[*] same as ppm

[1] Schroeder and Balassa (1966).

[2] Chapman (1926), Analyst: 543.

III. C. Food Chain Buildup - The trivalent arsenic as arsenite accumulates and is slowly oxidized to the pentavalent form in the mammalian body (Schreiber and Brouwer, 1964; and Schroeder and Balassa, 1966). The pentavalent arsenic as arsenate is rapidly excreted and probably does not accumulate in tissue. A possible exception exists with the rat since arsenate accumulation has been noted in studies with rats (Coulson, et al., 1935; Schroeder and Balassa, 1966).
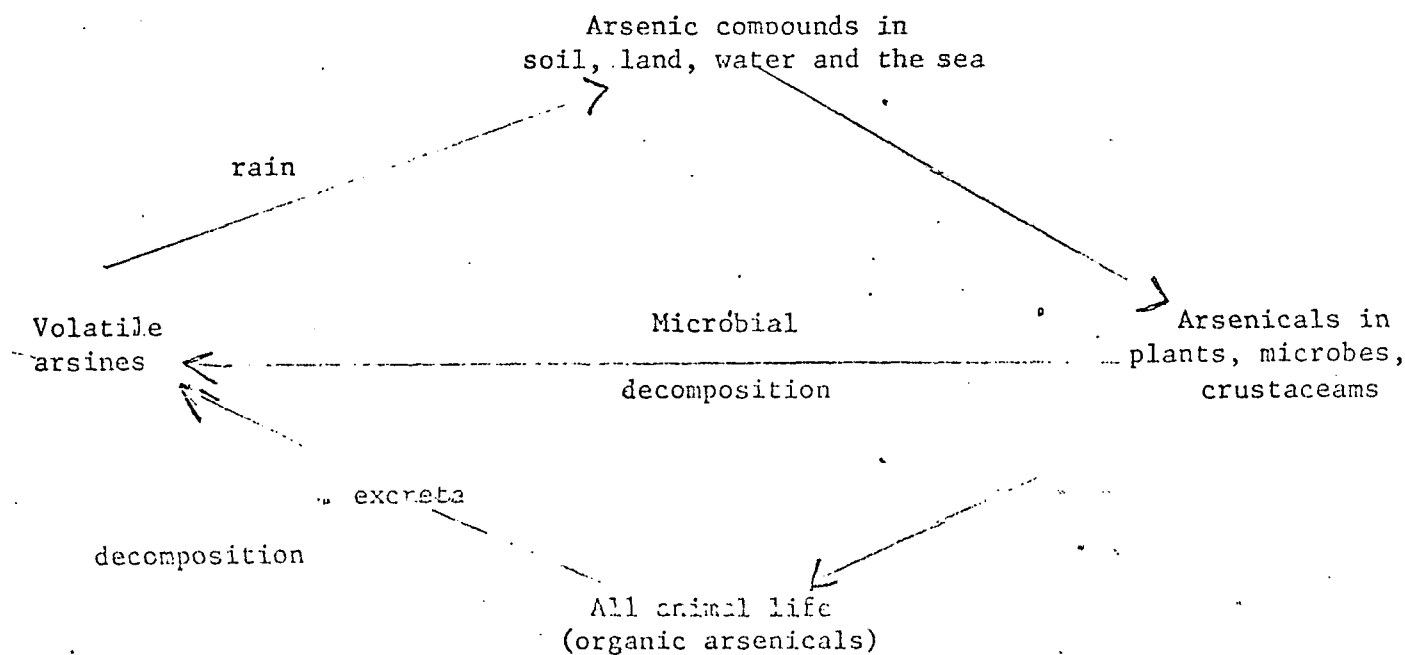
In the terrestrial environment the arsenites will accumulate in mammalian and avain tissues (Overby and Frederickson, 1963; Schroeder and Balassa, 1966). Macek (1969) stated that in order to be bio-magnified, "a compound must be persistent in the physical environment, available to the organism and persistent once assimilated into the biological system." Sodium arsenite is persistent in water and is available to fish. Gilderhus (1966) concluded from his study that sodium arsenite is persistent (50 percent) in fish for greater than 16 weeks and that pools treated with sodium arsenite retained 20-40 percent of the arsenic after 16 weeks. Organisms present in this system would be subjected to long-term exposure.

The potential exists for a food-chain buildup of arsenic in both the aquatic and terrestrial environment, but it must be recognized that higher members of the food chains have not shown residue levels as high as the lower forms in the chains. This would indicate that in actuality bio-magnification probably does not take place.

III. D. Fate and Movement in Terrestrial and Aquatic Systems -

Remembering that arsenicals are ubiquitous - existing in water, soil, air, plant and animal life - Frost (1967) proposed an As cycle in nature (Fig. 1).

Fig. 1. Arsenic Cycle in Nature

Arsenic compounds in
soil, land, water and the sea

rain

Volatile arsines

Microbial
decomposition

Arsenicals in plants, microbes, crustaceams

excreta

decomposition

All animal life
(organic arsenicals)

The earliest arsenical herbicide was sodium arsenite and it proved to be an excellent soil sterilant although it could also be used for selective weed control. Sodium, calcium, and lead arsenate have been used for pre-emergence control in grasses. Calcium and lead arsenate have also been used for insect control on turf and fruit, respectfully. Two organic arsenicals, monosodium methanearsonate (MSMA: also the disodium salt DSMA) and hydroxydimethylarsinic oxide (cacodylic acid) have been used extensively for weed control. Paris green has been widely used in aquatic areas as a mosquito larvicide and as an insecticide bait in terrestrial sites. Repeated applications of arsenicals to crops have resulted in an increase in the level of soil arsenic (Bishop and Chisholm, 1962; Ehman, 1967; Jones and Hatch, 1945; and Vandecaveye, 1936).

Heavy lead arsenate sprays have produced extremely high accumulation of arsenic residues in soils, especially orchards of the Pacific Northwest. Most of the arsenic residues in these specific soils were confined to the top 6-8 inches. Arsenic residues below 8 inches rarely exceed the natural occurrence level for arsenic (Boswell, 1952). Lead arsenate applied up to 30 pounds/1000 ft^2 in 1937 was highly effective for controlling white grubs in turf and after 10 years the arsenic content was still high enough to give very high control of white grubs (Neiswander, 1951).

The importance of the microflora for pesticide decomposition is well documented for many arsenicals (Dickens and Holtbold, 1967; Thom and Raper, 1932; and USDI, 1963). The arsenic herbicides, arsenic acid, methanearsonic acid, and dimethylarsinic acid are reportedly absorbed by soil surfaces. This would lead to the conclusion that high levels of arsenic would accumulate with repeated applications. This apparently does not happen and is indicative of the presence of some type of degrading mechanism. Microorganisms appear to have the ability to degrade arsenic (Alexander, 1961; Bird, 1948; Challenger, 1947; Thom and Raper, 1932; and Zussman et al., 1961). Thom and Raper concluded that an accumulation of arsenic in soil would be expected only when massive amounts were used or under special conditions unfavorable to the microflora. Further studies demonstrated that soil microorganisms are capable of degrading monosodium methanearsonic acid at the level of 1000 ppm. Dickens and Holtbold (1967) concluded that methanearsonates are decomposed under aerobic soil conditions and the rate of decomposition is directly dependent upon the availability of organic matter for microbial degradation.

Duble, Holt, and McBee (1969) found less than 0.1% of the 14C applied as DSMA released as volatile 14C 10 days after treatment of Bermudagrass and they concluded that the carbon-arsenic bond was stable in Bermudagrass. In soils, however, the carbon-arsenic bond is subject to biological systems. Von Endt, et al. (1968) found a rapid loss of 14C from 14C-MSMA which supported degradation by the microflora. Vineland Chemical Company [9] stated " . . . . since MSMA contains only 1 carbon atom, and the arsenic recovered is arsenate, and no other 14C products appeared, that the probable course of reaction and fate of the arsonate in the soil is oxidation by microorganisms of the methyl groups to CO_2 and arsenate as end products." Ehman (1967) also reported rapid inactivation of cacodylic acid and MSMA in soils. It has been suggested that inactivation may be due to bonding to some mineral structure, and ion exchange phenomenon, or biological degradation. The complete chemical fate of MSMA and cacodylic acid is not known.

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[9] Vineland Chemical Company; MSMA-DMA Weed Control.

Much work has been done on the fate of the inorganic arsenical, sodium
arsenite, since it was previously registered for aquatic weed control.
Cowell (1965) stated that application of sodium arsenite may have cumulative
effects on zooplankton. Gilderhaus (1966) determined the effects of long-
term exposures of sodium arsenite to fish and the aquatic environment. Fish,
water and bottom soils were analyzed to determine the fate of arsenic. Fish
suffered acute symptoms and the bottom fauna was substantially reduced.
Arsenic from sodium arsenite is removed very slowly from the water and
Gilderhaus interpolated that a single treatment of 4 ppm sodium arsenite
would deposit about 50 ppm arsenic in the top inch of bottom soil.

Several explanations have been suggested concerning the fate of paris green.
Benedetti (1934) claimed that arsenic is buried in the bottom mud. Misseroli
(1917) found that accumulation of arsenic did not take place because any
dissolved arsenic was volatilized by the microflora of the water. Morin
et al (1933) explained that no accumulation occurs because the aquatic
flora converts the arsenic to ethylarsenine. Herms and Gray (1940) stated
"In the quantities effective for control of mosquito larvae, Paris green
appears to have no effect on aquatic plants or animal life or upon livestock
and repeated applications do not appear to result in any accumulative effect."
Rathburn (1966) however, stated that small quantities of arsenic are added to
the soil as a result of applications of granular paris green. He further
stated that Paris green ". . . may occur unchanged as cupric acetoarsenite
or as various breakdown products caused by hydrolysis and the action of
chemicals present in the soil." Persistence of 2 percent paris green
applications is 24-25 days (Bendetti, 1934).

In a recent article, "Trace metals: unknown, unseen pollution threat"
(Anonymous, 1971), the health hazards of trace metals in the environment
were discussed. The author raised the question about arsenic and possible
hazards when arsenic undergoes methylation. ". . . microorganisms in
sediments containing arsenic convert the arsenic into deadly poisonous
dimethylarsine. . . ." This methylarsenic compound will go through the
water just the same as methylmercury does [accumulate in fish, and] cause
another problem: . . . As 5+ is first reduced to As^{3+}. Arsenite is then
methylated to form dimethylarsenic acid (As^+) . . . pollution hazards exist
when arsenic and its derivatives are introduced into environments where
anaerobic organisms are growing." (Fig. 2).

Fig. 2. <u>Arsenic</u> <u>is</u> <u>Methylated</u> <u>by</u> <u>Microorganisms</u> <u>in</u> <u>Waterways</u>

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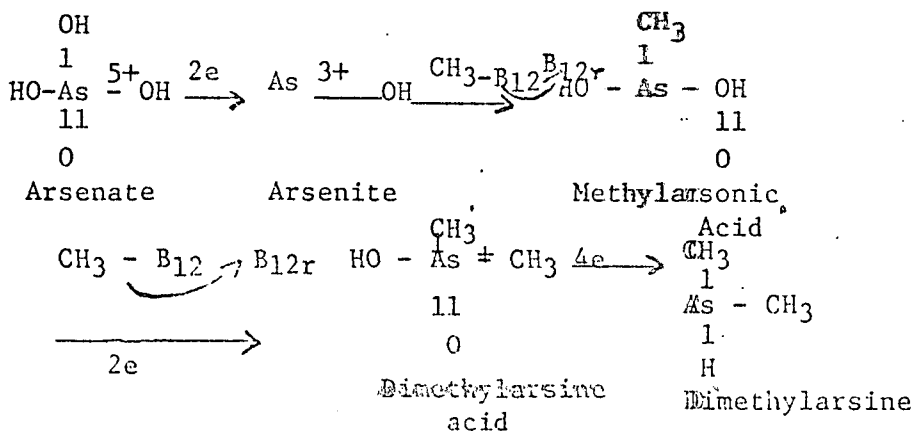
Arsenic pesticides such as sodium methylarsenate and calcium and lead arsenate could eventually find their way into anaerobic aquatic or terrestrial environments. Angino et al. (1970) questioned existing evidence that arsenic remains in the same oxidation state after entering sewage or the environment. They further stated, "When the amount of dissolved oxygen in many streams or in portions of certain streams is zero or nearly so, then we must consider the real possibility that arsenic present in water as the arsenate stands a good chance of being reduced to the arsenite form." Ehman (1967) also introduced the possibility of pentavalent arsenicals breaking down into other arsenicals.

III.E. Summary – Since arsenicals differ widely, we must be cautious about generalized statements. However, the following summary can be made:

1. Arsenic is widely distributed in water, soil, air, and plant and animals life.

2. Soils are capable of inactivating the arsenicals, but prolonged use of arsenicals have resulted in an accumulation of arsenic in the top layers of the soil.

3. Organic arsenicals are much less toxic than inorganic arsenicals; and, the pentavalent inorganic less toxic than trivalent inorganic arsenicals.

4. Substantial levels of arsenic have been found in fish and shellfish when compared to the natural level of arsenic in sea water. This would indicate that arsenic accumulates in aquatic organisms.

5. Pathological changes resulting from long-term exposure to sodium arsenite have been observed in fish; substantial residues of arsenic have been found in water, bottom soil and in fish; and bottom fauna and plankton populations have been reduced by arsenic (sodium arsenite) in the aquatic environment.

6. There appears to be a homeostatic mechanism within mammals for the arsenates. Arsenates are excreted relatively fast, but the arsenites accumulate in animal tissues.

7. The possibility exists that hazards may develop from the methylation of arsenic.

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SIGNIFICANCE OF ARSENICAL PESTICIDES
IN THE ENVIRONMENT

Arsenic has been recognized as a poison by the layman since ancient times. Hippocrates (460-377 B.C.) recommended a paste of sulphide $(AS_4 S_4)$ for the treatment of ulcers. It was at a much later date that the toxic properties of arsenical compounds came to be fully appreciated. The pure element was probably first prepared around 1250 by Albertus Magnus. The word "arsenic" appears to be derived from the Greek "arsenikon" meaning "potent" (Buchanan, 1962).

Native arsenic occurs in small quantities usually in association with other metals and in crystalline rocks and schists. It is widely distributed in combined form in certain mineral waters, coals and commercial zinc. Therefore, arsenic may be detected in the atmosphere of industrial cities using coal that contains pyrites.

Most arsenical compounds of industry are derived today as by-products of the treatment of arsenic-bearing ores of lead, copper and gold. Arsenic trioxide is the basic material for the synthesis of most of the arsenical compounds of commercial importance. The following presentations give the trends of use and significance of arsenical pesticides in the United States since the 1930's.

IV. A. Trends of Use - The world consumption of arsenic was increasing steadily until about 1943 when an estimated total of 70,000 tons were used. The United States was the principal producer and user of arsenical compounds at this time, which was just prior to the introduction of DDT and other less phytotoxic new insecticides. During the period of 1941-1944, the United States used an average of 42,000 tons of white arsenic. Of this tonnage the manufacture of insecticides took 27,000 tons, herbicides, 7,700 tons; glass manufacture, 3,000 tons; dyestuffs, 570 tons, and all other uses some 5,000 tons. The United States consumption had dropped to 29,000 tons by 1951 (Fairhall, 1957). The decreased use of arsenic in the United States by 1951 can be attributed to the emergence of DDT and a number of other modern insecticides for agricultural use after World War II.

There has continued to be some use of arsenic to make limited amounts of calcium arsenate and lead arsenate. The largest agricultural use of arsenic evidently is for manufacture of the methanearsonic acid salts. The methanearsonic acid is primarily used to produce selective post-emergence herbicides for use in cotton and on non-crop areas. It

is established that the use of disodium methanearsenate and monosodium acid, methanearsenate to control weeds of cotton and non-crop areas has increased greatly during the past decade (Arle and Hamilton, 1971). The following table summarizes pounds of the major arsenical pesticides produced since 1965.

Table 1 Production Records of Arsenicals for Agriculture
in United States 1965 - 1970

Product	Year	Total Production (Tons)
Lead arsenate, acid and basic*	1969	4,571
	1968	4,508
	1967	2,976
	1966	3,464
	1965	3,549

*U.S. Department of Commerce, March 29, 1971.

Product	Year	Total Production (Tons)
Calcium arsenate,* commercial	1969	709
	1968	1,699
	1967	1,020
	1966	1,445
	1965	2,096
Methanearsonic acid salts**	1970	15,225

*U.S. Department of Commerce, March 29, 1971.
**United States Tariff Commission, September 1971.

The United States Tariff Commission does not reveal production data on a product or class of compounds until there are several manufacturers, thereby protecting the confidential production data of a lone manufacturer. It was therefore significant that the methanearsonic acid salts had not been published as a separate entry until 1970. This entry and research publications on methanearsonic acid salts as herbicides, would indicate increased recent United States use of herbicidal compounds containing arsenic.

Arsenic acid is formulated as a 75 percent active liquid and applied at rates of 2-3 pints per acre to cotton as a preharvest desiccant.

This use is of special importance to the types of cotton grown in parts of Arkansas, in the Texas High Plains and Black Lands, and Oklahoma that require a stripper harvester.

IV. B. Arsenic in the Air - "Maximum permissible concentrations" of arsenic as a dust or fume or as arsine in working atmospheres have been a matter of some importance to workers in the field of industrial hygiene for some time. An international symposium under the auspices of W.H.O./I.L.O., discussed various aspects of the problem in 1959. Values set by this symposium were such that when averaged over an 8-hour working day, no demonstrable effect on the health may be expected for those exposed. The value proposed for inorganic arsenic in the form of vapor fume or dust was 0.5 mg/cubic meter of air (American Conference of Governmental Industrial Hygienists 1959) and 0.5 mg calculated as arsenious oxide (Imperial Chemical Industries, Great Britain). For calcium and lead arsenate lower values of 0.1 mg and 0.15 mg per cubic meter were adopted (Buchanan, 1962). Presence of arsenic in the air following use of either an insecticidal or herbicidal arsenic compound is not considered a factor of primary concern with respect to environmental impact.

