SUBSTITUTE CHEMICAL PROGRAM

INITIAL SCIENTIFIC AND MINIECONOMIC REVIEW OF CROTOXYPHOS (CIODRIN®)

JUNE 1975

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

EPA-540/1-75-015

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

PREFACE

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

The substitute chemical is reviewed for suitability considering all applicable scientific factors such as: chemistry, toxicology, pharmacology and environmental fate and movement; and socio-economic factors such as: use patterns and costs and benefits. EPA recognizes the fact that even though a compound is registered, it still may not be a practical substitute for a particular use or uses of a problem pesticide. The utilitarian value of the "substitute" must be evaluated by reviewing its biological and economic data. The reviews of substitute chemicals are carried out in two phases. Phase I conducts these reviews based on data bases readily accessible at the present time. An Initial Scientific Review and Minieconomic Review are conducted simultaneously to determine if there is enough data to make a judgment with respect to the "safety and efficacy" of the substitute chemical. Phase II is only performed if the Phase I reviews identify certain questions of safety or lack of benefits. The Phase II reviews conduct in-depth studies of these questions of safety and cost/benefits and consider both present and projected future uses of the substitute chemicals.

The report summarizes rather than interprets scientific data reviewed during the course of the studies. Data is not correlated from different sources. Opinions are not given on contradictory findings. Where applicable, the review also identifies areas where technical data may be lacking so that appropriate studies may be initiated to develop desirable information.

This report contains the Phase I Initial Scientific and Minieconomic Review of Crotoxyphos. Crotoxyphos was identified as a registered substitute chemical for certain cancelled and suspended uses of DDT.

The review covers all uses of crotoxyphos and is intended to be adaptable to future needs. Should crotoxyphos be identified as a substitute for a problem pesticide other than DDT, the review can be updated and made readily available for use. The data contained in this report was not intended to be complete in all areas. Data-searches ended in December, 1974. The review was coordinated by a team of EPA scientists in the Criteria and Evaluation Division of the Office of Pesticide Programs. The responsibility of the team leader was to provide guidance and direction and technically review information retrieved during the course of the study. The following EPA scientists were members of the review team: Richard K. Tucker (Team Leader); Merry Lou Alexander (Chemistry); O. E. Paynter, Ph.D. (Pharmacology and Toxicology); Richard Claggett (Fate and Significance in the Environment); E. David Thomas, Ph.D. (Registered Uses); Jeff Conopask (Economics).

Data research, abstracting, and collection were primarily performed by Midwest Research Institute (MRI), Kansas City, Missouri (EPA Contract #68-01-2448) under the direction of Mr. Thomas L. Ferguson. RvR Consultants, Shawnee Mission, Kansas, under a subcontract to MRI, assisted in data collection. The following MRI scientists were principal contributors to report: Chester R. Crawford, Ph.D., John Doull, Ph.D, David F. Hahlen, William B. House, Ph.D., Alfred Meiners, Ph.D. Rosmarie von Rümker, Ph.D. (RvR Consultants) also contributed to the report.

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

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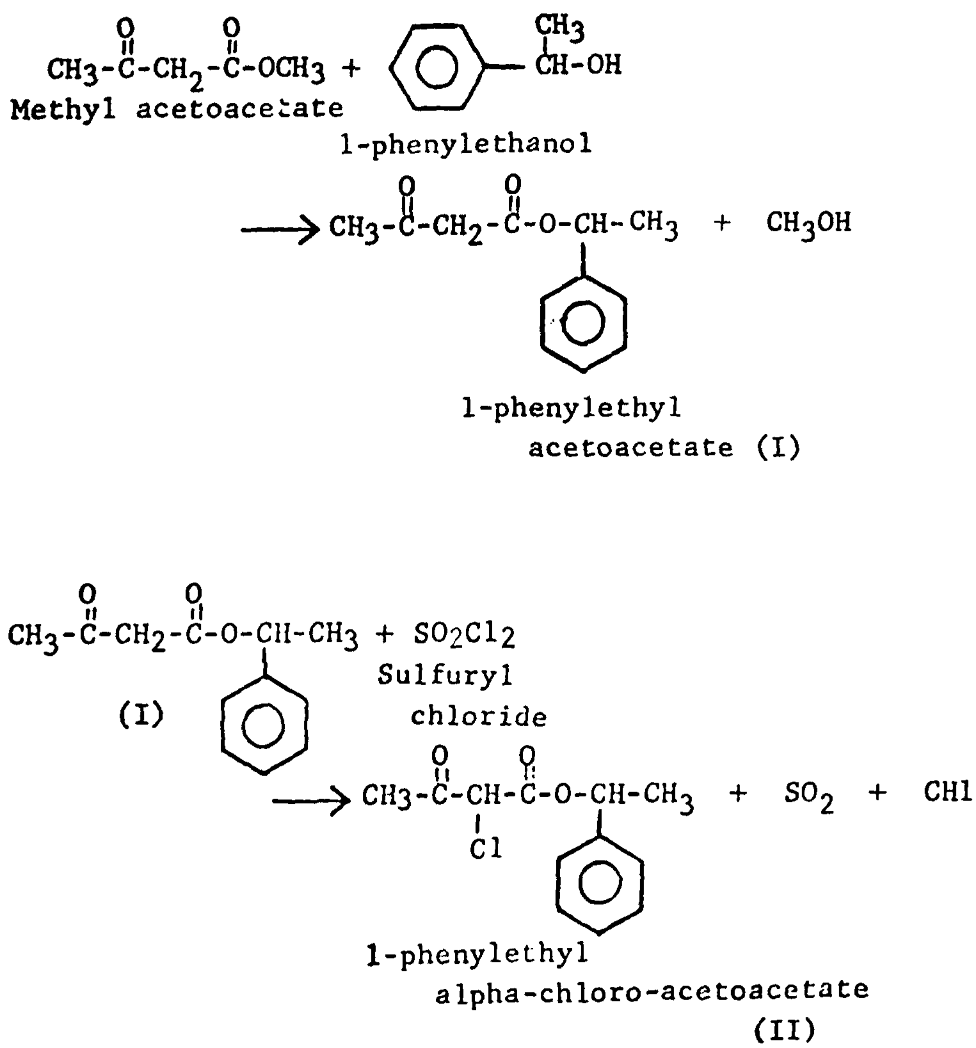
PART I. SUMMARY

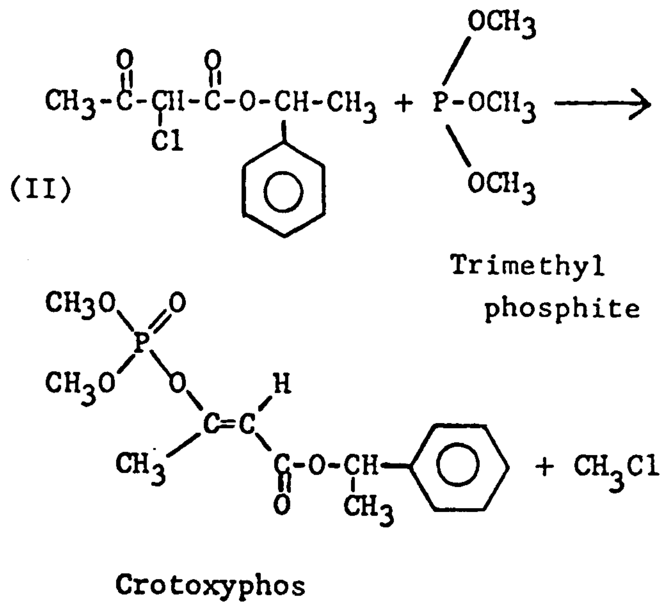
CONTENTS

This section contains a summary of the "Initial Scientific and Minieconomic Review" conducted on crotoxyphos (Ciodrin®, alpha-methylbenzyl 3-hydroxycrotonate dimethyl phosphate). The section summarizes rather than interprets scientific data reviewed.