The lead and arsenic content of air following use of lead arsenate in orchards of the State of Washington are presented in Table 2. (Neal, et al., 1941).

IV. C. Arsenic in Water - There are relatively little direct or documentable bits of information about the effect of lateral movement of soil and water from fields treated with methanearsonic acid herbicides or from orchards with accumulations of arsenic. Being highly soluble in water, it may be theorized that disodium methanearsonate and monosodium acid, methanearsonate tend to move downward into the soil in the initial stages of the first rain rather than remain with the surface soil that may be washed from the field as runoff beings. Once leached into the soil, the methanearsonates change to less soluble inorganic compounds that are tightly adsorbed by soil colloids and organic matter. It is considered that this adsorption inhibits downward movement of the arsenic toward the water table (Arnott and Leaf, 1967; Dickens and Hiltbolt, 1967).

Sodium arsenite has been used to control submerged plants in ponds and lakes. Findlay Lake, New York was sprayed with sodium arsenite during May 17-20, 1958, resulting in a miximum arsenic concentration of 7.0 mg/1 liter of water. Arsenic content of the water had dropped to 1.5 mg/liter of water one week after treatment and in diminishing amounts during the balance of the summer. The herbicide was applied again on May 29, 1959. In none of the fish caught from Findlay Lake on May 29, 1959, and June 19, 1959, was an amount of arsenic found equal to that

	Milligrams per 10 cubic meters			
	Lead		Arsenic	
	Average	Range	Average	Range
Mixing	57.4	0.9 –467.3	18.5	0.2 –110.7
Burning containers	35.8	10.2 –76.5	166.7	48.6 –261.2
Spraying	4.5	1.3 –14.3	1.4	0.4 – 4.8
Thinning	3.0	0.4 –17.0	0.8	0.1 – 3.2
Picking	29.3	7.7 –75.2	8.8	2.6 – 19.0
Dumping:				
October	1.9	0.4 – 6.9	0.6	0.1 –1.9
December	0.3	0.01 –1.1	0.1	0.02–0.2
Sorting and Packing (October)	0.16	0.07– 0.22	0.06	0.03–0.08
Blanks	0.011	0.001–0.03	0.003	0.001–0.01

Note: Factors influencing exposure were:- (1) degree of care used in opening
and shaking containers; (2) amount of material and number of bags used per
mix; (3) amount and direction of breeze; (4) dry or wet mixing; and (5) location
in shed or outdoors.

present in edible salt water fish. The maximum found was 1.0 μg/gr. of viscera from fish on June 19, 1959, Ullman, et al., 1961).

Recent work by Dr. B. C. McBride and Dr. R. S. Wolfe, University of Illinois has shown that arsenic, as well as selenium, may be acted on by bacteria in nature to produce highly poisonous compounds. Micro-organisms in sediments that contain arsenic convert the arsenic into the highly toxic dimethyl arsine. The work evidently showed that methanobacteria act upon a variety of arsenic compounds to produce the dimethyl arsine. Thus, this recent work warns that pollution hazards exist for aquatic and terrestrial environments that have large amounts of arsenic introduced where anaerobic organisms are growing (Anonymous, July 1971).

IV. D. Arsenic in Soil - It has been indicated that one of the beneficial environmental aspects of using methanearsonic acid herbicides includes lessening of the need for other herbicides with greater residual phyto-toxicity. However, review of papers cited for this section would indicate continued extensive use of arsenic insecticides and herbicides in soil may represent a serious potential phytotoxic hazard that eventu-ally will reduce the productivity of land, especially in the cotton belt.

In an extensive review of pesticide residues in soils, there was a report that one commercial apple orchard received more than 3,500 pounds of lead arsenate per acre over a 25-year period. Accumulation of this form of the arsenic was not too surprising and explainable because of its immobility and insolubility. Further, apple trees usually grew unaffected in soil containing relatively high levels of inorganic arsenic residues because the arsenic remained largely in the upper six or eight inches of soil (Sheets and Harris, 1965). It has been found that recovery of old orchard soils for forage or food-crop production is difficult and slow and many remain unproductive. ˜)
(this h... ... Calcium arsenate)
Before emergence of DDT and more recent modern insecticides, inorganic arsenicals, were used extensively on cotton and tobacco for insect control. Undocumented reports from the lower Mississippi Valley have implicated arsenic residues in abnormalities that occur sporadically in rice growing on old cotton land. The recently introduced organic arsenicals, especially monosodium acid, methanearsonate, may add to the arsenic residues already present in the soils of this area (Sheets and Harris, 1965).

It has recently been reported that arsenic buildup in soils after years of pesticidal use reached 1.8 - 830 ppm arsenic while untreated areas ranged from 0.5 to 14 ppm arsenic in areas tested within North America.

Further, arsenic residues in 58 surface soil samples taken from soils
with a history of arsenic application averaged 165 ppm arsenic.
(Woolson, Axley, and Kearney, in press).

A review of arsenic applied to experimental fields from three states
provides valuable information. A variety of organic arsenicals were
applied to Alabama soils, and two years after the last treatment, 95
percent of that applied was recovered in the surface 15 cm. Ca_3 (As
04)$_2$ was applied to Mississippi soils around 1930 and only 28 percent
of the amount applied was recovered. The Mississippi soil had a history
of flooding and silting. In Wisconsin, 72 percent of applied Na As O_2
was recovered about four months after application (Woolson, Axley and
Kearney, in press).

Such factors as soil texture and presence of iron, aluminum, calcium,
phosphorus and humus might be expected to affect fixation of arsenic in
soil and thus its phytotoxicity. There have been numerous reports that
the presence of small arsenic concentrations in soil have been beneficial
to the growth of peas, radishes, wheat, corn sorghum, soybeans, cotton
and potatoes (Woolson, Axley, and Kearney, 1971a).

It has been reported that loss of methanearsonic acid from soil via
photodecomposition and/or volatilization is none (Barrier, 1970).

It has been shown that organic arsenicals have about the same leaching
and fixing characteristics in the soil as inorganic arsenates. In
addition, it has been shown that the monosodium acid, methanearsonate
(MSMA) goes to the inorganic arsenate form so that ultimately the
behavior and fate of inorganic arsenate is of prime importance regard-
less of the source of the arsenic (Woolson, Kearney and Axley, 1971).

The metabolism of cacodylic acid applied to soil under aerobic conditions
appeared to proceed through C - arsenic cleavage as well as through a
volatile arsine production. The metabolism of cacodylic acid under
anaerobic conditions appeared to proceed through reduction to arsine or
dimethylarsine (Kearney and Woolson, 1971b).

A fungus, several actinomycetes and bacteria have been isolated and
shown to metabolize monosodium acid, methanearsonate. Further studies
with cacodylic acid demonstrated metabolism by soil microorganisms.
Some of the soil organisms were arsine producing (Kearney and Woolson,
1971a).

Hurtig recently reported on a survey of different soil and crop types
of 32 farms in Southwestern Ontario, Canada, relative to occurrence of
arsenic following use of lead arsenate for insect control. The survey
included five field crops tobacco, pasture, greenhouse and orchards.

General]. all soils examined has less than 10 ppm arsenic except the highest recorded for vegetables (26.6 ppm) and orchards which ranged from 10.2 to 121 ppm (Hurtig, 1969).

IV. E. Arsenic in Plants - In plants, 10-12 ppm arsenic by dry weight have been regularly reported. Certain azotobacter, yeast, fungi and molds, including species of aspergillis, can exist in high concentrations and reduce the arsenic to volatile hydrides. On a dry weight basis algae have been found to contain 0.1 - 2.6 ppm arsenic and other seaweeds 0.7 - 12 ppm arsenic. Certain English, Japanese, New Zealand and California marine algae have been found to contain 17-95 ppm of arsenic whereas freshwater algae have less (Schroeder and Balassa, 1967).

Organic arsenicals are translocated in many plant species. Studies have shown that in crabgrass and soybeans monosodium acid, methane-arsonate [76] As translocated to a greater extent at 85°F. than at 60°F. Other investigators reported that ammonium arsenate [77] A_s moved throughout the bean plant whether applied to leaves or roots. Disodium methanearsonate is taken up from nutrient solution by roots of Johnson grass and translocated to all part of the plant.

In cotton, various levels of arsenic residues derived from organic arsenicals are found throughout the plant depending on the stage of development of the plant at the time of application. Arsenic residues in cotton seed are low when applications are made before development of the first flower bud. However, if applications are made after square formation, residues increase and may reach 40 ppm in seed from bolls closed at time of application and sampled at maturity (Duble et al., 1968).

A comparative study of absorption, transport and metabolism in beans revealed that cacodylic acid and monosodium acid, methanearsonate (MSMA) were transported about equally from the leaves to the terminal bud and expanding leaves whereas negligible amounts of sodium arsenite and arsenate were translocated. The latter two compounds caused more rapid contact injury to the treated leaves than either organic arsenical. Both cacodylic acid and MSMA were more phytotoxic per mole of tissue arsenic when foliarly-applied than when root-applied (Sachs and Michael, 1971).

Arsenic sprays are often applied to grapefruit trees in Florida to reduce the acid content of the fruit in order to improve flavor and permit early harvest. Symptoms of arsenic toxicity frequently appear when the treatment is used repeatedly in consecutive years. The foliar symptoms of toxicity appears first on the south and southwest side of the trees. The first leaf symptoms are a slight mottling with darker green areas adjacent to the lateral veins. This resembles manganese deficiency except

that the symptoms of manganese deficiency appear first on the young leaves, whereas symptoms of arsenic toxicity appears on mature leaves in the summer and fall. Arsenic toxicity to grapefruit can be prevented by several means: (1) spray with recommended amounts of arsenic during alternate seasons only; (2) in serious cases of arsenic toxicity eliminate use for several seasons until the trees regain their vigor; and, (3) application of an adequate amounts of borax tends to reduce symptoms of arsenic toxicity (Deszyck, 1958).

CHAPTER IV

SIGNIFICANCE OF ARSENICAL PESTICIDES
IN THE ENVIRONMENT

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RESIDUES IN CROPS AND FOOD ITEMS

According to Lehman (1965), the toxicology of arsenic has been exhaustively studied. It has been shown that as an average, natural foods contain 0.6 ppm arsenic calculated on a dry-weight basis. The daily urinary excretion of arsenic is an index of the amount ingested and estimated to be up to 0.5 mg. A third important aspect is arsenic's cumulative properties. Based on data reported for a rat study (Morris and Wallace, 1938), 4.36% of ingested arsenic (as the arsenate) could be expected to be retained in the body.

V. A. Tolerances

V. A. 1. Established Tolerances - Following are the established tolerances presented in this chapter (for more details see exhibits 1-10):

a. A tolerance of 4 ppm of combined As_2O_3 for residues of the defoliant orthoarsenic (arsenic) acid in or on cotton (420.180).

b. A tolerance of 0.7 ppm (expressed as As_2O_3) for residues of the herbicide methanearsonic acid in or on cotton, from application of the disodium and monosodium salts of methanearsonic acid in the production of cotton (420.289).

c. Tolerances of 3.5 ppm of combined As_2O_3 for residues of the insecticides calcium arsenate, copper arsenate, magnesium arsenate and sodium arsenate on specified raw agricultural commodities (420.192, 420.193, 420.195, and 420.196, respectively). Tolerances for lead arsenate (420.194) on vegetables and tree fruits were based mainly on the cumulative action of lead.

d. Tolerances for total residues of combined arsenic (calculated as As), contributed in food by veterinary medicine uses under Sections 121.253, 121.254, 121.262, and 121.310 are established under Section 135g.33 as follows: 0.5 ppm in muscle and eggs and 1 ppm in edible by-products of chickens and turkeys; and, 2 ppm in liver and kidney of swine, and 0.5 ppm in muscle and by-products of swine other than liver and kidney.

V. A. 2. Tolerances Pending - The following arsenic tolerances are now under consideration:

a. Tolerances for residues of elemental arsenic at 2 ppm in or on cotton, 1 ppm in liver and kidney and 0.5 ppm in meat, fat, and meat by-products (except liver and kidney) of cattle from use of the defoliant cacodylic acid (dimethylarsinic acid) on cottonseed.

b. Tolerances of 0.5 ppm residues of arsenic (as As) in meat, fat, and meat by-products of cattle and horses (except liver and kidney); and 2 ppm in the kidney and liver of cattle and horses resulting from the dermal application of arsenical dip solutions (sodium arsenite) for tick control of these livestock imported from Mexico and in the tick eradication program in the Texas area. The use of the arsenical solutions are to be supervised by authorized personnel according to prescribed ARS (USDA) procedures. The animals may remain in the Texas quarantine area from 3 weeks to 10 months and are subject to repeated dip treatments during this time. Such animals are usually range-fed and are shipped to feed lots for feeding for periods from 3 to 6 months prior to slaughter. All animals recieve a final dip before leaving the quarantine area. Horsemeat is not generally available in the U.S. for human consumption. Arsenic residues in cattle result mainly from feed rations containing cottonseed meal which are fed to cattle in feed lots or on the farm.

V. A. 3. Policy Considerations for Arsenic Residues - Section 420.3(d)(4), 21 CFR revised as of January 1, 1971, states: "When a tolerance is established for more than one pesticide containing arsenic found in, or on a raw agricultural commodity, the total amount of such pesticide shall not exceed the highest established tolerance calculated as As_2O_3."

V. B. Acceptable Daily Intake (ADI) - Since no acceptable daily intake (FAO/WHO, 1968) has been established for either arsenic or lead, no recommendation for tolerances can be made at this time.

The safety of established and pending tolerances for arsenic residues on specified items of the normal daily diet were based on toxicological evaluation of rat, dog and other livestock feeding studied submitted by the petitioner and other available published data (Morris and Wallace, 1938; WHO/FAO, 1968; Morris, et al., 1938; Calvery, et al., 1938; Byron et al., 1967; Anon, 1963). Based upon 4.36% retention of arsenic (as arsenate), it would be expected that only a small amount of arsenic would be retained in the body and that this amount would be an insignificant contribution to the total body load of arsenic (0.3 ppm) obtained from normal sources. Data (Morris, et al., 1938) indicate that much larger amounts of arsenic are stored in rats receiving calcium arsenate (a pentavalent arsenic compound) than in those receiving arsenic trioxide (a trivalent arsenic compound) when fed at the same level.

V. C. Pesticide Monitoring.

V. C. 1. FDA Market Basket Survey - Pesticide residue levels detected in ready-to-eat foods were stated (Corneliussen, 1970) to remain at relatively low levels during the 5th year of the Total Diet Study. Samples were collected from 30 markets in 24 different United States cities and analyzed at 5 sampling sites: Boston; Kansas City, Mo.; Los Angeles; Baltimore; and Minneapolis. The method sensitivity for arsenic as As_2O_3

was 0.1 ppm. Residue levels of arsenic (As_2O_3) for each of the following class of food items (6 composite samples at each of the 5 sampling sites) were found to be:

Dairy products: 1/6 composites (Boston, Minneapolis) - 0.1 ppm

Meat, fish, and poultry: 4/6 composites (Boston - average 0.2 ppm range from 0.2 to 0.4 ppm); 4/6 composites (Los Angeles - average 0.1 ppm, range from 0.1 to 0.4 ppm); 4/6 composites (Baltimore - average 0.4 ppm, range from 0.2 to 1.0 ppm); 3/6 composites (Minneapolis - average 0.1 ppm, 0.1 ppm).

Grain and cereal products: 4/6 composites (Boston - 0.1 ppm) 1/6 composites (Los Angeles - 0.1 ppm); 2/6 composites (Minneapolis - 0.1 to 0.2 ppm).

Potatoes: 1/6 composites (Boston, Los Angeles, Minneapolis) - 0.1 ppm.

Leafy vegetables: 2/6 composites (Boston; 1/6 composites), (Los Angeles, Minneapolis) - 0.1 ppm.

Legume vegetables: 2/6 composites (Boston); 1/6 composites (Los Angeles) - 0.1 ppm.

Root vegetables: 2/6 composites (Boston); 1/6 composites (Minneapolis) 0.1 ppm.

Garden fruits: 3/6 composites (Boston); 1/6 composites (Los Angeles) - 0.1 ppm.

Fruits: 2/6 composites (Boston, Los Angeles); 1/6 composites (Minneapolis) - 0.1 ppm.

Oils, fats and shortenings: 1/6 composites (Boston, Minneapolis) - 0.1 ppm.

Sugars and adjuncts: 3/6 composites (Boston); 1/6 composites (Baltimore Minneapolis) - 0.1 ppm.

Beverages: 2/6 composites (Boston); 1/6 composites (Baltimore) - 0.1 ppm.

In this report, as in earlier reports, the arsenic values were reported on an "as in" basis for 3 food classes: Dairy products, meat, fish and poultry, and, oils, fats, and shortening, even though the earlier tabulations (Duggan, et al., 1967) indicated a "fat basis."

V. C. 2. USDA Consumer and Marketing Service Surveys

V. C. 2. a. Arsenic Residues in Beef - The Meat and Poultry Inspection
Program is conducting a survey (1971) to determine the nature, extent
and levels of mercury, lead, cadmium, selenium, arsenic, antimony,
copper and zinc in beef. This is to evaluate any present or potential
public health hazard that may exist and to determine background levels
of these elements. The survey is to include:

(1) Analyses of 3000 samples randomly obtained from beef slaughter-
ing plants throughout the U.S. The number of samples to be taken at
each plant is based on the seasonal production capacity of the plant.

(2) Analyses of 50 samples to be obtained from beef slaughtering
plants in each of five geographical areas selected on the basis of
known data regarding heavy metals. The data collected for the random
samples (2176/3000) through June 28, 1971, are summarized in TABLE IV. 2.
The data on the samples from selected areas have not been fully evaluated.
The analytical data for the random samples indicate that lead, cadmium
and copper are present in all the samples analyzed and that arsenic
occurs randomly at relatively low levels. Arsenic residues in beef
result mainly from feed containing cottonseed meal and from arsenical
dips used for tick control of cattle imported from Mexico. It will be
necessary to obtain more residue data during subsequent yearly surveys
to ascertain if the arsenic residues in tissues will increase appreciably
following more extensive use of arsenicals as herbicides for cotton or
in cattle dips.