Production and Use

Crotoxyphos is manufactured in the United States by Shell Chemical Company, a division of Shell Oil Company, under the tradename Ciodrin®. One process that has been reported for its manufacturer involves the following three-step reaction sequence:





The chemical properties of crotoxyphos are similar to those of many other organophosphates. It readily undergoes hydrolysis. This hydrolysis is more rapid in basic than in acidic aqueous systems; the half-life is 180 hr at pH 9, 410 hr at pH 6, and 540 hr at pH 2. In soils, the degradation rate of crotoxyphos is even more rapid, i.e., about two orders of magnitude faster than the above hydrolysis rates.

Technical crotoxyphos is a liquid of over 80% purity. The major formulations of crotoxyphos are emulsifiable concentrates, (1 to 3.2 lb/gal), ready-to-use solutions (1 to 3%), and dusts (3%). A 20% dust concentrate is also available for further formulation. Crotoxyphos is often formulated with other insecticides.

Crotoxyphos is used to control various types of flies, ticks, lice and certain mites around livestock. About 80% of the total domestic usage, however, is estimated to be on dairy cattle. Crotoxyphos is also used on beef cattle, hogs and sheep. It is not used on crops.

The estimated domestic use of crotoxyphos in 1971 was 901,000 lb of active ingredient, compared to only 141,000 lb in 1966. By geographic region, the North Central states were estimated to use 50% of the total 1971 usage, followed (in decreasing order of use) by the Northeast, South Central, Southwest, Southeast, and Northwest states. An assessment of supply increase potential is currently not possible.

Toxicity and Physiological Effects

Crotoxyphos is a toxic organophosphate insecticide. The toxicity of crotoxyphos to rats is as follows:

Route of entry	Measurement	Value
Oral	LD_{50}	38.4-125 mg/kg
Dermal	LD_{50}	202-375 mg/kg
Subcutaneous	LD_{50}	148.8 mg/kg
Inhalation	LC_{50} (1 hr)	670 mg/liter

Crotoxyphos in the diet of rats up to 250 ppm caused no inhibitory effect on brain cholinesterase. Feeding at a level of 750 ppm, however, caused a marked depression. Microscopic examination of tissues from animals exposed to all dose levels revealed no pathological changes due to crotoxyphos.

The cholinesterase "no effect" level appears to be 7 ppm for rats.

Crotoxyphos fed in the diet of rats for 10 months at the level of 0.01 mg/kg caused no effects on cholinesterase activity. However, feeding 3.84, 1.92, and 0.77 mg/kg caused inhibition of cholinesterase activity, increase in vitamin C levels in liver and kidney, and reduced rate of hippuric acid synthesis.

Acute oral LD_{50} reported for mice ranges from 39.8 to 89 mg/kg.

The acute oral LD_{50} of crotoxyphos to cats is 802 mg/kg.

The LD_{50} of crotoxyphos to chicks has been reported to be 111 mg/kg and for hens, 147 mg/kg. A one-week feeding study of chicks at levels of 50, 100, 200, and 400, and 800 ppm crotoxyphos in the diet showed that 800 ppm caused a 50% inhibition of plasma cholinesterase.

Crotoxyphos does not appear to induce demyelination of peripheral nerves of chicken.

Feeding crotoxyphos in the diet of dogs for 12 weeks at levels of 5, 15, and 45 ppm caused no effect on growth or organ weights at any level of exposure. However, 15 and 45 ppm caused a depression of plasma and RBC cholinesterase activity. Feeding 135 ppm for 2 weeks did not affect brain cholinesterase. Microscopic examination of tissues at all dose levels in the 12 week study revealed no pathological changes that could be attributed to crotoxyphos. The cholinesterase "no effect" level in dogs appears to be 5 ppm.

Numerous studies have been undertaken to determine the safety of crotoxyphos to a variety of domestic animals. Sheep and goats were dipped in 1% emulsion of crotoxyphos. Swine and young dairy calves were sprayed with 0.5 and 2% emulsions. The only signs of toxicity were diarrhea and muscular weakness in some dairy calves when sprayed with the 2% emulsion.