V. C. 2. b. Arsenic Residues in Poultry and Swine - Surveys were con-
ducted for arsenic residues in 1966, 1968, and 1970 in swine and in
1968, 1969, and 1970, in young chickens. Tolerance limits were set at
1.5 ppm in chicken livers and 2.0 ppm in swine livers. Violative residues,
found mainly in the livers, were more pronounced in chickens than swine
and were attributed to lack of proper withdrawal. In 1970, about 5% of
liver samples in 261 swine and 7.4% of liver samples in 431 young
chickens were found to contain violative residues.

TABLE 1 - RESIDUES OF SEVERAL METALS IN BEEF

METALS		LIVER					MUSCLE (DIAPHRAGM)					KIDNEY				ALL TISSUES	
	N	INCIDE. RATE	AVE. (PPM)	LOW (PPM)	HIGH (PPM)	N	INCIDE. RATE	AVE. (PPM)	LOW (PPM)	HIGH (PPM)	N	INCIDE. RATE	AVE. (PPM)	LOW (PPM)	HIGH (PPM)	N	INCIDE. RATE
ARSENIC (AS)	145	6.664	0.093	0.02	0.22	0	0.0	0.0	0.0	0.0	21	0.965	0.077	0.05	0.17	135	7.133
CADMIUM (CD)	2122	97.518	0.207	0.01	3.17	1765	81.112	0.082	0.01	0.90	2153	98.943	0.546	0.01	7.82	2171	99.770
MERCURY (HG)	395	18.153	0.023	0.01	1.79	566	26.011	0.028	0.01	1.85	1164	53.493	0.026	0.01	5.25	1456	66.912
LEAD (PB)	2155	99.081	0.536	0.01	3.74	2080	95.588	0.361	0.01	2.96	2145	98.575	0.625	0.02	3.38	2176	100.000
ANTIMONY (SB)	0	0.0	0.0	0.0	0.0	0	0.0	0.0	0.0	0.0	0	0.0	0.0	0.0	0.0	0	0.0
COPPER (CU)**	2031	99.904	34.923	1.30	115.30	2081	99.904	1.818	0.03	29.90	2081	99.904	4.176	0.08	24.20	2082	99.952
COPPER (CU)**	322	100.000	42.494	3.90	104.10	322	100.000	1.816	0.60	3.70	322	100.000	4.155	0.08	20.30	322	100.000

** COPPER WAS NOT ANALYZED IN THE FIRST 4 SAMPLES

TOTAL NUMBER OF ANIMALS - 2176

DATA COLLECTED THROUGH 6/28/71

7

CHAPTER V

Bibliography (Residues)

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Exhibit 1

SUBPART C--PESTICIDE REGULATIONS--Page 36
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page in your reprint.

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§ 120.180   Orthoarsenic acid.

A tolerance of 4 parts per million of
combined As_2O_3 is established for residues
of the defoliant orthoarsenic acid in or
on the raw agricultural commodity cot-
tonseed.

§ 120.181   CIPC; tolerance for residues.

A tolerance of 50 parts per million
is established for residues of the plant
regulator CIPC (isopropyl N(3-chloro-
phenyl) carbamate) in or on potatoes
from postharvest application.

§ 120.182   Endosulfan; tolerances for residues.

Tolerances are established for the total
residues of the insecticide endosulfan
(6,7,8,9,10,10 - hexachloro - 1,5,5a,6,9,9a -
hexahydro-6,9-methano - 2,4,3 - benzodi-
oxathiepin-3-oxide) and its metabolite
endosulfan sulfate (6,7,8,9,10,10-hexa-
chloro - 1,5,5a,6,9,9a-h e x a h y d r o-6,9-
methano-2,4,3-benzodioxathiepin-3,3-di-
oxide) in or on raw agricultural
commodities as follows:

2 parts per million in or on apples,
apricots, artichokes, beans, broccoli,
brussels sprouts, cabbage, cauliflower,
celery, cherries, collards, cucumbers, egg-
plants, grapes, kale, lettuce, melons,
mustard greens, nectarines, peaches,
pears, peas (succulent type), peppers,
pineapples, plums, prunes, pumpkins,
spinach, strawberries, summer squash,
sunflower seed, tomatoes, turnip greens,
watercress, and winter squash.

* 1 part per million in or on alfalfa hay
and cottonseed. *

0.5 part per million in milk fat (re-
flecting negligible residues in milk) and
in or on sugarcane.

0.3 part per million in or on alfalfa
(fresh).

0.2 part per million in or on carrots,
sweet corn (kernels plus cob with husks
removed), sweetpotatoes; and in meat,
fat, and meat byproducts of cattle, goats,
hogs, horses, and sheep.

** 0.2 part per million (negligible resi-
dues) in or on filberts, macadamia nuts,
pecans, potatoes, safflower seed, and
walnuts. **

U. S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
FOOD AND DRUG ADMINISTRATION

Exhibit 2

(§§ 420.282 thru 420.289)

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page in your reprint.

§ 420.282   2-Chloro-*N,N*-diallylaceta-
mide; tolerances for residues.

Tolerances are established for negligi-
ble residues of the herbicide 2-chloro-
N,N-diallylacetamide in or on the raw
agricultural commodities cabbage, castor
beans, celery, corn grain (includes pop-
corn), fresh corn including sweet corn
(kernels plus cobs with husk removed),
corn forage or fodder (including sweet
corn, field corn, and popcorn), dried
beans, lima beans, lima bean forage,
onions, peas, pea forage, potatoes, snap
beans, snap bean forage, sorghum grain,
sorghum forage, soybeans, soybean for-
age, sugarcane, sweetpotatoes, and to-
matoes at 0.05 part per million.

§ 420.283   2,3,6-Trichlorophenylacetic
acid; tolerances for residues.

A tolerance of 0.1 part per million is
established for negligible residues of the
herbicide 2, 3, 6-trichlorophenylacetic
acid in or on sugarcane, such residues
resulting from application of its dimeth-
ylamine or sodium salts.   *

§ 420.284   Zinc phosphide; tolerances
for residues.

A tolerance of 0.01 part per million is
established for residues of phosphine in
or on the raw agricultural commodity
sugarcane from use of the rodenticide
zinc phosphide in sugarcane fields.

§ 420.285   *N'*-(4-Chloro-o-tolyl)-*N,N*-
dimethylformamidine; tolerances for
residues.

Tolerances are established for com-
bined residues of the insecticide *N'*-(4-
chloro-o-tolyl) - *N,N*-dimethylformami-
dine and its metabolites containing the 4-
chlorotoluidine moiety (calculated as the
insecticide) from application of the in-
secticide as the free base or as the hydro-
chloride salt in or on raw agricultural
commodities as follows:

8 parts per million in or on pears.

3 parts per million in or on apples.

3 parts per million in or on broccoli,
brussels sprouts, cabbage, and cauli-
flower.

* § 420.286   1-Chloro-2-nitropropane; tol-
erances for residues.

A tolerance of 0.05 part per million is
established for negligible residues of the
fungicide 1-chloro-2-nitropropane and
its metabolite 2-nitropropanol (regu-
lated as 1-chloro-2-nitropropane) in or
on the raw agricultural commodities
cottonseed and melons.   *

§ 420.287   Decachlorooctahydro-1,3,4-
metheno-2H-cyclobuta[cd]pentalen-
2-one; tolerance for residues.

A tolerance of 0.01 part per million is
established for negligible residues of the
insecticide   decachlorooctahydro-1,3,4,-
metheno - 2H-cyclobuta[cd]pentalen-2-
one in or on the raw agricultural com-
modity bananas.

§ 420.288   2-(Thiocyanomethylthio)ben-
zothiazole; tolerances for residues.

A tolerance of 0.1 part per million is
established for negligible residues of the
fungicide 2-(thiocyanomethylthio)ben-
zothiazole in or on cottonseed.

§ 420.289   Methanearsonic acid; toler-
ances for residues.

A tolerance of 0.7 part per million (ex-
pressed as As₂O₃) is established for resi-
dues of the herbicide methanearsonic
acid in, or on cottonseed, from applica-
tion of the disodium and monosodium
salts of methanearsonic acid in the pro-
duction of cotton.   *

Amendment published in Federal Register:
* November 18, 1970; 35 F.R. 17708

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Exhibit 3

§ 120.189 Coumaphos; tolerances for residues.

Tolerances are established for residues of the insecticide coumaphos (O,O-diethyl O-3-chloro-4-methyl-2-oxo-2H-1-benzopyran-7-yl phosphorothioate) and its oxygen analog (O,O-diethyl O-3-chloro-4-methyl-2-oxo-2H-1-benzopyran-7-yl phosphate) in or on raw agricultural commodities as follows:

1 part per million in or on meat, fat, and meat byproducts of cattle, goats, hogs, horses, poultry, and sheep.

0.5 part per million in milk-fat reflecting negligible residues in milk.

0.1 part per million in eggs.
(See also § 121.304 of this chapter.)

§ 120.190 Diphenylamine; tolerances for residues.

Tolerances for residues of the fungicide diphenylamine are established as follows:

10 parts per million in or on apples from preharvest or postharvest use, including use of impregnated wraps, for scald control.

Zero in milk and meat.

§ 120.191 Folpet; tolerances for residues.

Tolerances for residues of the fungicide folpet (N-(trichloromethylthio) phthalimide) in or on raw agricultural commodities are established as follows:

50 parts per million in or on celery, cherries, leeks, lettuce, onions (green), shallots.

25 parts per million in or on apples avocados, blackberries, blueberries, boysenberries, crabapples, cranberries, currants, dewberries, gooseberries, grapes, huckleberries, loganberries, raspberries, strawberries, tomatoes.

* 15 parts per million in or on citrus fruits, cucumbers, garlic, melons, onions (dry bulb), pumpkins, summer squash, winter squash. *

420
§ 120.192 Calcium arsenate; tolerances for residues.[2]

A tolerance of 3.5 parts per million of combined As_2O_3 is established for residues of the insecticide calcium arsenate in or on each of the following raw agricultural commodities: Asparagus, beans, blackberries, blueberries (huckleberries), boysenberries, broccoli, brussels sprouts, cabbage, carrots, cauliflower, celery, collards, corn, cucumbers, dewberries, eggplants, kale, kohlrabi, loganberries, melons, peppers, pumpkins, raspberries, rutabagas (with or without tops) or rutabaga tops, spinach, squash, strawberries, summer squash, tomatoes, turnips (with or without tops) or turnip greens, youngberries.

* § 120.191 is amended by deleting the paragraph "15 parts per million in or on citrus * ° °"

Amendment published in Federal Register:
* December 14, 1968; 33 F.R. 18578

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page in your reprint.

§ 120.193 Copper arsenate; tolerances
for residues.

A tolerance of 3.5 parts per million of combined As_2O_3 is established for residues of the insecticide and fungicide copper arsenate in or on each of the following raw agricultural commodities: Brussels sprouts, cabbage, carrots, cauliflower, kohlrabi, tomatoes.

§ 120.194 Lead arsenate; tolerances for
residues.

Tolerances for residues of lead arsenate (primarily an insecticide) in or on raw agricultural commodities are established as follows:

7 parts per million of combined lead in or on apples, apricots, asparagus, avocados, blackberries, blueberries (huckleberries), boysenberries, celery, cherries, cranberries, currants, dewberries, eggplants, gooseberries, grapes, loganberries, mangoes, nectarines, peaches, pears, peppers, plums (fresh prunes), quinces, raspberries, strawberries, tomatoes, youngberries.

1 part per million of combined lead in or on citrus fruits.

§ 120.195 Magnesium arsenate; tolerance for residues.

A tolerance of 3.5 parts per million of combined As_2O_3 is established for residues of the insecticide magnesium arsenate in or on the raw agricultural commodity beans.

§ 120.196 Sodium arsenate; tolerance for residues.

A tolerance of 3.5 parts per million of combined As_2O_3 is established for residues of the insecticide sodium arsenate in or on the raw agricultural commodity grapes.

*In § 120.193, "(with or without tops) or carrot tops" is deleted.

(§§ 135g.29 thru 135g.43)

Amendments published in Federal Register: PART 135g--TOLERANCES FOR   Page 17
* May 13, 1971; 36 F.R. 8781   RESIDUES OF NEW ANIMAL DRUGS IN FOC
* * June 19, 1971; 36 F.R. 11811   Remove old page 17 and insert this
                                              new page in your reprint.

Exhibit 5

§ 135g.29 Testosterone propionate.

(a) No residues of testosterone propionate may be found in the uncooked edible tissues of heifers.

(b) The method of examination prescribed for the quantitative determination of testosterone propionate is as follows: Prepare an extract of the tissues as described in § 135g.28(b) (1) and (2) and bioassay the extractive in an ethyl alcohol vehicle by inunction on the day-old chick's comb by the method published in "Methods in Hormone Research," New York, Academic Press, volume II, page 286 (1962).

§ 135g.30 Estradiol benzoate.

(a) No residues of estradiol benzoate may be found in the uncooked edible tissues of heifers, lambs, and steers.

(b) The method of examination prescribed for the quantitative determination of estradiol benzoate is as follows: Incorporate the finely ground tissues in the diet of immature mice, and assay by the mouse uterine weight method of E. J. Umberger, G. H. Gass, and J. M. Curtis, published in "Endocrinology," volume 63, page 806 (1958).

§ 135g.31 Chlorobutanol.

A tolerance of zero is established for residues of chlorobutanol in milk from dairy animals.

§ 135g.32 Salicylic acid.

A tolerance of zero is established for residues of salicylic acid in milk from dairy animals.

§ 135g.33 Arsenic.

Tolerances for total residues of combined arsenic (calculated as As) in food are established as follows:

(a) In edible tissues and in eggs of chickens and turkeys:

(1) 0.5 part per million in uncooked muscle tissue.

(2) 1 part per million in uncooked edible byproducts.

(3) 0.5 part per million in eggs.

(b) In edible tissues of swine:

(1) 2 parts per million in uncooked liver and kidney.

(2) 0.5 part per million in uncooked muscle tissue and byproducts other than liver and kidney.

§ 135g.34 Erythromycin.

Tolerances for residues of erythromycin in food are established as follows:

(a) 0.1 part per million (negligible residue) in uncooked edible tissues of swine.

(b) Zero in uncooked edible tissues of chickens, turkeys, and beef cattle; in uncooked eggs; and in milk. * *

§ 135g.35 Sulfaethoxypyridazine.

A tolerance of zero is established for residues of sulfaethoxypyridazine in the uncooked edible tissues of swine and cattle and in milk.

§ 135g.36 Furazolidone.

A tolerance of zero is established for residues of furazolidone in the uncooked edible tissues of swine.

§ 135g.37 Prednisolone.

A tolerance of zero is established for residues of prednisolone in milk from dairy animals.

§ 135g.38 Estradiol monopalmitate.

(a) No residues of estradiol monopalmitate may be found in the uncooked edible tissues of chickens.

(b) The method of examination prescribed for the quantitative determination of estradiol monopalmitate is as follows: Incorporate finely ground tissues of the treated chickens in the diet of immature mice and assay by the mouse uterine weight method of E. J. Umberger, J. H. Gass, and J. M. Curtis published in "Endocrinolgoy," volume 63, page 806 (1958).

§ 135g.39 Thiabendazole.

Tolerances are established at 0.1 part per million for negligible residues of thiabendazole in uncooked edible tissues of cattle, goats, sheep, and swine, and at 0.05 part per million for negligible residues in milk.

§ 135g.40 Prednisone.

A tolerance of zero is established for residues of prednisone in milk from dairy animals.

§ 135g.41 Methylparaben.

A tolerance of zero is established for residues of methylparaben in milk from dairy animals.

§ 135g.42 Propylparaben.

A tolerance of zero is established for residues of propylparaben in milk from dairy animals.

§ 135g.43 Ipronidazole.

No residues of ipronidazole (2-isopropyl-1-methyl-5-nitroimidazole) and its metabolite (1-methyl-5-nitroimidazole-2-isopropanol) are found in the uncooked edible tissues of turkeys as determined by the following method of analysis:

I. METHOD OF ANALYSIS

A. The assay procedure is suitable for the recovery and analysis of ipronidazole (1-methyl-2-isopropyl-5-nitroimidazole) and its metabolite 1-methyl-5-nitroimidabole-2-isopropanol from turkey tissue with a lower limit of 2 parts per billion using a 100-gram sample. Ipronidazole and its metabolite are extracted from muscle, liver, kidney, skin, fat, and blood with benzene in the presence of borax. The extract is purified by column chromatography on silica gel and the two compounds are determined separately by gas-liquid chromatography (GLC).

B. The following aspects of the procedure must be carefully observed to insure good recoveries and reproducible results:

§ 121.253 Arsanilic acid.

Arsanilic acid may be safely used in animal feed when incorporated therein in accordance with the following conditions:

(a) The additive is the chemical p-aminobenzenearsonic acid ($C_6H_8AsNO_3$) conforming to the following specifications (on the dry basis):

(i) The additive contains not less than 34 percent and not more than 34.8 percent of arsenic (As), equivalent to not less than 93.5 percent and not more than 100.8 percent $C_6H_8AsNO_3$.

(ii) The additive contains not more than 0.025 percent arsenic as inorganic arsenite, calculated as As_2O_3 and not more than 0.05 percent arsenic as inorganic arsenate, calculated as $AsO_4\equiv$.

(b) Permitted uses of arsanilic acid alone and with certain other additives are described in tabular form in this section, and these tables are to be read as follows:

(1) The numbered line items establish the required limitations and indications for use of the principal ingredient as the medicament alone or with an additional ingredient added for increased effectiveness.

(2) The lettered line items establish the required limitations and indications for use of secondary ingredients that may be added to the indicated principal ingredient. Where principal and secondary ingredients have been mixed, the applicable limitations and indications for use from both the numbered items and lettered items apply. If duplicate limitations occur, these may be appropriately combined.

(3) Permitted combinations of principal ingredient and secondary ingredients are individually listed. Unless specifically provided by the regulations, the principal ingredient may not be mixed with two or more secondary ingredients.

(4) Where cross-references specify a particular table and item number of another section, use of only the principal ingredient of the numbered item is authorized thereby.

(5) The term "principal ingredient" as used in this section refers to the additive named in the heading of this section and is not intended to imply that the ingredient is of a greater value than any other additives named in this section.

(c) It is used or intended for use in feeds, as follows:

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new page in your reprint.

ARSANILIC ACID IN COMPLETE CHICKEN AND TURKEY FEED

Principal Ingredient	Grams per ton	Combined with—	Grams per ton	Limitations	Indications for use
1.1 Arsanilic acid.	90 (0.01%)	--------------	----------	For chickens; withdraw 5 days before slaughter; as sole source of organic arsenic.	Growth promotion and feed efficiency; improving pigmentation.
1.2 Arsanilic acid.	90 (0.01%)	Amprolium.	113.5-227 (0.0125%-0.025%)	For broiler chickens; for replacement chickens where immunity to coccidiosis is not desired; withdraw 5 days before slaughter; as sole source of organic arsenic.	Growth promotion and feed efficiency; improving pigmentation; prevention of coccidiosis.
1.3 Arsanilic acid.	90 (0.01%)	Amprolium + ethopabate.	113.5-227 (0.0125%-0.025%) 3.6 (0.0004%)	For broiler chickens; withdraw 5 days before slaughter.	Do.
1.4 Arsanilic acid.	90 (0.01%)	Amprolium.	36.3-113.5 (0.004%-0.0125%)	For replacement chickens; withdraw 5 days before slaughter; as sole source of organic arsenic; as follows:	Growth promotion and feed efficiency; improving pigmentation; development of active immunity to coccidiosis.

Growing conditions	Amount of amprolium in feed for birds, by age groups		
	Up to 5 weeks of age	From 5 to 8 weeks of age	Over 8 weeks of age
	Grams per ton	*Grams per ton*	*Grams per ton*
Severe exposure to coccidiosis.	113.5 (0.0125%)	72.6-113.5 (0.008%-0.0125%)	36.3-113.5 (0.004%-0.0125%)
Moderate exposure to coccidiosis.	72.6-113.5 (0.008%-0.0125%)	54.5-113.5 (0.006%-0.0125%)	36.3-113.5 (0.004%-0.0125%)
Slight exposure to coccidiosis.	36.3-113.5 (0.004%-0.0125%)	36.3-113.5 (0.004%-0.0125%)	36.3-113.5 (0.004%-0.0125%)

Principal Ingredient	Grams per ton	Combined with—	Grams per ton	Limitations	Indications for use
1.5 Arsanilic acid.	90 (0.01%)	Zoalene.	113.5 (0.0125%)	For broiler chickens, withdraw 5 days before slaughter; as sole source of organic arsenic.	Growth promotion and feed efficiency; improving pigmentation; prevention and control of coccidiosis.
1.6 Arsanilic acid.	90 (0.01%)	Zoalene.	36.3-113.5 (0.004%-0.0125%)	For replacement chickens; in complete feed only; grower ration not to be fed to birds over 14 weeks of age; withdraw 5 days before slaughter; as sole source of organic arsenic; as follows:	Development of active immunity to coccidiosis; growth promotion and feed efficiency; improving pigmentation.

Growing conditions	Starter ration	Grower ration
	Grams per ton	*Grams per ton*
Severe exposure.	113.5 (0.0125%)	75.4-113.5 (0.008%-0.0125%)
Light to moderate exposure.	75.4-113.5 (0.008%-0.0125%)	36.3-75.4 (0.004%-0.008%)

* In § 121.253(c), the words "under 5 1/2 weeks of age nor" are deleted from item 1.6 under "Limitations" in the table.

ARSANILIC ACID IN COMPLETE CHICKEN AND TURKEY FEED—Continued

Principal Ingredient	Grams per ton	Combined with—	Grams per ton	Limitations	Indications for use
1.7 Arsanilic acid	90 (0.01%)	Amprolium	72.6-113.6 (0.006%) 0.0125%)	For broiler chickens; withdraw 5 days before slaughter; as sole source of organic arsenic.	Growth promotion and feed efficiency; improving pigmentation; prevention coccidiosis caused by E. tenella only.
1.8 Arsanilic acid	90 (0.01%)	Buquinolate	75 (0.00625%)	For broiler chickens; withdraw 5 days before slaughter; do not feed to laying hens; as sole source of organic arsenic.	As an aid in the prevention of coccidiosis caused by E. tenella, E. maxima, E. necatrix and E. acervulina; growth promotion and feed efficiency improving pigmentation.
a. 1.1, 1.2, 1.3, 1.4, 1.5 or 1.6.	-----------	Penicillin	2.4-50	As procaine penicillin	Growth promotion and feed efficiency.
b. 1.1, 1.2, 1.3 or 1.4.	-----------	Penicillin+ streptomycin.	14.4-50	As procaine penicillin+ streptomycin sulfate; 14.4-50 gm. of combination containing 16.7% of penicillin.	Do.
c. 1.5 or 1.6.	-----------	Penicillin+ bacitracin.	3.6-50	Not less than 0.6 gm. of penicillin nor less than 3.0 gm. of bacitracin; as procaine penicillin+ bacitracin, bacitracin methylene disalicylate, manganese bacitracin, or zinc bacitracin.	Growth promotion and feed efficiency.
d. 1.5 or 1.6.	-----------	Bacitracin	4-50	As bacitracin, bacitracin methylene disalicylate, or zinc bacitracin.	Do.
e. 1.1, 1.5, or 1.6.	-----------	do	4-50	As manganese bacitracin	Do.
* f. 1.1, 1.2, 1.3, 1.4, 1.5, 1.6.	-----------	Erythromycin	92.6-185	§ 121.292(d), table, items 1.1, 1.2, 2.1, 2.2, 4.1, 4.2.	§ 121.292(d), table, items 1.1, 1.2, 2.1, 2.2, 4.2.
g. 1.1, 1.2, 1.3, 1.4, 1.5, 1.6.	-----------	Erythromycin	4.6-18.5	As erythromycin thiocyanate.	Growth promotion and feed efficiency. *
2.1 Arsanilic acid.	90 (0.01%)	-----------	-----------	For turkeys; withdraw 5 days before slaughter; as sole source of organic arsenic.	Growth promotion and feed efficiency; improving pigmentation.
2.2 Arsanilic acid.	90 (0.01%)	Amprolium	113.5-227 (0.0125%- 0.025%)	do	Growth promotion and feed efficiency; improving pigmentation; preventing of coccidiosis.
2.3 Arsanilic acid.	90 (0.01%)	Zoalene	113.5-170.3 (0.0125%- 0.01875%)	For turkeys grown for meat purposes only; withdraw 5 days before slaughter; as sole source of organic arsenic.	Growth promotion and feed efficiency; improving pigmentation; prevention and control of coccidiosis.

(d) To assure safe use, the label and labeling of the additive, any combination of additives, and any feed additive supplement, feed additive concentrate, feed additive premix, or complete feed prepared therefrom shall bear, in addition to the other information required by the act, the following:

(1) The name of the additive or additives.

(2) A statement of the quantity or quantities contained therein.

(3) Adequate directions and warnings for use.

(e) Section 121.3158 establishes the limitation for residues of the additive in food for human consumption.

Exhibit 7

§ 121.254   Sodium arsanilate.

Sodium arsanilate may be safely used in animal feed when incorporated therein in accordance with the following conditions.

(a) The additive is the chemical sodium p-aminobenzenearsonate ($C_6H_7AsNNaO_3$) conforming to the following specifications (on the dry basis):

(i) The additive contains not less than 30.87 percent and not more than 31.65 percent of arsenic (As), equivalent to not less than 98.5 percent and not more than 101 percent of $C_6H_7AsNNaO_3$.

(ii) The additive contains not more than 0.025 percent arsenic as inorganic arsenite, calculated as As_2O_3 and not more than 0.05 percent arsenic as inorganic arsenate, calculated as $AsO_4\equiv$.

(b) Permitted use of sodium arsanilate alone and with certain other additives is described in tabular form in this section and this table is to be read as follows:

(1) The numbered line items establish the required limitations and indications for use of the principal ingredient as the medicament alone or with an additional ingredient added for increased effectiveness.

(2) The lettered line items establish the required limitations and indications for use of secondary ingredients that may be added to the indicated principal ingredient. Where principal and secondary ingredients have been mixed, the applicable limitations and indications for use from both the numbered items and lettered items apply. If duplicate limitations occur, these may be appropriately combined.

(3) Permitted combinations of principal ingredient and secondary ingredients are individually listed. Unless specifically provided by the regulations, the principal ingredient may not be mixed with two or more secondary ingredients.

(4) Where cross-references specify a particular table and item number of another section, use of only the principal ingredient of the numbered item is authorized thereby.

(5) The term "principal ingredient" as used in this section refers to the additive named in the heading of this section and is not intended to imply that the ingredient is of a greater value than any other additives named in this section.

(c) It is used or intended for use in feeds, as follows:

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SODIUM ARSANILATE IN COMPLETE CHICKEN AND TURKEY FEED

Principal Ingredient	Grams per ton	Combined with—	Grams per ton	Limitations	Indications for use
1. Sodium arsanilate. .	90 (0.01%)	---------------	---------------	For chickens and turkeys; withdraw 5 days before slaughter. ☆ as sole source of organic arsenic. ☆	Growth promotion and feed efficiency; improving pigmentation.
a. Sodium arsanilate.	90	Amprolium...	36.3-227 (0.004%-0.025%).	For chickens and turkeys; as prescribed in § 121.210, table 1, items 1.1, 2.1, 3.1, 4.1.	§ 121.210, table items 1.1, 2.1, 3.1, 4.1.
b. Sodium arsanilate.	90	Zoalene.......	36.3-170.3 (0.004%-0.01875%).	For chickens and turkeys; as prescribed in § 121.207, table, items 1, 2, 3.	§ 121.207, table, items 1, 2, 3.

(d) To assure safe use, the label and labeling of the additive, any combination of additives, and any feed additive supplement, feed additive concentrate, feed additive premix, or complete feed prepared therefrom shall bear, in addition to the other information required by the act, the following:

(1) The name of the additive or additives.

(2) A statement of the quantity or quantities contained therein.

(3) Adequate directions and warnings for use.

Amendment published in Federal Register:
November 25, 1964; 29 F.R. 15815

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§ 121.262 3-Nitro-4-hydroxyphenylar-
sonic acid.

3-Nitro-4-hydroxyphenylarsonic acid
may be safely used in animal feed when
incorporated therein in accordance with
the following conditions:

(a) The additive is the chemical
4-hydroxy-3-nitrobenzene arsonic acid,
$C_6H_6AsNO_5$, conforming to the following
specifications, on a dry basis:

(1) The additive contains not less
than 28.0 percent and not more than
28.7 percent arsenic, equivalent to not
less than 93.3 percent and not more than
100.8 percent of $C_6H_6AsNO_5$.

(2) The additive contains not more
than 0.025 percent arsenic as inorganic
arsenite, calculated as As_2O_3, and not
more than 0.05 percent arsenic as inor-
ganic arsenate, calculated as As_2O_5.

(b) Permitted uses of 3-nitro-4-hy-
droxyphenylarsonic acid alone and with
certain other additives are described in
tabular form in this section, and these
tables are to be read as follows:

(1) The numbered line items establish
the required limitations and indications
for use of the principal ingredient as the
medicament alone, or with an additional
ingredient added.

(2) The lettered line items establish
the required limitations and indications
for use of secondary ingredients that
may be added to the indicated principal
ingredient. Where principal and sec-
ondary ingredients have been mixed, the
applicable limitations and indications
for use for both the numbered items and
lettered items apply. If duplicate lim-
itations occur, these may be appropri-
ately combined.

(3) Permitted combinations of prin-
cipal ingredients and secondary ingre-
dients are individually listed. Unless
specifically provided for by the regula-
tion, principal ingredients may not be
mixed with two or more secondary
ingredients.

(4) Where cross-references specify a
particular table and item number of an-
other section, use of only the principal
ingredient or ingredients of the num-
bered item is authorized thereby.

(5) The term "principal ingredient"
as used in this section refers to the addi-
tive named in the title of this section,
and is not intended to imply that the
ingredient is of greater value than any
other additives named in this section.

(c) It is used or intended for use in
feed as follows:

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* March 31, 1971; 36 F.R. 5906   Remove old page 48 and insert this new
page in your reprint.

TABLE 1—3-Nitro-4-Hydroxyphenylarsonic Acid in Complete Chicken and Turkey Feed

Principal ingredient	Grams per ton	Combined with—	Grams per ton	Limitations	Indications for use
1.1 3-Nitro-4-hydroxyphenylarsonic acid.	22.7-45.4 (0.0025%-0.005%)			For chickens; withdraw 5 days before slaughter; as sole source of organic arsenic.	Growth promotion and feed efficiency; improving pigmentation.
1.2 3-Nitro-4-hydroxyphenylarsonic acid.	45.4 (0.005%)	3,5-Dinitrobenzamide [1] + Sulfanitran	227 (0.025%) / 272 (0.03%)	For chickens; not to be fed to laying chickens; withdraw 5 days before slaughter; from feed additive premixes containing not more than 25 percent 3,5-dinitrobenzamide, 30 percent sulfanitran, and 5 percent 3-nitro-4-hydroxyphenylarsonic acid; as sole source of organic arsenic.	Prevention of coccidiosis caused by E. tenella, E. necatrix, and E. acervulina; growth promotion and feed efficiency; improving pigmentation.
1.3 3-Nitro-4-hydroxyphenylarsonic acid.	22.7-45.4 (0.0025%-0.005%)	Zoalene	113.5 (0.0125%)	For broiler chickens; withdraw 5 days before slaughter; as sole source of organic arsenic.	Prevention and control of coccidiosis; growth promotion and feed efficiency; improving pigmentation.
1.4 3-Nitro-4-hydroxyphenylarsonic acid.	22.7-45.4 (0.0025%-0.005%)	...do	36.3-113.5 (0.004%-0.0125%)	For replacement chickens; in complete feed only; grower ration not to be fed to birds over 14 weeks of age; withdraw 5 days before slaughter; as sole source of organic arsenic; as follows:	Development of active immunity to coccidiosis; growth promotion and feed efficiency; improving pigmentation.

Growing Conditions	Starter ration	Grower ration
	Grams per ton	Grams per ton
Severe exposure	113.5 (0.0125%)	75.4-113.5 (0.0083%-0.0125%)
Light to moderate exposure	75.4-113.5 (0.0083%-0.0125%)	36.3-75.4 (0.004%-0.0083%)

Principal ingredient	Grams per ton	Combined with—	Grams per ton	Limitations	Indications for use
1.5 3-Nitro-4-hydroxyphenylarsonic acid.	22.7-45.4 (0.0025%-0.005%)	Sulfanitran + Aklomide	181.6 (0.02%) / 227 (0.025%)	For chickens; not to be fed to laying chickens; withdraw 5 days before slaughter; from feed additive premixes containing not more than 20 percent sulfanitran, 25 percent aklomide, and 2.5 percent to 5.0 percent 3-nitro-4-hydroxyphenylarsonic acid; as sole source of organic arsenic.	As an aid in the prevention of coccidiosis caused by E. tenella, E. necatrix, and E. acervulina; growth promotion and feed efficiency; improving pigmentation.
1.6 3-Nitro-4-hydroxyphenylarsonic acid.	22.7-45.4 (0.0025%-0.005%)	Aklomide	227 (0.025%)	For broiler chickens only; withdraw 5 days before slaughter; as sole source of organic arsenic.	Aid in the prevention of coccidiosis caused by E. tenella and E. necatrix; growth promotion and feed efficiency; improving pigmentation.
1.7 3-Nitro-4-hydroxyphenylarsonic acid.	22.7-45.4 (0.0025%-0.005%)	Amprolium	113.5-227 (0.0125%-0.025%)	For broiler chickens; for replacement chickens where immunity to coccidiosis is not desired; withdraw 5 days before slaughter; as sole source of organic arsenic.	Prevention of coccidiosis; growth promotion and feed efficiency; improving pigmentation.
1.8 3-Nitro-4-hydroxyphenylarsonic acid.	22.7-45.4 (0.0025%-0.005%)	Amprolium + Ethopabate	113.5-227 (0.0125%-0.025%) / (0.0004%)	For broiler chickens; for replacement chickens where immunity to coccidiosis is not desired; withdraw 5 days before slaughter; as sole source of organic arsenic; not to be fed to laying chickens.	Do.

[1] No residues are detected by the method of analysis set forth in § 121.263 (e).

Amendment published in Federal Register:
* May 20, 1970; 35 F.R. 7734
* * June 20, 1970; 35 F.R. 10146

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TABLE 1—3-NITRO-4-HYDROXYPHENYLARSONIC ACID IN COMPLETE CHICKEN AND TURKEY FEED—Continued

Principal Ingredient	Grams per ton	Combined with—	Grams per ton	Limitations	Indications for use
1.9 3-Nitro-4-hydroxyphenyl-arsonic acid.	22.7–45.4 (0.0025%–0.005%)	Amprolium	36.3–113.5 (0.004%–0.0125%)	For replacement chickens; withdraw 5 days before slaughter; as sole source of organic arsenic; as follows:	Growth promotion and feed efficiency; improving pigmentation; development of active immunity to coccidiosis.