Yearling cattle, adult cattle, horses, and pigs have also been exposed to various concentrations of dips and sprays, for varying lengths of time. Pigs, horses and adult cattle exhibited cholinesterase depression during treatment or post-treatment period.

The metabolism of crotoxyphos can be summarized as follows:

1. Crotoxyphos is absorbed from the gastro-intestinal tract and from intact skin in mammals.

2. The deesterified carboxylic acid of crotoxyphos is a minor metabolite with weak cholinesterase-inhibiting activity.

3. The major metabolites of crotoxyphos are dimethylphosphoric acid, acetoacetic acid and hydroxyethylbenzene.

Crotoxyphos feed to pregnant cattle failed to produce abortions.

Crotoxyphos failed to induce reverse mutation in Escherichia coli WP_2 on solid medium.

Crotoxyphos did not cause any teratogenic effects in embryos when eggs were injected on day 4 or day 5 of incubation.

No data was found on oncogenic effects of crotoxyphos or effects on humans.

Food Tolerances and Acceptable Intake

In the United States, tolerances for crotoxyphos have been established for meat, fat and meat by-products of cattle, goats, hogs and sheep, and for milk. All tolerances are 0.02 ppm. An acceptable daily intake (ADI) has not been established for crotoxyphos. Crotoxyphos has not been reported as a significant residue in any class of food. However, analytical systems routinely used by Food and Drug Administration laboratories to monitor pesticide residues in food and feedstuffs do not detect crotoxyphos. Thus, absence of crotoxyphos residue data does not necessarily mean that it is not present.

Environmental Effects

An evaluation of crotoxyphos toxicity to fish and other aquatic species is summarized as follows:

Species	Exposure Time (hr)	Toxicity Calculation	Toxicity Measure (ppb)
Sheepshead	24	EC_{50}	>1,000
(*Cyprinodon variegatus*)	48	EC_{50}	>1,000
Bluegill	24	LC_{50}	390
(*Lepomis macrochirus*)	96	LC_{50}	152
Channel catfish	24	LC_{50}	3,700
(*Ictalurus punctatus*)	96	LC_{50}	2,600
Cutthroat trout	24	LC_{50}	92
(*Salmo clarki*)	96	LC_{50}	51
Rainbow trout	24	LC_{50}	101
(*Salmo gairdneri*)	96	LC_{50}	72.4
Fathead minnow	24	LC_{50}	15,500
(*Pimephales promelas*)	96	LC_{50}	11,900
Largemouth bass	24	LC_{50}	1,800
(*Micropterus salmoides*)	96	LC_{50}	1,100
Brown shrimp	24	EC_{50}	220
(*Penaeus aztecus*)	48	EC_{50}	32
Eastern oyster			
(*Crassostrea virginica*)	96	no adverse affect at 1,000	
Scud	24	LC_{50}	49
(*Gammarus lacustris*)	48	LC_{50}	29
	96	LC_{50}	15
Stonefly	24	LC_{50}	1.0-10
(*Pteronarcys sp.*)	96	LC_{50}	1.0-10

The only data found on the effects of crotoxyphos on wildlife was acute oral LD_{50} of 790 mg/kg for young mallard drakes (Anas platyrynchos).

Commercial labels of insecticides that contain crotoxyphos as the active ingredient contain the warning: "This product is toxic to fish and wildlife."

Crotoxyphos has been shown to be "moderately toxic" to the honeybee (Apis mellifera). The LD_{50} value, based on contact effect, was 2.26 μg/bee for 48 hr exposure at 80°F and 65% relative humidity.

No data was found on the effect of crotoxyphos on lower terrestrial organisms.