Growing conditions	Amount of amprolium in feed for birds by age groups		
	Up to 5 weeks of age	From 5 to 8 weeks of age	Over 8 weeks of age
	Grams per ton	Grams per ton	Grams per ton
Severe exposure to coccidiosis.	113.5 (0.0125%)	72.6–113.5 (0.008%–0.0125%)	36.3–113.5 (0.004%–0.0125%)
Moderate exposure to coccidiosis.	72.6–113.5 (0.008%–0.0125%)	54.5–113.5 (0.006%–0.0125%)	36.3–113.5 (0.004%–0.0125%)
Slight exposure to coccidiosis.	36.3–113.5 (0.004%–0.0125%)	36.3–113.5 (0.004%–0.0125%)	36.3–113.5 (0.004%–0.0125%)

Principal Ingredient	Grams per ton	Combined with—	Grams per ton	Limitations	Indications for use
1.10 3-Nitro-4-hydroxyphenyl-arsonic acid.	22.7–45.4 (0.0025%–0.005%)	Buquinolate	75 (0.00825%)	For broiler chickens; withdraw 5 days before slaughter; do not feed to laying chickens; as sole source of organic arsenic.	As an aid in the prevention of coccidiosis caused by E. tenella, E. maxima, E. necatrix, and E. acervulina; growth promotion and feed efficiency; improving pigmentation.
1.11 3-Nitro-4-hydroxyphenyl-arsonic acid.	45.4 (0.005%)	Clopidol	113.5 (0.0125%)	For broiler chickens; do not feed to chickens over 16 weeks of age; withdraw 5 days before slaughter; as sole source of organic arsenic.	Growth promotion and feed efficiency; improving pigmentation; aid in the prevention of coccidiosis caused by E. tenella, E. necatrix, E. acervulina, E. maxima, E. brunetti, and E. mivati.
1.12 3-Nitro-4-hydroxyphenyl-arsonic acid.	45.4 (0.005%)	Clopidol	113.5 (0.0125%)	For replacement chickens intended for use as caged layers; do not feed to chickens over 16 weeks of age; withdraw 5 days before slaughter; as sole source of organic arsenic.	Aid in the prevention of coccidiosis caused by E. tenella, E. necatrix, E. acervulina, E. maxima, E. brunetti, and E. mivati; growth promotion and feed efficiency; improving pigmentation.
1.13 3-Nitro-4-hydroxyphenyl-arsonic acid.	45.4 (0.005%)	Decoquinate	27.2 (0.003%)	For broiler chickens; do not feed to laying chickens; withdraw 5 days before slaughter; as sole source of organic arsenic.	As an aid in the prevention of coccidiosis caused by E. tenella, E. necatrix, E. mivati, E. acervulina, E. maxima, and E. brunetti; growth promotion and feed efficiency; improving pigmentation.
✱ 1.14 3-Nitro-4-hydroxyphenylarsonic acid.	45.4 (0.005%)	Monensin	110 (as monensic acid activity).	For broiler chickens; do not feed to laying chickens; withdraw 5 days before slaughter; as sole source of organic arsenic.	Growth promotion and feed efficiency; improving pigmentation; as an aid in the prevention of coccidiosis caused by E. necatrix, E. tenella, E. acervulina, E. brunetti, E. mivati, and E. maxima. ✱

Amendment published in Federal Register:
* May 27, 1971; 36 F.R. 9620

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TABLE 1—3 NITRO-/ HYDROXYPHE? SLARSONE ACID IN COMPLETE CHICKEN AND TURKEY FEED—Continued

Principal Ingredient	Grams per ton	Combined with—	Grams per ton	Limitations	Indications for use
1.15 3-Nitro-4-hydroxy-phenyl-arsonic acid.	22.7 (0.0025%)	Sulfadimeth-oxine+ ormetoprim	113.5 (0.0125%) 68.1 (0.0075%)	For broiler chickens; not for laying chickens; discontinue use of medicated feed 5 days before slaughter; as sole source of organic arsenic.	As an aid in the prevention of coccidiosis caused by all Eimeria species known to be pathogenic to chickens, namely, E. tenella, E. necatrix, E. acervulina, E. brunetti, E. mivati, and E. maxima and bacterial infections due to H. gallinarum (infectious coryza) and E. coli, growth promotion and feed efficiency; improving pigmentation.
1.16 3-Nitro-4-hydroxy-phenyl-arsonic acid.	45.4 (0.005%)	Amprolium....... + Ethopabate....... + Lincomycin.......	113.5 (0.0125%) 3.6 (0.0004%) 2-4	For floor-raised broiler chickens; not for laying chickens; as lincomycin hydrochloride monohydrate; withdraw 5 days before slaughter; as sole source of amprolium and organic arsenic.	For increase in rate of weight gain; improved feed efficiency and pigmentation; as an aid in the prevention of coccidiosis in floor-raised broiler chickens.
*1.17 3-Nitro-4-hydroxy-phenyl-arsonic acid.	45.4 (0.005%)	Nequinate........	18.16 (0.002%)	For broiler chickens only; feed continuously as sole ration throughout the starting period; withdraw 5 days before slaughter; as sole source of organic arsenic.	An aid in the prevention of coccidiosis caused by E. tenella, E. necatrix, E. acervulina, E. maxima, E. brunetti, and E. mivati in broiler chickens; growth promotion and feed efficiency; for improving pigmentation. *
a. 1.1, 1.3, 1.4....	22.7–45.4	Penicillin........	2.4–50	As procaine penicillin	Growth promotion and feed efficiency.
b. 1.1...........	22.7–45.4	......do...........	50–100	§ 121.256, table, item 3.1.	§ 121.256, table 1, item 3.1.
c. 1.1...........	22.7–45.4	Penicillin+ streptomycin.	14.4–50	As procaine penicillin and streptomycin sulfate.	Growth promotion and feed efficiency.
d. 1.1...........	22.7–45.4	Chlortetracycline	10–50	As chlortetracycline hydrochloride	Do.
e. 1.1...........	22.7–45.4	......do...........	50–200	§ 121.208, table 1, items 2, 6.	§ 121.208, table 1, items 2, 6.

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TABLE 1—3-NITRO-4-HYDROXYPHENYLARSONIC ACID IN COMPLETE CHICKEN AND TURKEY FEED—Continued

Principal Ingredient	Grams per ton	Combined with—	Grams per ton	Limitations	Indications for use
f. 1.1, 1.3, 1.4	22.7-45.4	Penicillin+ bacitracin.	3.6-50	As procaine penicillin plus bacitracin, bacitracin methylene disalicylate, manganese bacitracin, or zinc bacitracin.	Growth promotion and feed efficiency.
g. 1.1	22.7-45.4	......do............	50-100	§ 121.232, table 1, items 2.2, 5.2; § 121.233, table 1, items 2.2, 5.2; § 121.252, table 1, items 2.2, 5.2.	§ 121.232, table 1, items 22, 5.2; § 121.233, table 1, items 2.2, 5.2; § 121.252, table 1, items 2.2, 5.2.
h. 1.1	22.7-45.4	Bacitracin..........	50-100	§ 121.232, table 1, items 2.1, 5.1; § 121.233, table 1, items 2.1, 5.1; § 121.252, table 1, items 2.1, 5.1.	§ 121.232, table 1, items 2.1, 5.1; § 121.233, table 1, items 2.1, 5.1; § 121.252, table 1, items 2.1, 5.1.
i. 1.1, 1.3, 1.4, 1.8	22.7-45.4	......do............	4-50	As bacitracin, bacitracin methylene disalicylate, zinc bacitracin, or manganese bacitracin.	Growth promotion and feed efficiency.
j. 1.1	22.7-45.4	Oxytetracycline...	50-200	§ 121.251, table 1, item 6.	§ 121.251, table 1, item 6.
* k. 1.11	......	Bacitracin..........	4	For broiler chickens; as bacitracin methylene disalicylate.	Growth promotion and feed efficiency. *
2.1 3-Nitro-4-hydroxyphenylarsonic acid.	22.7-45.4 (0.0025%-0.005%)	....	....	For turkeys; withdraw 5 days before slaughter; as sole source of organic arsenic.	Growth promotion and feed efficiency; improving pigmentation.
2.2 3-Nitro-4-hydroxyphenylarsonic acid.	22.7-45.4 (0.0025%-0.005%)	Zoalene..........	113.5-170.3 (0.0125%-0.018%)	For turkeys grown for meat purposes only; withdraw 5 days before slaughter; as sole source of organic arsenic.	Growth promotion and feed efficiency; improving pigmentation; prevention and control of coccidiosis.
a. 2.1	22.7-45.4	Penicillin..........	2.4-50	As procaine penicillin.	Growth promotion and feed efficiency.
b. 2.1	22.7-45.4	......do............	50-100	§ 121.256, table 1, item 4.1.	§ 121.256, table 1, item 4.1.
c. 2.1	22.7-45.4	Penicillin+ streptomycin.	14.4-50	As procaine penicillin and streptomycin sulfate.	Growth promotion and feed efficiency.
d. 2.1	22.7-45.4	Chlortetracycline.	10-50	As chlortetracycline hydrochloride.	Do.
e. 2.1	22.7-45.4	......do............	50-200	§ 121.208, table 1, items 3, 7.	§ 121.208, table 1, items 3, 7.
f. 2.1	22.7-45.4	Penicillin+ bacitracin.	3.6-50	Not less than 0.6 gm. of penicillin nor less than 3.0 gm. of bacitracin; as procaine penicillin plus bacitracin, bacitracin methylene disalicylate, manganese bacitracin, or zinc bacitracin.	Growth promotion and feed efficiency.
g. 2.1	22.7-45.4	......do............	50-100	§ 121.256, table 1, item 4.2.	§ 121.256, table 1, item 4.2.
h. 2.1	22.7-45.4	Bacitracin..........	4-50	As bacitracin, bacitracin methylene disalicylate, manganese bacitracin, or zinc bacitracin.	Growth promotion and feed efficiency.
i. 2.1	22.7-45.4	......do............	50-100	§ 121.232, table 1, item 3.1; § 121.233, table 1, item 3.1; § 121.252, table 1, item 3.1.	§ 121.232, table 1, item 3.1; § 121.233, table 1, item 3.1; § 121.252, table 1, item 3.1.
j. 2.1	22.7-45.4	Oxytetracycline...	50-100	§ 121.251, table 1, item 3.	§ 121.251, table 1, item 3.
k. 2.1	22.7-45.4	Amprolium.......	113.5-227	§ 121.210, table 1, item 1.1.	§ 121.210, table 1, item 1.1.

(d) To assure safe use, the label and labeling of the additives, any combination of additives, and any feed additive supplement, feed additive concentrate, feed additive premix, or complete feed prepared therefrom shall bear, in addition to the other information required by the act, the following:

(1) The name of the additive or additives.

(2) A statement of the quantity or quantities contained therein.

(3) Adequate directions and warnings for use.

Exhibit 10

(§ 120.3)

(2) Where tolerances are established in terms of inorganic bromide residues only from use of organic bromide fumigants on raw agricultural commodities, such tolerances are sufficient to protect the public health and no additional concurrent tolerances for the organic pesticide chemicals from such use are necessary. This conclusion is based on evidence of the dissipation of the organic pesticide or its conversion to inorganic bromide residues in the food when ready to eat.

(d) (1) Where tolerances are established for both calcium cyanide and hydrogen cyanide on the same raw agricultural commodity, the total amount of such pesticides shall not yield more residue than that permitted by the larger of the two tolerances, calculated as hydrogen cyanide.

(2) Where tolerances are established for residues of both O,O-diethyl S-[2-(ethylthio)ethyl] phosphorodithioate and demeton (a mixture of O,O-diethyl O-(and S-)[2-(ethylthio)ethyl] phosphorothioates) on the same raw agricultural commodity, the total amount of such pesticides shall not yield more residue than that permitted by the larger of the two tolerances, calculated as demeton.

(3) Where tolerances are established for both terpene polychlorinates (chlorinated mixture of camphene, pinene, and related terpenes, containing 65-66 percent chlorine) and toxaphene (chlorinated camphene containing 67-69 percent chlorine) on the same raw agricultural commodities, the total amount of such pesticides shall not yield more residue than that permitted by the larger of the two tolerances, calculated as a chlorinated terpene of molecular weight 398.6 containing 67 percent chlorine.

* (4) Where a tolerance is established for more than one pesticide containing arsenic found in, or on a raw agricultural commodity, the total amount of such pesticide shall not exceed the highest established tolerance calculated as As_2O_3. *

(5) Where tolerances are established for more than one member of the class of dithiocarbamates listed in paragraph (e) (3) of this section on the same raw agricultural commodity, the total residue of such pesticides shall not exceed, that permitted by the highest tolerance established for any one member of the class, calculated as zinc ethylenebisdithiocarbamate.

(6) Where tolerances are established for residues of both S,S,S-tributyl phosphorotrithioate. All such arsenic... compounds and also... agricultural commodity, the total amount of

such pesticides shall not yield more residue than that permitted by the higher of the two tolerances, calculated as S,S,S-tributyl phosphorotrithioate.

(c) Except as noted in subparagraphs (1) and (2) of this paragraph, where residues from two or more chemicals in the same class are present in or on a raw agricultural commodity the tolerance for the total of such residues shall be the same as that for the chemical having the lowest numerical tolerance in this class, unless a higher tolerance level is specifically provided for the combined residues by a regulation in this part.

(1) Where residues from two or more chemicals in the same class are present in or on a raw agricultural commodity and there are available methods that permit quantitative determination of each residue, the quantity of combined residues that are within the tolerance may be determined as follows:

(i) Determine the quantity of each residue present.

(ii) Divide the quantity of each residue by the tolerance that would apply if it occurred alone, and multiply by 100 to determine the percentage of the permitted amount of residue present.

(iii) Add the percentages so obtained for all residues present.

(iv) The sum of the percentages shall not exceed 100 percent.

(2) Where residues from two or more chemicals in the same class are present in or on a raw agricultural commodity and there are available methods that permit quantitative determinations of one or more, but not all, of the residues, the amounts of such residues as may be determinable shall be deducted from the total amount of residues present and the remainder shall have the same tolerance as that for the chemical having the lowest numerical tolerance in that class. The quantity of combined residues that are within the tolerance may be determined as follows:

(i) Determine the quantity of each determinable residue present.

(ii) Deduct the amounts of such residues from the total amount of residues present and consider the remainder to have the same tolerance as that for the chemical having the lowest numerical tolerance in that class.

(iii) Divide the quantity of each determinable residue by the tolerance that would apply if it occurred alone and the quantity of the remaining residue by the tolerance for the chemical having the lowest numerical tolerance in this class and multiply by 100 to determine the percentage of the permitted amount of residue present.

Although the less toxic arsenicals have had a therapeutic use for over 2,000 years, the toxic nature of the soluble inorginic compounds has been known and exploited for much longer. Industrial applications for arsenic compounds have increased the total of the toxic experiences but it was not until the 20th century that the fundamental mechanisms of the action of arsenic were beginning to be brought to light. In the past half century, first stimulated by the interest in the mode of action of the organic arsenical drugs used in the treatment of syphilis then by the need to combat the possible use of offensive arsenical warfare agents by discovering effective antidotes, a great deal has come to be known about the action of arsenic on biological systems (Buchanan, 1962).

VI. A. Absorption - Systemic poisoning has been produced by the absorption of arsenic compounds from the lungs, the gastrointestinal tract, and across the skin.

VI. A.1. Oral Absorption - The degree of absorption from the gastrointestinal tract and the toxicity of the ingested arsenical is closely related to the solubility at the pH of the stomach and the intestinal tract. Arsenic sulfides, found in ores, are very insoluble and are not toxic. Elemental arsenic is considered by most authorities to be nonpoisonous and after ingestion, appears to pass through the alimentary tract largely unchanged, though it is possible that a small amount may be changed into the irritant trioxide (Buchanan, 1962).

Buchanan (1962) states that arsenic trioxide is absorbed across the gastro-intestinal tract and that absorption is more rapid if the oxide is in finely divided form. However, Harrison, et al. (1958), in comparing the toxicities of the crude arsenic trioxide and pure arsenic trioxide, found the pure compound to be more toxic than the crude form. The particle size distribution of the two samples indicated that the pure arsenic trioxide contained many more large particles than the crude white arsenic.

The absorption of the arsenates is probably similar to the corresponding phosphate compound but no quantitative information is available (Clarkson and Distefano, 1971).

VI. 2. Dermal Absorption - The percutaneous absorption of arsenicals resulting in systemic toxicity is generally not considered important although poisonings have been reported by this route. Arsenic may be absorbed through the skin when it is applied in ointments or lotions. The soluble arsenic compounds are readily absorbed from all mucous membranes, including the lung surfaces, at a rate and to an extent dependent upon the form in which they are ingested (Stewart and Stolman, 1960).

VI.3. Respiratory Absorption - Approximately 75 percent of inhaled arsenic trioxide is retained in the lungs (Clarkson and Distefano, 1971). Ciliary movement may remove inhaled arsenic from the bronchial passages and introduce them into the alimentary canal. Therefore, some of the effects noted from inhalation exposure may be derived from gastrointestinal absorption. Rozenshtein (1970) demonstrated that as little as 4 $\mu g/m^3$ of arsenic trioxide in the inspired air has untoward effects on the unconditioned reflexes and cholinesterase levels in rats. All levels of 1 ug/m^3 was shown to have no effect. Benko (1970) demonstrated systemic absorption in mice from the inhalation exposure to 180 $\mu g/m^3$ arsenic trioxide dust. Arsine, which is a gas, may readily be absorbed through the lungs and produces very toxic effects.

VI.B. Distribution - Utilizing radiolabeled arsenic, Lanz, et al. (1950), demonstrated that 95 to 99 percent of the arsenic of whole blood is combined with the globin of hemoglobin in the erythrocytes. This study was carried out in rats and confirms the findings of Hunter, et al. (1942). However, this does not hold true for other animals and humans (Hunter, et al., 1942). Almost all of the arsenic of serum is bound to the serum proteins (Stewart and Stollman, 1960).

After acute exposure arsenic is deposited in descending order in the liver, kidney, intestine, spleen, and lung (Clarkson and Distefano, 1971). Arsenic appears in the hair about two weeks after the first exposure where it is bound to the -SH linkage of keratin. Chronic exposure leads to accumulation in hair, bone, and skin. Arsenic may be found in high concentrations in the hair years after cessation of exposure and after most of the metal has been removed from the soft tissues (Clarkson and Distefano, 1971).

Apparently arsenic levels do not remain high in tissues after the cessation of arsenic intake. Inorganic arsenic fed to cows raised the arsenic levels of the liver and kidney during an 8 week feeding period, but 15 days after the last feeding the levels returned to normal (Peoples, 1962; 1964).

Arsenic fed in low levels (5 ppm) to mice failed to accumulate in the tissues. At high levels the arsenic content of tissues first increased then declined (Benko, 1968-70). Schroeder (1968) demonstrated that arsenic accumulated in the aortas of rats. In humans who had Salvarsan treatments, the liver levels of arsenic were found to be normal.

The estimates of the "normal" arsenic content of hair, nails, and urine have been made by various investigators and show a reasonable measure of agreement. Watrous and McCaughey (1945) have quoted a normal range of arsenic in the urine of 0.014 to 0.046 mg/l. Buchanan (1962) cites arsenic values found in human tissues and fluids by Smales and Pate as follows:

Urine	0.013	- 0.33 mg/l
Blood	0.09	- 0.50 mg/l
Hair	0.5	- 2.1 ppm
Fingernails	0.82	- 3.5 ppm
Toenails	0.52	- 5.6 ppm

Normal fasting serum levels of human males and females range from 3.5 to
7.2 ug of arsenic per 100 ml. From autopsy samples arsenic levels measured
in ug/100 g in kidney ranges from 2.6 to 3.7; liver 3.0 to 3.9; heart 2.4
to 3.7; brain 2.4 to 3.7; lung 1.8 to 2.9; and thigh muscle 3.1 to 5.8
(Kingsley and Schaffert, 1951).

Arsenic passes the blood-brain barrier only slowly. Brain levels are
among the lowest in the body. Arsenic in brain tissue, however, is retained
for longer periods than it is in other soft tissues and is associated with
the mesoglial mesenchyma, where it may cause degenerative changes (Clarkson
and Distefano, 1971).

VI. C. Metabolism and Excretion - There is evidence indicating pentavalent
arsenic is reduced in the tissues to the trivalent state. Ehrlich first
advanced this theory to explain the action of pentavalent arsonic acids
which are relatively nontoxic to trypanosomes in vitro but are active in vivo.
In 1923, Voegtlin, et al., demonstrated that although the organic pentavalent
compounds of arsenic were toxic in vivo, the time required for this toxic
action to appear was longer than in the case of trivalent compounds. This
latter theory may not be tenable due to the different mechanism of toxicity
of the two types of compounds.

Winkler (1962) found that arsenic is stored in tissues of rats in the pentavalent
form even when fed as trivalent arsenic. This indicates there may be an
oxidation of trivalent arsenic to the pentavalent state.

Overby and Frost (1962) and McChesney and Banks (1962) have demonstrated
that there is no cleavage of organically found arsenic in the body. The
reverse, the conversion of inorganic arsenic to organically bound arsenic
probably occurs.

Excretion occurs by all physiologic routes - feces, urine, sweat, and milk.
Some volatile arsenic may be exhaled from the lungs. Arsenic is also removed
from the body by the normal loss of hair and skin, especially in cases of
chronic poisoning. The urine and feces contain most of the excreted arsenic.
In general, the arsenite salts are lost mainly via the feces and the arsenates
via the urine. Arsenate excretion is more rapid than arsenite excretion and
probably occurs via the phosphate excretory mechanisms. Approximately 10
days are required to eliminate a single dose of arsenic from the body and
as much as 70 days are needed to eliminate the body burden after cessation
of repeated exposure (Sollman, 1957).

The arsenic in the urine is in the inorganic form if elemental arsenic has
been administered. About 10 to 15 percent of the arsenic found in the bile
is in the trivalent form. None of the arsenic is detected in the organic

form or as a complex or conjugated compound. Since the rate of excretion of arsenic is important in determining toxicity, it has been found that when various arsenicals are administered intravenously to rats the trivalent sodium arsenite was excreted less readily than the pentavalent arsenical (Schreiber and Brouwer, 1964). The rate of excretion of pentavalent arsenic was 41 to 64 percent, found predominantly in the urine. Only 9 to 24 percent of trivalent arsenic was excreted in the urine.

VI. D. <u>The Biochemical Basis for Toxicity</u> - Trivalent arsenic compounds, inorganic and organic, possess a high affinity of neighboring thiol (SH) groups. The reactions are of the following type:

$$R-As\,O \quad + \quad \begin{matrix} HS\!-\!\!-\!CH_2 \\ HS\!-\!\!-\!CH \\ HS\!-\!\!-\!CH_2 \end{matrix} \quad \longrightarrow \quad R\ As\!\!<\!\!\begin{matrix} S\!-\!\!-\!CH_2 \\ S\!-\!\!-\!CH \\ HO\!-\!\!-\!CH_2 \end{matrix} \quad + \quad H_2O$$

This reaction of arsenic with the essential components of enzyme systems is the basis for the toxic action of trivalent arsenic in the body. Experiments with arsenical compounds have shown them to have a marked effect on a wide range of enzyme systems and the pyruvate oxidase system, e.g. that of brain cells, in particular, is greatly inhibited by low concentrations of trivalent arsenic compounds (Peters, Sinclair, and Thomspon, 1946).

An important means by which trivalent arsenic exerts its poisonous effects is by the inhibition of pyruvate oxidation which is an essential stage of the mechanism of energy transformation in the living cell. Strong support for this view is provided by the finding an increase in the blood level of pyruvate in cases of experimental poisoning. This has also been observed in man (Buchanan, 1962).

A great many other enzyme systems in the body are also affected by arsenic in this manner. D-amino acid oxidase, 2-glutamic acid oxidase, monoamine oxidase and transaminase are all inhibited by trivalent arsenic and are reactivated by glutathione. Urease is highly sensitive to trivalent arsenic as are also choline oxidase, choline dehydrogenase and glucose oxidase. All of these enzymes possess thiol groups as a common factor in this inactivation. On the other hand, enzymes not possessing thiol groups essential to their activity, are not inactivated by trivalent arsenic (Buchanan, 1962).

Unlike trivalent arsenic, the toxicity of pentavalent arsenic is not due to its binding to thiol (SH) groups. Therefore, the arsenate ion does not affect enzyme systems in the way the arsenite ion does (Johnstone, 1963).

Rather, the unstable arsenyl ions may replace the more stable phosphoryl ions in a number of systems resulting in the uncoupling of oxidative phosphorylation. This substitution has been shown to take place in vitro. Under certain conditions, arsenic can substitute for nitrogen in choline and lecithin. It may be seen, therefore, that the toxicity of pentavalent arsenic does not necessarily depend on its reduction to trivalent arsenic in the body as postulated by Ehrlich.

VI. E. <u>Toxicity to Laboratory Animals</u> - The absorption, distribution, metabolism, excretion, and the action of arsenic at cellular and subcellular levels has previously been discussed. This section will deal with the toxic effects of arsenic on the intact animal.

VI. E. 1. <u>Acute Toxicity</u> - In general, the inorganic arsenicals are more toxic than the organic compounds. Of the inorganic arsenic compounds, the trivalent compounds are more toxic than the pentavalent compounds.

Frost (1967) reported that at their respective LD_{50} levels of 700, 16, and 0.8 mg/kg, tryparsamide, benzenearsonic acid, and benzenearsenoxide gave similar levels of arsenic in rabbit tissues. This has been confirmed in other species with other arsenicals. It appears that target enzymes, although farm more susceptible to trivalent than to pentavalent arsenicals, bind a similar level of arsenic at the point of death.

The first and principal symptoms of acute arsenic toxicity are those of inflammation of the digestive tract. Autopsy rarely shows extensive corrosion, and the gastroenteritis may be obtained by intravenous or sub-cutaneous administration. This does not exclude all local action, since some arsenic is excreted into the alimentary canal, but the quantity is not sufficient to account for the symptoms. The inflammation is due to the systemic action on the capillaries, which is strongest in the intestines, regardless of the route of arsenic administration. Capillary paralysis results in the production of exudation into the connective tissue. This raises the epithelium and causes it to be thrown off in shreds or false membranes. The exudation is then poured into the lumen of the intestine and largely coagulates. This distention, as well as the circulatory changes, causes increased peristalsis and watery diarrhea. The vessels of the kidney participate in the capillary dilatation. The glomercular capillaries are swollen and fill the capsule; the urine is albuminous and scanty. Nephritis results.

Table 1 lists the acute LD_{50} of various arsenic compounds.

Table 1. Acute Oral Toxicities of Arsenical Pesticides in Rats[*]

Compound	LD_{50} (mg/kg)
Inorganic	
Arsenic trioxide	138
Arsenic pentoxide	8
Calcium arsenate	10-100
Paris green (copper acetoarsenite)	20-100
Lead arsenate	10-100
Sodium arsenite	10- 50
Organic	
Cacodylic acid	1350
Methanearsonic acids:	
Calcium hydrogen salt (CMS)	4000
Ammonium salt (AMA)	749
Disodium salt (DSMA)	2800
Monoammonium salt (MAMA)	750
Monosodium salt (MSMA)	1800

[*]Gaines (personal communication)

VI. E. 2. Subacute Toxicity - Von Glahn, et al. (1938) reviewed the
subacute toxicity studies of arsenicals. They state that the earliest
reported experiment was that of Ziegler and Obolonsky in 1888. In this
experiment, small doses of arsenic were administered subcutaneously and
orally to dogs and rabbits. In the rabbits, fatty changes of the liver
cells in the central part of the lobule was observed after a few days; at
the end of 9 days, shrinking and hyaline degeneration of individual liver
cells, with fragmentation of the nuclei, were present. After 14 days, in
addition to the fat droplets, there were necroses, the necrotic liver
cells having a spongy appearance. In the livers of the rabbits surviving
for 16 days, small groups of swollen liver cells without nuclei, an
increase of connective tissue and proliferation of bile ducts were found.
One of the rabbits survived for 20 days. In addition to the alterations
described, many multinucleated cells were present in the sinusoids.
Another rabbit remained alive for 25 days; degeneration of single hepatic
cells and numerous giant cells were seen. The only hepatic lesion produced
in dogs following the administration of arsenic in doses from 0.01 to 0.1
gm over a period of 90 days was vascular degeneration of liver cells and
fatty degeneration of liver cells and fatty infiltration. The fat was not

abundant as in the liver of rabbits. Podwyssotzky, in the same year, reported somewhat similar results in guinea pigs after subcutaneous injection of sodium arsenite in amounts from 0.005 to 0.1 gm. Some of the animals lived but a short time - from 3 to 6 days. Necrotic areas were found in the livers, the connective tissues was increased, and bile ducts were proliferating. Mitoses were present in fibroblasts and the epithelium of bile ducts. Later the masses of necrotic liver cells were sharply delimited, as though sequestrated, and were invaded by newly formed bile ducts and connective tissue. In the animals whose period of survival was from 15 to 25 days, the necrotic liver cells had disappeared for the most part and were replaced by recently formed liver cells and scar tissue.

Wolkow (cited by Von Glahn, et al. 1938) administered a solution of potassium arsenite by subcutaneous injection to eighteen rabbits. Doses of from 0.003 to 0.003 to 0.005 gm of arsenious acid were well tolerated; following large doses of from 0.1 to 0.02 gm, the animals lived only a few days. Nine of the animals were put to death at varying intervals, the longest period being 36 days. The other nine rabbits were allowed to succumb from the effects of the arsenic. In this group the longest period of survival after the beginning of the experiment was 60 days.

The most constant finding was fatty degeneration of the liver cells and Kupffer cells, usually in all parts of the lobule. Areas of necrosis of liver cells were found as early as the second day in five of the animals given the larger doses. The necroses were situated most often at the periphery of the lobule; the necrotic cells were frequently swollen, the cytoplasm was clear and transparent, and their nuclei stained faintly and were scarcely visible. Leukocytes had collected at the periphery of each area of necrosis and had also penetrated between the necrotic cells. These foci of necrosis were sharply defined from the surrounding cells. The stroma remained in the necrotic areas; fine fat droplets were not conspicuous in the necrotic cells. Mitoses were observed in a few of the liver cells, and in three of the animals multinucleated liver cells were found. Inflammatory reactions in the bile ducts were moderately frequent. The connective tissue of the portal areas was increased in three animals, and bile ducts were proliferated.

Stoeber (cited by Von Glahn, et al., 1938) injected sodium arsinite intravenously into rabbits. Some of the animals lived for 7-1/2 months. In the animals in which the poisoning was subacute, there were observed swelling, hemosiderosis of the Kupffer cells and also phagocytosis of erythrocytes by these cells. More striking were enlarged pigment-containing phagocytes at the periphery of the lobule and in the portal areas. The pigment held within the phagocytes was in part iron containing. The portal areas were widened by fibroblasts and fibrocytes, and bile ducts were proliferating. Small areas of necrosis involving a few liver cells

were found scattered throughout the lobule but were more frequent close to the efferent vein and portal area. The Kupffer cells were well preserved in these areas. After from 3 to 6 weeks, the liver cell layer bordering the portal area was irregular. The epithelial cells of the precapillary bile ducts contained fine droplets of fat, and these ducts were surrounded by sparse numbers of leukocytes.

VI. E. 3. <u>Chronic Toxicity</u> - Sollmann (1921) studied the effects of chronically administered daily doses of arsenic trioxide on albino rats. The doses ranged, in mg/kg/day from 0.0000475 to 0.0049, while the duration of the studies ranged from 9 to 24 weeks.

It was found that when arsenic trioxide was administered to the rats over this time period, a distinct retardation of growth and checking of appetite resulted from small doses; i.e., 0.00005 to 0.0005 mg/kg; and a more marked loss of weight with doses of 0.0015 to 0.005 mg/kg. No mortality was attributable to arsenic trioxide in this experiment.

Utilizing dogs, Joachimoglu (1916) found that more arsenic was absorbed from the gastrointestinal tract when increasing doses were given. One dog, for example, received daily doses of arsenic which were increased weekly from 10 mg to 400 mg. When the dog received 40 mg of arsenic trioxide, it excreted 4.58 mg arsenic daily in his urine. When the dose was increased to 400 mg arsenic daily, it excreted 19.8 mg in the urine. However, these figures show that the percent of urinary excretion decreases with increasing oral doses and more is excreted in the feces. On microscopic examination, the gastrointestinal tract was either normal or showed degenerative changes. The amount of arsenic absorbed varied greatly with the animals. Apparently decreased absorption of arsenic by the gastrointestinal tract is not responsible for the tolerance to arsenic.

Von Glahn, <u>et al</u>. (1938), in studying the effects of various diets on the liver of rabbits, fed ten animals a diet of cabbage only. Pigment was increased in the liver cells of most of the animals, and in many of them large phagocytes containing pigment were present in the sinusoids. The experiment was repeated three times, but similar changes were not produced. Thinking that the cabbage fed to the first series of rabbits may have contained an arsenical pesticide, the authors attempts to repeat their results by feeding low levels of copper arsenate, sodium arsenate, or lead arsenate. The arsenic level in the diets was adjusted to the arsenic levels found in their analysis of cabbage (4.32 mg/kg). Copper arsenate was administered at levels of 5.6 mg (1.4 mg arsenic) and 9.3 mg (2.33 mg arsenic); sodium arsenate was administered at 6.8 mg (.5 mg arsenic); lead arsenate was administered at 7.2 mg (1.4 mg arsenic) and 12 mg (2.33 mg arsenic).

Of the forty-six rabbits fed hay and oats and given a daily dose of one
of the arsenates only four-9 percent-failed to acquire cirrhosis. Two
of these four lived only a short time. That the arsenate did, however,
produce damage in the livers of three of these four animals was indicated
by the presence of necrosis. The analyses for the arsenic contents of
the livers of the rabbits that received the arsenates show clearly that
the extent of the damage done was directly related to the arsenic present.
It was determined that arsenic alone was responsible and that the lead
and copper did not play any part in the production of the lesions.

Morris, et al. (1938) studied the storage of arsenic when low levels of
arsenic were fed as either calcium arsenate or arsenic trioxide. In this
study 215 mg of arsenic per kilogram of body weight, as either arsenic
trioxide or calcium arsenate, was added to the control diet of albino
rats. The average number of days on the diet was 54 for those on calcium
arsenate and 42 for those on arsenic trioxide. In both the calcium
arsenate and arsenic trioxide groups, large quantities of arsenic were
stored in the various organs. The liver and kidneys stored by far the
largest amount per gram of dry weight. The livers of the experimental
animals of the calcium arsenate series were 41 percent larger than those
of the controls, while the brains were 8 percent smaller. Much larger
amounts of arsenic were stored in animals receiving calcium arsenate than
in those receiving arsenic trioxide when fed at the same level.

In a study of the effect of several abnormal trace elements (germanium, tin,
and arsenic) on rats, Schroeder, et al. (1968) fed albino rats 5 μg/ml of
sodium arsenite in their drinking water for over two years. Arsenic, in
this experiment, was not found to be carcinogenic. No arsenic keratoses
appeared, and this element was not toxic in terms of growth and life span.
In evaluating the differences between the test and control animals, the
following criteria were considered: limited growth, lessened survival and
longevity, elevated serum cholesterol and glucose levels, excess proteinuria,
excess number of tumors, fatty changes in the liver and renal lesions. In
this light, femalerats fed arsenic showed no significant differences from
the controls; male rats and elevated serum cholesterol levels only. Glucose
levels, however, were lower than; the controls. These very few changes
occurred in the presence of a remarkable accumulation of arsenic in the
tissues, demonstrating that arsenite, given at this level is not toxic to
rats.