The degradation of crotoxyphos has been evaluated in nonsterilized and sterilized samples of three different soils, Poygan silty clay loam (33.6% clay; 10.0% organic matter; pH 7.2); Kewaunee clay (48.7% clay; 3.8% organic matter; pH 6.4); and Ella loamy sand (5.2% clay; 1.6% organic matter; pH 3.8). The half-lives (in hr) of crotoxyphos in these soils were as follows:

	Poygan silty clay loam	Kewaunee clay	Ella loamy sand
Nonsterilized	2.00	5.50	71.0
Sterilized	3.75	6.00	77.0

Studies concerning the pathways of chemical breakdown of crotoxyphos indicated that dimethylphosphoric acid, *cis*-hydroxycrotonic acid, and 1-phenylethanol are the final degradation products in soils.

Half-lives of crotoxyphos in aqueous systems (temperature not specified) are reported as: 540 hr at pH 2; 410 hr at pH 6; and 180 hr at pH 9. At 100°F, the half-life is 35 hr at pH 9 and 87 hr at pH 1.

No data was found on crotoxyphos residues in water, air, or non-target plants or on its bioaccumulation, biomagnification, or environmental transport.

Limitations in Available Scientific Data

The review of scientific literature was based on available sources given limitations of time and resources.

Data was not found in a number of pertinent areas:

1. Acute toxicity of both technical and formulated crotoxyphos (eye irritation to rabit, primary skin irritation to rabbit, and inhalation LC_{50} for at least two species in a dynamic flow system).

2. Subacute inhalation to rats. (If cattle are to be sprayed in confined areas, a subacute inhalation test should be carried out.)

3. Data on the environment effects of crotoxyphos, including effects on fish, lower aquatic organisms, wildlife, cattle metabolism, beneficial arthropods, and lower terrestrial organisms.

4. Data on the presence, fate, and persistence of crotoxyphos residues in water, sediment, and other elements of aquatic ecosystems.

5. Data on the presence, fate, and persistence of crotoxyphos residues in air.

6. Data on bioaccumulation, biomagnification, or environmental transport mechanisms.

Efficacy and Cost Effectiveness

Crotoxyphos is an organophosphate insecticide that is used primarily for control of biting flies, ticks, and lice on cattle. Its effectiveness depends upon the method of application, number of applications, concentration, and point of application on the animal.

Good control of horn flies on cattle was achieved with a variety of application devices. One application every 3 to 5 days provided good control when applied with a low volume sprayer. Dust bags containing 3% crotoxyphos gave good control when they were frequently contacted by the cattle. Back rubbers also provide good control of horn flies. Stable flies on cattle are effectively controlled with crotoxyphos. However, crotoxyphos does not appear to give any residual control and must be applied daily.

Face fly control of up to 85% can be achieved on cattle with back rubbers or dust bags containing crotoxyphos. Frequent contact by the animal is necessary for control. Economic benefits from the control of flies on beef cattle range from a loss of 2.3¢/day/head to a gain of 25.0¢/day/head. For dairy cows, the economic benefits range from a loss of 34.4¢/day/head to a gain of 13.9¢/day/head. These rates, based on 1972 cost data, are for the use of crotoxyphos during the fly season. However, the data derived is incomplete and should be looked on with caution.

Crotoxyphos gives 99 to 100% control of cattle ticks and gives good residual control for 3 weeks. Control of the lone star tick for up to 1 week can also be achieved with crotoxyphos. Complete control of winter ticks on cattle and horses has been achieved with crotoxyphos. Similar results were experienced with horse ticks. A 2% crotoxyphos oil reduced cattle grubs on cattle by 74 to 96%. Chorioptic mange mites and several biting lice were completely controlled by crotoxyphos for up to 6 weeks.