Calvery, et al. (1938) studied the chronic effects on dogs of feeding diets
containing lead acetate, lead arsenate, and arsenic trioxide. The basic
problem in this study was to determine the toxicity of lead and arsenic
when used as sprays and spray residues. Dogs were used in the study. Lead
acetate, lead arsenate or arsenic trioxide was added to the basic diet at
the following levels: lead acetate, 12.8, 38.4, and 64 mg of lead/kg diet;
lead arsenate, 64 mg of lead/kg of diet; arsenic trioxide, 28.8 and 107.5
mg arsenic/kg of diet.

It was found that the storage and retention of arsenic by the dogs when
fed arsenic trioxide and lead arsenate was much less than that of the
rats fed arsenic trioxide and calcium arsenate. The very low storage
was either due to failure of absorption or rapid elimination, and explains
the low susceptibility of dogs to chronic arsenic toxicity. At the levels
used in the experiment, there was no difference between the toxicity of
lead acetate and lead arsenate. However, earlier experiments in rats at
higher levels showed that lead arsenate was far more toxic.

Fairhall and Miller (1941) studied the relative toxicity of the molecular
components of lead arsenate. Albino rats were used in the experiment.
The diets were uniform except that lead arsenate was added to the diet
of one group (10 mg/day), an equivalent amount of lead as lead arsenate
was added to the diet of the second, and an amount of arsenate equivalent
to that of the lead arsenate group was added as calcium arsenate to the
third group. The animals remained on the diets for two years.

Based upon the mortality rates over the 2-year period, the order of
toxicity of the three substances at equivalent levels of intake was as
follows: calcium arsenate was most toxic, lead arsenate less, and lead
carbonate least toxic.

Pathologic studies showed significant changes in the kidney and spleen.
The large hyperregenerative cells with large vesicular nuclei and
cytoplasmic brown pigment granules in the renal convoluted tubules were
most frequent in rats fed lead carbonate, less with lead arsenate, and
least with calcium arsenate. The large oxyphil intranuclear inclusions
appeared in the same order in animals fed lead carbonate and lead arsenate
but were absent in the calcium arsenate group. These changes are typical
of lead toxicity.

Splenic hemosiderosis, considered indicative of blood destruction, occurred
in the greater amounts in rats fed calcium arsenate and lead arsenate than
in those fed lead carbonate. Splenic myelosis was distinctly reduced in
the lead carbonate series but not appreciably diminished in the calcium
arsenate and lead arsenate series or in the control groups. If splenic
hemosiderosis is accepted as signifying blood destruction and splenic
myelosis is accepted as a sign of blood formation, it appears that the
action of lead carbonate on the spleen in rats may be both hypoplastic and
hemolytic while that of the arsenate radical is primarily hemolytic.

The distribution of lead and arsenic in the tissues of the 1-and 2-year
groups indicated less storage of lead than of arsenic in the soft tissues
of animals fed lead arsenate. The kidney content of arsenic in the calcium
arsenate group was distinctly greater than that of the lead arsenate group,
both in the 1-year and 2-year animals.

It would appear that the arsenate radical either decreases the absorption or increases the excretion of lead.

VI. E. 4. <u>Teratogenicity Studies</u> – Ferm and Carpenter studied the teratogenic effects of sodium arsenate in the golden hamster. Virgin female golden hamsters were mated with male hamsters. On the 8th day of gestation the pregnant hamsters were injected into the lingual vein with 5 mg/kg or 20 mg/kg of sodium arsenate in distilled water. Exencephaly, a specific malformation in the heads of the offsprings was produced. The dosage level appeared to be critical since 5 mg/kg induced no malformations while a dose of 40 mg/kg kills all embryos <u>in utero</u>. The exencephalic lesion was markedly consistent and specific and often within a single litter a majority of the survivors showed a strikingly similar defect. Secondary effects of this nervous system lesion included occasional bulging of the eyeballs and a relative protrusion of the tongue and mandible similar to that seen in hypervitaminosis-A-treated animals. No other gross external malformations were noted in other organ systems. The maternal animals tolerated all dose levels of arsenic very well. Maternal weight gain was normal. Histological examination of the placental membranes revealed no abnormality.

Fern and Carpenter (1971) made a more complete study of the teratogenic effects of sodium arsenate on the golden hamster in an attempt to determine the possible mechanism of arsenic as a teratogen.

Virgin female hamsters were bred to males during the night and the day following the evening of breeding was considered the first day of gestation. On the eighth day of gestation, the pregnant females were anesthetized and injected intravenously with dibasic sodium arsenate. The dose varied between 15 and 25 mg/kg of body weight. The time of injection on this day was recorded, the day being divided into 6 hour periods. The female animals were killed on the morning of the 15th day of gestation.

Dibasic sodium arsenate had a marked effect both upon resorption and malformation rates in the hamster. The rates increased with increasing doses. The observation that the resorption rate decreases in those litters which are treated at later stages of development may be best understood in that early in the 8th day of gestation, the hamster embryo develops very rapidly, progressing from primitive streak stage to an embryo with a completely closed neural tube and a beating heart within a 24-hour period. It is during this period that the embryo is most susceptible to lethal and teratogenic influences. Thereafter, this susceptibility decreases with time. The time of injection had a profound influence on the teratogenic profile. The overall malformation rate remained constant over the 12-hour period (8th day) but the frequency with which specific malformations occurred varied considerably with time. There was marked increase in rib

malformations in the last six hour period of the 8th day. However, the frequency of all other malformations (genitourinary, anencephaly, and exencephalia) decreased through the 12-hour time span. Malformations of the cranium were the most common developmental anomaly found.

VI. E. 5. Cancer Studies - Attempts to demonstrate cancer in experimental animals with arsenic have not been successful. Frost (1967) contends that no carcinogenesis from arsenic in animals has been reported. However, Kraybill and Shimbin (1964), in a review, indicated that hepatomas had been induced in trout from the feeding of carbarsone in the diet. The control group had zero hepatomas in a group of 300, whereas the carbarsone treated group had 5 hepatomas in 50 exposed.

VI. F. Toxicity to Humans - The symptoms and effects of acute and chronic arsenical poisoning in man are quite similar to those found in experimental animals. Systemically arsenicals relax the capillaries and increase their permeability, thus stimulating inflammation. This change is most conspicuous in the splanchnic area. In acute poisoning it results in violent gastroenteritis. The dilation of capillaries introduces change in the circulation which cause secondary disturbances in the function of more remote organs, particularly in the nervous system. Fatty degeneration of the cells is seen, especially in glands and muscles, with other disturbances of nutrition and metabolism, particularly in chronic poisoning. There may also be direct paralysis of the heart (Sollmann, 1964).

VI. F. 1. Acute Poisoning - The mortality in clinically acute arsenical poisoning in people is high, about 50 to 75 percent. The fatal dose varies, especially with the solubility of the preparation. Of the trioxide, 5 to 50 mg are toxic; 0.1 to 0.3 gm is usually fatal, but recovery may occur after much larger quantities (Sollmann, 1957). The arsenites are more soluble and are more rapidly toxic than the corresponding arsenates.

Even when administered in comparatively large doses, there is a characteristic delay ranging from half an hour to several hours in the onset of symptoms following ingestion of trivalent arsenic. The first symptom is frequently a feeling of throat constriction, followed by difficulty in swallowing and epigastric discomfort. Thereafter, violent abdominal pain accompanied by vomiting and a watery diarrhea occurs. Blood may be present in the stools or vomitus. These symptoms are accompanied by others of systemic upset, including a sensation of giddiness, muscular cramps, possibly the effect of the severe loss of fluid in the watery stools and headache. In those dying from the acute effects, shock, manifesting itself by a cold clammy skin, feeble pulse and weak sighing respirations, supervene, and death may be preceded by terminal convulsions. In these cases, death usually takes place within 24 hours. In less acute cases, the victim may survive for two to four days (Buchanan, 1962).

The number of reported cases of arsenical poisoning in the United States in 1969 is shown in Table 2. It should be noted that, although sodium arsenite and arsenic trioxide accounted for about one-fourth of the poisonings, they accounted for all of the deaths resulting from identified arsenical compounds.

Table 2. Reported Cases of Arsenical Poisoning, U.S.A., 1969[*]

Arsenical	Reported Cases	Reported Deaths
Lead arsenate	83	0
Sodium arsenate	79	0
Sodium arsenite	38	5
Arsenic (unspecified)	34	1
Arsenic trioxide	23	2
Calcium arsenate	7	0
Disodium methyl arsenate	5	0
Paris green	2	0

[*]Poison Control Center Statistics, National Clearing House for Poison Control Centers, FDA, DHEW.

A number of cases of acute poisonings are summarized with the most pre-valent symptoms of poisoning and also some unusual findings given.

Barnhart and Weiderkopf (1961) describe a patient who ingested a large quantity of an unspecified arsenical insecticide. His stomach was pumped 45 minutes later. Nevertheless, the patient developed a neuropathy with pain and impaired function of the hands and feet and full recovery was incomplete 2 years after the initial poisoning.

Capellini, et al. (1955) reported 34 cases of lead arsenate poisoning in workers producing insecticides. The concentration of lead and arsenic in the workroom air was from 8 to 11 mg/l. The average length of exposure varied from 2 to 6 months. The symptomology of lead arsenate poisoning was quite varied since signs of both lead and arsenic intoxication occurred.

Barry and Herndon (1962) found ECG changes in 3 patients that had taken arsenic trioxide in an attempt to commit suicide. These changes disappeared within 20 days in the two patients that recovered. Similar ECG changes were reported by Glazener, et al. (1968).

Sodium arsenate in the form of "Ant Buttons" was ingested by two children. Both recovered after acute symptoms of poisoning. The report states that "Ant Buttons" is a trade-name for an insecticide which utilize crown caps as containers (Jacobiziner and Raybin, 1961). A similar case was reported by Jenkins (1965). The registration for this product has been cancelled.

Because of the increasing incidence of cases of arsenic poisonings, arsenic insecticides were outlawed in Germany in 1942. Arsenical insecticides are still in use in Italy and France.

VI. F. 2. <u>Chronic Poisoning</u> - The symptoms of chronic arsenical poisoning may be divided into three phases of appearance (Cushny, 1949, cited in Buchanan, 1962).

In the first phase, the victim complains of weakness, loss of appetite, some nausea and occasional vomiting. There may be a sense of heaviness in the stomach and some diarrhea.

In the second stage of chronic poisoning, conjunctivites and a catarrhal state of the exposed mucous membranes of the nose, larynx and respiratory passages are common. The patient presents himself with symptoms of coryza, hoarseness and mild tracheitis or bronchitis. These symptoms are not uncommon in those exposed to arsenical dust in the course of their occupation and in such circumstances, they might be confused as symptoms resulting from irritation from local contact rather than effects of chronic systemic poisoning. Perforation of the nasal septum is a common finding in such individuals. Skin manifestations are common at this stage of poisoning. These may consist chiefly of eczematoid features of varying degrees of severity but vesicular lesions tend to predominate. Melanosis of the skin is a common finding following many years use of arsenic medicinally or contact with arsenical dust. This is an indication of systemic absorption of arsenic and not the result of local action.

The third stage of poisoning is marked by the onset of the manifestations of peripheral neuritis. Initially, the neuritis affects mainly the hands and feet and is patchy elsewhere and is sensory in character. Motor paralysis does not normally appear except in the more severe cases when the first muscles to be affected are generally the extensor muscles of the toes, then the peronei muscles.

Improvement may be expected on withdrawal from further exposure to arsenic, but is often very slow and may be incomplete, especially where motor paralyses have appeared and the muscles have given a reaction of degeneration.

A few cases of chronic arsenical poisoning will be summarized. One of the most unusual cases of contamination of food products occurred at Lancashire, Straffordshire, England in 1900 in which several thousand

persons became ill and about 70 persons died from drinking contaminated
beer. The beer contained as much as 15 ppm arsenic and the glucose used
in the fermentation contained about 400 ppm arsenic. The ultimate source
of the contamination was found to be in the sulfuric acid used in prepara-
tion of the sugar. The sulfuric acid which contained about 1.4 percent
arsenous acid was manufactured from pyrites containing arsenic impurities.

Smelter operations have commonly been associated with adverse effects
from arsenic exposure. Such a situation was reported in this country
in 1962 when a gold mine and smelter was reopened and the emission
control equipment was inadequate to control atmospheric pollution from
SO_2 and As_2O_2 (Birmingham et al., 1965). In this case, air levels taken
at the plant showed 60 to 13,000 micrograms per cubic meter of arsenic.

A study was made of 40 school children in the area. Out of these students,
32 had dermatosis associated with arsenic cutaneous exposure. The systemic
arsenic poisoning was discounted when it was proved to be a contact
dermatitis. One interesting aspect of this environmental exposure is that
children who were bussed to a high school in a distant town did not have
the continuous exposure of the 40 children in the local elementary school
had no dermatitis. As to the children showing dermatitis, the skin
irritation was in the folds of skin and where the skin was moist. In a
few cases, the conjunctivae and nasal mucosae were irritated. There were
no cases of keratoses, epitheliomas, or melanodermas present. Among the
refinery workers, there were typical symptoms of arsenic exposure.

A similar air pollution episode was recorded at a copper mine in northern
Chile (Oyanguren and Perez, 1966). The air levels of arsenic were quite
high. In a survey of 124 workers, the symptoms of arsenic exposure were
melanosis - 7.25 percent, arsenical dermatitis - 5.65 percent, and
perforation of the nasal septum - 1.65 percent. There were no cutaneous
manifestations encountered among a control group or among members of the
mining community.

Heyman, et al. (1956) reviewed 41 cases of peripheral neuropathy caused by
arsenical intoxication. All of the patients were from North Carolina where
arsenical dusts and sprays are extensively employed as pesticides. Seven
of the victims could relate the onset of nausea and vomiting with the use
of arsenical pesticides on tobacco. Fourteen others also were employed
around crops utilizing arsenical pesticides. Twenty-two patients in the
study treated with BAL failed to show any dramatic improvement on an
accelerated recovery of sensory and motor function.

Micks, et al. (1956) review four cases of chronic arsenical poisoning in
farmers resulting from the use of arsenic containing pesticides on crops.

They state that the intermittent natur of the exposures, which occurred during a period of years, provided optimum conditions for chronic poisoning.

The most prominent symptom exhibited was paralysis of the legs and hands, which occurred in 3 of the patients. The paralysis began in the feet and involved the hands shortly thereafter. BAL in addition to vitamin therapy and other symptomatic treatment. By this time, however, the arsenic had already produced marked pathological changes which were irreversible. Since all of the patients were farmers, the occupational hazards associated with arsenical insecticides were pointed out as well as the characteristic symptoms of chronic arsenic poisoning.

In a study conducted by the U.S. Public Health Service, Neal et al. (1941) failed to reveal any positive association between lead and arsenic exposure and certain adverse effects which might have been anticipated from such exposure by orchard workers applying lead arsenate. However, Farner, et al. (1949) in a four month medical study on a group of Mexican Nationals employed in Washington State's orchard industry during 1945, established a definite health hazard from exposure to lead arsenate. An increasing incidence of lead intoxication as the season progressed was demonstrated.

VI. F. 3. Cancer - There is considerable confusion in the literature about the role of arsenicals in carcinogenesis or in the development of cancer. The earliest published claim of arsenic cancer was made by Paris (1820) in which he reported occasional cases of cancer of the scrotum in copper smelters. Huchinson (1887) was the first to report skin cancer following prolonged internal administration of arsenical preparation. Neubauer (1947) reported a collection of 143 published cases of arsenic cancer including a number of workers exposed to pesticides. It appears that skin cancer resulting from systemic arsenic poisoning is first manifested in non-malignant keratosis (on palms of hands and soles of feet) and eventuates into a neoplasm.

Snegireff and Lombard (1951) studied the records of two industrial plants and found that where workers in one plant were exposed to arsenic, 18 of 146 deaths (12.3 percent) were caused by cancer. In another plant where workers were not exposed to arsenic, 12 of 109 deaths (11.0 percent) were caused by cancer. They concluded that these were not significantly different.

In another study Pinto and Bennett (1963) compared mortality and cancer rates for the years 1946-1960 of 38 copper smelting plant workers who were exposed to arsenic with 191 workers not exposed to arsenic. The percentage of deaths due to cancer in the arsenic exposed workers was 15.8 percent and 19.4 percent in those not exposed to arsenic. The fact that the workers were

exposed to arsenic was confirmed by urinalysis. The mean urine values of arsenic for the exposed workers was 0.82 mg/l and for the non-exposed workers 0.13 mg/l. Cancer death rates for men of similar age ranges for the whole state was 15.9 percent, virtually the same rate as for the arsenic exposed group.

Neal, et al. (1941) did not observe any increase in cancer among the 1200 people studied in the Wenatchee, Washington area during extensive use of lead arsenate.

On the other hand, Braun (1958) and Roth (1956) reported what they considered an unusually high incidence of internal cancers including malignant tumors of the liver and lungs. These were apparently always preceded by benign keratosis of the skin. It appears that the arsenic exposure was directly connected with the use of arsenical pesticides as well as the consumption of wine made from grapes contaminated with arsenic. In a brief review of arsenic cancer, Hueper (1966) concluded there is abundant and reliable evidence that arsenic is a human carcinogen.

CHAPTER VI

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ARSENIC TOXICOLOGY

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Supplemental Information For
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Agency, March 17, 1972.

During a recent meeting relative to the status of the Special Pesticide Review Group's Arsenic Pesticides Report, several items of essential information were indicated. Those attending the meeting with Mr. Charles Fabricant were: Mr. Harold Alford, Dr. H. E. Fairchild, Dr. O. G. Fitzhugh, Mr. L. E. Miller, and Dr. W. M. Upholt.

This supplemental information report presents the added material developed to date. This supplement discusses the following subjects in the order given: (1) significant arsenical pesticide production history; (2) basic producers of arsenical pesticides; (3) export-import data for arsenical pesticides; (4) pesticide use patterns and history of use in the United States—arsenical pesticides; (5) comparative use costs of arsenical pesticides and the registered alternative pesticides; and, (6) Environmental Protection Agency registrants of arsenical pesticides.