PART II. INITIAL SCIENTIFIC REVIEW

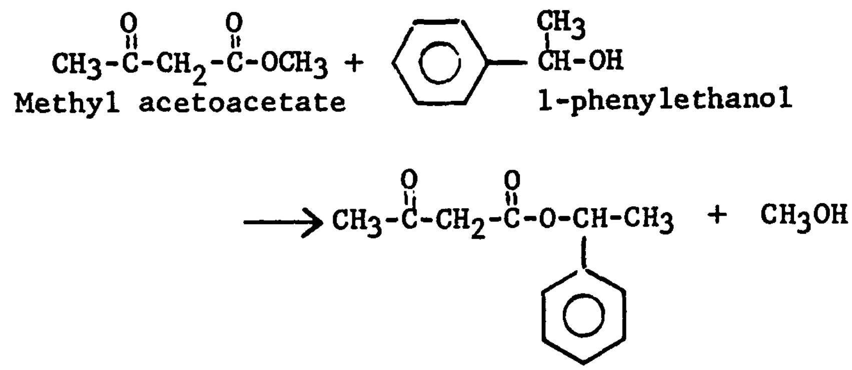
SUBPART A. CHEMISTRY

CONTENTS

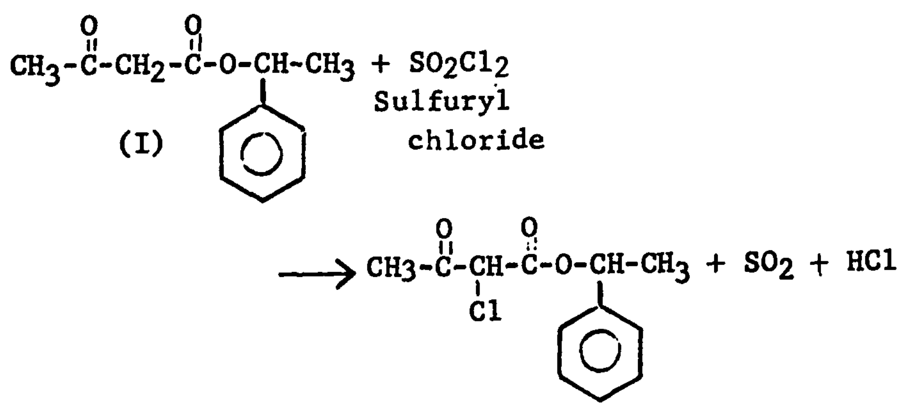
This section contains a detailed review of available data on the chemistry and presence of crotoxyphos in foods. Eight subject areas have been examined: Synthesis and Production Technology; Physical Properties of Crotoxyphos; Analytical Methods; Composition and Formulation, Chemical Properties, Degredation Reactions and Decomposition Processes; Occurrence of Residue in Food and Feed Commodities; Acceptable Daily Intake and Tolerances. The section summarizes rather than interprets data reviewed.

Synthesis and Production Technology

Crotoxyphos is manufactured in the United States by the Shell Chemical Company. According to Porter (1967)[1/] crotoxyphos is prepared by the following reaction sequence:

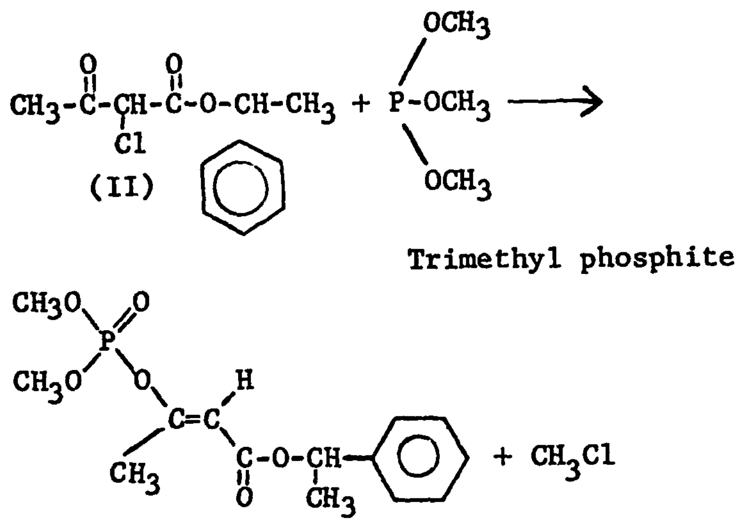


1-phenylethyl
acetoacetate (I)



1-phenylethyl alpha-
chloroacetoacetate (II)

1/ Porter, P. E., "Ciodrin® Insecticide," Analytical Methods for Pesticides, Plant Growth Regulators, and Food Additives, Vol. V, Additional Principles and Methods of Analysis, Chap. 11, Academic Press, Inc., New York (1967).