PRODUCTION HISTORY

Calcium Arsenate and Lead Arsenate

Table I of this report gives the production records for calcium arsenate and lead arsenate during the period of 1950 through 1970. These production data go back to the period when DDT and other more recent chlorinated hydrocarbon pesticides were still in the development stage.

Note (Table I) that the production of calcium arsenate once was well in excess of forty million pounds. Prominent uses of this pesticide were on cotton and vegetables. Much of the recent production is needed for baits to control snails, slugs and other pests of crops in the West.

Lead arsenate was the principal insecticide used on fruits prior to the development of DDT. Note the continued decline in use of lead arsenate from 1950 to the mid-1960's. Recently, entomologists in several states, especially in the fruit growing areas of the East, have encouraged a return to the use of lead arsenate for integrated spray programs. Further explanation of this subject appears in Chapter I of the Special Pesticide Review Group's Arsenic Report.

Methanearsonate Herbicides

Production data for the methanearsonate herbicides (MSMA, DSMA, AMA) only became publicly available in 1970. The United States Tariff Commission has reported 30,454,000 pounds were produced in 1970. More details on production of this class of pesticides will be found on page 95 of the Special Pesticide Review Group's Arsenic Report. Principal uses of the methanearsonate herbicides are in cotton and for industrial weed control, especially pests such as johnsongrass.

Table I. 1/ Annual Production for Calcium Arsenate and Lead
and Lead Arsenate in the United States, 1950-1970

	Calcium Arsenate (1,000 pounds)	Lead Arsenate (1,000 pounds)
1950	45,348	39,434
1951	40,900	25,416
1952	7,634	14,286
1953	7,212	14,196
1954	2,758	15,620
1955	3,770	14,776
1956	27,106	11,756
1957	19,478	11,920
1958	10,432	14,938
1959	6,424	12,904
1960	6,590	10,062
1961	7,944	10,446
1962	4,660	9,930
1963	3,310	7,842
1964	6,958	9,258
1965	4,192	7,098
1966	2,890	7,328
1967	2,008	5,952
1968	3,398	9,016
1969	1,418	9,142
1970*	3,059	4,185

*Preliminary and subject to revision
1/ Taken from "the Pesticide Reviews," Agricultural Stabilization
and Conservation Service, United States Department of Agriculture,
Washington, D.C. 1950-1970.

<u>Sodium Arsenite and Miscellaneous Arsenicals</u>

Following are the available data on sodium arsenite as a pesticide in the United States.

Stocks of All Manufacturers and Formulators of
    Sodium Arsenite

<u>Year</u>	<u>1,000</u> <u>Pounds</u>
1962	2,809
1963	2,680

A sodium arsenite report in 1966 from the United States Department of Agriculture stated "usage in agriculture is declining because of the hazard from run-off and from the attraction of the salty taste to livestock. Some is applied to kill off potato foliage before harvest; small quantities are used as an algaecide in farm ponds." (U.S.D.A. The Pesticide Review, 1966. 33 pp. October 1966).

Another compilation of data indicating a decline of inorganic arsenic herbicidal preparations between 1958 and 1963 follows: *

Products	1958		1963	
	Quantity 1,000 pounds	Value 1,000 dollars	Quantity 1,000 pounds	Value 1,000 dollars
Arsenical preparations	46,681	2,045	24,959	2,326

*U.S.D.A. the Pesticide Review, 1966. 33pp. October 1966.

There was a brief report in 1968 (U.S.D.A., the Pesticide Review, 1968) that arsenic trioxide was in short supply in late 1966 and most of 1967. The short supply of arsenic trioxide was due to a strike in the copper industry and increased demand for production of organic arsenical herbicides (such as MSMA and DSMA).

The United States Department of Agriculture has reported (U.S.D.A. the Pesticide Review, 1969) as follows "usage of inorganic arsenical pesticides has been declining steadily in recent years due to replacement with more efficient organic pesticides."

Lead Arsenate

Following are the basic producers of lead arsenate:

Allied Chemical Corporation
Agricultural Division
40 Rector Street
New York, New York 10006

Chevron Chemical Company
Ortho Division
200 Bush Street
San Francisco, California 94120

FMC Corporation
Niagara Chemical Division
100 Niagara Street
Middleport, New York 14105

Los Angeles Chemical Company
4545 Ardine Street
South Gate, California 90280

Nihon Nohyaku Company, Ltd.
(Japan Agricultural Chemicals Company, Ltd.)
5th Floor Eitaro Bldg., No. 4, 1-Chome
Nihumbashitori Chuo-Ku, Tokyo, Japan

Procida (Groupe Roussel)
Saint-Marcel
13-Marseille 11°, France

Rhodia Inc., Chipman Division
120 Jersey Avenue
New Brunswick, New Jersey 08903

The Sherwin-Williams Company
116 St. Clair Avenue
Cleveland, Ohio 44101

Woolfolk Chemical Works, Ltd.
East Main Street
P.O. Box 938
Fort Valley, Georgia 31030

Calcium Arsenate

Following are the basic producers of calcium arsenate:

Allied Chemical Corporation
Agricultural Division
40 Rector Street
New York, New York 10006

Commercial Chemical Company
P.O. Box 86
Memphis, Tennessee 38101

Los Angeles Chemical Company
4545 Ardine Street
South Gate, California 90280

Pennwalt Corporation
Agricultural Chemicals Division
2901 Taylor Way
Tacoma, Washington 98401

Rhodia Inc., Chipman Division
120 Jersey Avenue
New Brunswick, New Jersey 08903

Woolfolk Chemical Works, Ltd.
East Main Street
P.O. Box 938
Fort Valley, Georgia 31030

Basic Copper Arsenate

No longer being manufactured because the tolerance has
been cancelled.

Ammonium Arsenite

Basic producer information is not available from usual
sources. Refer to registrants of Pesticides Regulation Division for
those supplying the material for pesticidal purposes.

Arsenic Acid

Following are the basic producers of arsenic acid:

Allied Chemical Corporation
Agricultural Division
40 Rector Street
New York, New York 10006

Commercial Chemical Company
P.O. Box 86
Memphis, Tennessee 38101

Pennwalt Corporation
Agricultural Chemicals Division
2901 Taylor Way
Tacoma, Washington 98401

Rhodia Inc., Chipman Division
120 Jersey Avenue
New Brunswick, New Jersey 08903

The Sherwin-Williams Company
116 St. Clair Avenue
Cleveland, Ohio 44101

Woolfolk Chemical Works, Ltd.
East Main Street
P.O. Box 938
Fort Valley, Georgia 31030

Arsenic Pentoxide

Basic producer information is not available from the usual sources. Refer to registrants of the Pesticides Regulation Division for those supplying the material for pesticidal purposes.

Arsenic Trioxide

Following is a basic supplier of arsenic trioxide:

American Smelting and Refining Company
120 Broadway
New York, New York 10005

Sodium Pyroarsenate

Basic producer information is not available from the usual sources. Refer to registrants of the Pesticides Regulation Division for suppliers of the material for pesticidal use.

Wolman Salts

Following is the basic producer of Wolman Salts:

Koppers Company, Inc.
1501 Koppers Building
Pittsburgh, Pennsylvania 15219

Cacodylic Acid

Following is the basic producer of cacodylic acid:

The Ansul Company
1 Stanton Street
Marinette, Wisconsin 54149

Sodium Arsenite

Following are the basic producers of sodium arsenite:

Allied Chemical Corporation
Agricultural Division
40 Rector Street
New York, New York 10006

Chemical Formulators, Inc.
P.O. Box 26
Nitro, West Virginia 25143

Chemical Insecticide Corporation
30 Whitman Avenue
Edison, New Jersey 08817

Chevron Chemical Company
Ortho Division
200 Bush Street
San Francisco, California 94120

FMC Corporation
Niagara Chemical Division
100 Niagara Street
Middleport, New York 14105

Pennwalt Corporation
Agricultural Chemicals Corporation
2901 Taylor Way
Tacoma, Washington 98401

Procida (Groupe Roussel)
Saint-Marcel
13-Marseille 11°, France

Rhodia Inc., Chipman Division
120 Jersey Avenue
New Brunswick, New Jersey 08903

The Sherwin-Williams Company
116 St. Clair Avenue
Cleveland, Ohio 44101

Potassium Arsenite

Basic producer information is not available from the usual sources. Refer to the registrants of the Pesticides Regulation Division for suppliers of the material for pesticidal use.

Sodium Arsenate

Following are the basic producers of sodium arsenate:

Procida (Groupe Roussel)
Saint-Marcel
13-Marseille 11°, France

Rhodia Inc., Chipman Division
120 Jersey Avenue
New Brunswick, New Jersey 08903

Paris Green

Following are the basic producers of Paris green:

Los Angeles Chemical Company
4545 Ardine Street
South Gate, California 90280

Procida (Group Roussel)
Saint-Marcel
13-Marseille 11°, France

Rhodia Inc., Chipman Division
120 Jersey Avenue
New Brunswick, New Jersey 08903

The Sherwin-Williams Company
116 St. Clair Avenue
Cleveland, Ohio 44101

DSMA (Disodium Methanearsonate)

Following are the basic producers of DSMA:

The Ansul Company
1 Stanton Street
Marinette, Wisconsin 54149

W. A. Cleary Corporation
P.O. Box 749
New Brunswick, New Jersey 08903

Diamond Shamrock Corporation
Agricultural Chemical Division
300 Union Commerce Building
Cleveland, Ohio 44115

Vineland Chemical Company
P.O. Box 745
West Wheat Road
Vineland, New Jersey 08306

MSMA (Monosodium Methanearsonate)

Following are the basic producers of MSMA:

The Ansul Company
1 Stanton Street
Marinette, Wisconsin 54149

Diamond Shamrock Corporation
Agricultural Chemical Division
300 Union Commerce Building
Cleveland, Ohio 44115

Vineland Chemical Company
P.O. Box 745
West Wheat Road
Vineland, New Jersey 08306

AMA (Amine Methanearsonate)
Following is the basic producer of AMA:
Vineland Chemical Company
P.O. Box 745
West Wheat Road
Vineland, New Jersey 08306

Sodium Hypoarsenate

Basic producer information is not available from the usual
sources. Refer to registrants of the Pesticides Regulation Division for
suppliers of the material for pesticidal use.

<u>Disodium Arsenate</u>

Basic producer information is not available from the usual sources. Refer to registrants of the Pesticides Regulation Division for suppliers of the material for pesticidal use.

<u>10, 10'-oxybisphenoxarsine</u>

Following is the basic producer of 10,10'-oxybisphenoxarsine:

Scientific Chemicals Division
Ventron Instruments Corporation
3800 South Racine Avenue
Chicago, Illinois 60609

<u>EXPORT-IMPORT DATA FOR ARSENICALS</u>

The available export data for the arsenicals are presented in the following tables.

Exports of Calcium Arsenate

Year	1,000 dollars	1,000 pounds
1961	58	
1962	104	942
1963	18	187
1965 1/	613	1,430
1966 1/	805	3,187
1967 1/	898	1,580
1968 1/	782	2,277
1969	1,758.2	5,466.7

1/ Inorganic insecticides which includes lead arsenate, calcium arsenate and inorganic fumigants and rodenticides.

Exports of Lead Arsenate

Year	1,000 dollars	1,000 pounds
1961	183	
1962	249	1,423
1963	135	803

Exports of Inorganic Herbicides, Including Sodium
    Arsenite

Year	1,000 dollars	1,000 pounds
1965	276	724
1966	362	1,496
1967	342	1,000
1968	606	2,325.3
1969	1,244.9	2,870.4

The above export tables for calcium arsenate, lead
arsenate and the inorganic herbicides, including sodium arsenite,
indicate an increase in exports as demands decreased in the United
States.

Pesticide Use Patterns and History of Use In the United States--Arsenical Pesticides

The basic information relating uses of the arsenical pesticides
to pest and host crop or other specialized uses are given in Chapter I
of the Group's Arsenic Pesticides Report. The registered alternate
pesticides are given in Chapter I for each of the arsenical pesticides
now registered by the Environmental Protection Agency.

Chapter IV of the Group's Arsenic Pesticides Report gives
specific information on trends of arsenical pesticides use. Also, in
Chapter IV, the use of arsenical pesticides has been related to hazard
or safety for air, water, soil and plants.

The increased use of lead arsenate on fruits, especially for
plum curculio control in the Eastern United States, can be expected if
the chlorinated hydrocarbon insecticide alternates are removed from
availability for use. This is a subject which the Special Pesticides
Review Group had to consider most seriously in arriving at conclusions
on lead arsenate for the Administrator.

COMPARATIVE USE COSTS OF ARSENICAL PESTICIDES AND THE REGISTERED ALTERNATE PESTICIDES

The registered alternates for the arsenical pesticides are
indicated for each major pest controlled in Chapter I of the Special
Pesticides Review Group's Arsenic Report. Chapter I of this Report
also gives available impact information on crop yields or economic
costs whenever developed and made available.

Following are newly developed comparative costs (per acre or other convenient comparison) for appropriate arsenical pesticide and selected alternates now registered (Note: rates and costs per acre will not assure grower of equivalent pest control):

Comparisons for Lead Arsenate Insecticide Uses

Crop	Pesticide	Range of Dosage Rates (lbs. per 100 gal. or per acre)	Total Cost Per Treatment (dollars)
Fruit crops	Lead arsenate	2-6 lbs. per 100 gals.	$.52 – $1.56
	Carbaryl	1/2 –1-1/2 lbs. per 100 gal.	.50 – 1.50
	Guthion	0.3 – 0.5 lbs. per 100 gal.	.84 – 1.40
	Diazinon	0.25 – 0.5 lbs per 100 gal.	1.00 – 2.00
	Malathion	0.5 – 1.0 lbs per 100 gals	.34 – .68
	Parathion	0.15 – 0.5 lbs per 100 gals	.06 – .20
	Methoxychlor	1-1.5 lbs per 100 gals	.66 – .99
	Rotenone	1.25 –2.2 lbs per 100 gals	.14 – .24
Vegetable crops, ornamentals and field crops	Lead arsenate	3-10 lbs per acre	.78 – 2.60
	Carbaryl	.5 – .5 – 2 lbs per acre	.50 – 2.00
	Diazinon	.4 – .5 lbs per acre	1.60 – 2.00
	Malathion	1-2 lbs per acre	.68 – 1.36
	Lindane	.2 – .4 lbs per acre	.27 – .548
	Parathion	.3 – 1 lb. per acre	.12 – .40

(continued)

Crop	Pesticide	Range of Dosage Rates (lbs. per 100 gal. or per acre)	Total Cost
	Toxaphene	2-4 lbs per acre	$.44 – $ .88
	Methoxychlor	1-2-1/4 lbs per acre	.66 – 1.48
Lawns and ornamental turf	Lead arsenate	80-430 lbs per acre	$20.80 – $118.80
	Carbaryl	4-20 lbs per acre	4.00 – 20.00
	Chlordane	10 lbs per acre	$5.90
	Diazinon	2-2/3 – 7-3/4 lbs per acre	6.90 – 19.40
	Heptachlor	10 lbs per acre	$10.30
	Toxaphene	25 lbs per acre	$5.50

Comparisons for Calcium Arsenate Insecticide Uses

Crop	Pesticide	Range of Dosage Rates (lbs per 100 gal. or per acre)	Total Cost Per treatment (dollars)
Vegetable crops	Calcium arsenate	3-5-1/2 lbs per acre	$.42 – $.77

For competitive costs see "Comparisons for Lead Arsenate Insecticide Uses" under "vegetable crops."

Crop	Pesticide		Total Cost
Lawns and ornamental turf	Calcium Arsenate	430 lbs per acre	$60.20

For competitive costs see "Comparisons For Lead Arsenate Insecticide Uses" under "lawns and ornamental turf."

Miscellaneous Wood Preservative Arsenical Pesticide Uses – Compared to Alternates

Arsenic Compound	Cost	Alternate	Cost
Arsenic pentoxide	$.64/lb.	creosote pentachlorophenol	$.25/gal. .17/lb.
Arsenic trioxide	$.047/lb.	Same as for arsenic pentoxide.	

Comparisons in MSMA and DSMA Non-Crop, Industrial
Sites, Rights-of-Ways, Driveways and Sidewalks

Pesticide	Range of Dosage Rates (lbs per acre)	Total Cost Per Treatment (dollar)
MSMA*	2-5 lbs (100 gals. water)	$2.75 - $6.88
DSMA*	2-5 lbs (100 gals. water)	$2.75 - $6.88
Simazine	6-12 lbs	$15 - $30
Monuron	6-12 lbs	$12 - $24

*Usually used to supplement other herbicides for johnsongrass control.

Comparisons of Arsenical Pesticides For Lawns
and Ornamental Turf

Pesticide	Range of Dosage Rates (lbs of actual per acre)	Total Cost Per Treatment (dollar)
MSMA	2-5 lbs	$2.75 - $6.88
DSMA	5-15 lbs	$6.88 - $20.63
Lead arsenate	70-200 lbs	$18.20 - $52.00
Calcium arsenate	80-600 lbs	$11.20 - $84.00

Comparisons for MSMA and DSMA to Control Weeds
in Cotton (Post-Emergence)

Pesticide	Range of Dosage Rates (lbs of actual/acre)	Total Cost Per Treatment (dollar)
MSMA*	1-2 lbs	$1.38 - $2.75
DSMA*	2-3 lbs	$2.75 - $4.13
Treflan	3 lbs	$13.95
Monuron	2-2-1/2 lbs	$4.00 - $5.00

*Primary use is supplement to other herbicides for johnsongrass control.

REGISTRANTS OF ARSENICAL PESTICIDES

The Pesticides Regulation Division has made a preliminary review of the arsenical pesticides now registered. Mr. Harold Alford has indicated in a recent letter to Dr. William Upholt that approximately 700 products are currently registered containing one or more of approximately 34 arsenical compounds. The Pesticides Regulation Division has initiated a summarization of the arsenical pesticide registrants.