Crotoxyphos

The preceding procedure represents the most likely production method, but no production details are available. The Shell Oil Company owns patents on the compound (as a composition of matter) and has patents on methods for its production. (Whetston and Harman, 1960; Whetstone and Stiles, 1961; Tieman and Stiles, 1962; Whetstone and Harman, 1963).[1-4] The patented production method is essentially as has been described.

1/ Whetstone, R., and D. Harman, "Insecticidally Active Esters of Phosphorus Acids and Preparation of the Same," U.S. Patent No. 2,956,073 (to Shell Oil Company, 11 October 1960).

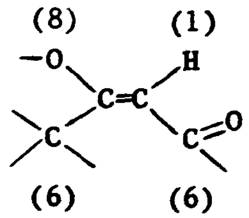
2/ Whetstone, R., and A. R. Stiles, "Arylphosphate Compounds," U.S. Patent No. 2,982,686 (to Shell Oil Company, 2 May 1961).

3/ Tieman, C. H., and A. R. Stiles, "Preparation of Vinyl Esters of Phosphorus Acids Useful as Insecticides," U.S. Patent No. 3,068,268 (to Shell Oil Company, 11 December 1962).

4/ Whetstone, R., and D. Harman, "Organo-Phosphorus Insecticide," U.S. Patent No. 3,116,201 (to Shell Oil Company, 31 December 1963).

U.S. Patent 3,068,268 (Tieman and Stiles, 1962) outlines an improved process for preparing crotoxyphos. Essentially, this process involves the toxification step (3) for the purpose of increasing the yield of the more active (E) isomer of crotoxyphos.

According to Beynon et al. (1973)[1/], the terms E and Z are used to avoid confusion with the terms <u>cis</u> and <u>trans</u> based on other conventions. In order to determine the configuration of a double bond, it is necessary to determine which two groups attached to the double bond have the higher priority. The determination of the priority of the groups according to sequence rules is straightforward for crotoxyphos. One need only consider the atomic numbers of the atoms attached directly to the carbon atoms of the double bond. For crotoxyphos, one must consider the atomic numbers of the four atoms in parentheses.



E-isomer of crotoxyphos

The sequence rules are based on the atomic numbers of the atoms; the atoms of higher atomic number have higher priority. The oxygen atom has the highest priority on the one carbon atom of the double bond and the carbon atom has the highest priority on the other. Thus, for such a structure, the configuration is described in terms of the oxygen and carbon atoms. The structure with these atoms on the same side of the double bond is called Z ("Zusammen," together) and that with them on the opposite side is called E ("Entgegen," opposite). The more-active isomer of crotoxyphos has the E configuration.

Melnikov (1971)[2/] also reports the above reaction sequence, but states that another method can be used for the production of crotoxyphos:

$$\underset{\text{ONa}}{CH_3C}{=}CHCO_2\underset{CH_3}{CH}C_6H_5 + (CH_3O)_2\overset{O}{\overset{\|}{P}}Cl \longrightarrow (CH_3O)_2\overset{O}{\overset{\|}{P}}O\underset{CH_3}{C}{=}CHCO_2\underset{CH_3}{CH}C_6H_5 + NaCl$$

sodium enolate of phenylethyl acetoacetate	dimethylchloro-phosphate	crotoxyphos

1/ Beynon, K. I., D. H. Hutson, and A. N. Wright, "The Metabolism and Degradation of Vinyl Phosphate Insecticides," <u>Residue Rev.</u>, 47:55-142 (1973).

2/ Melnikov, N. N., <u>Chemistry of Pesticides</u>, Vol. 36 of <u>Residue Rev.</u>, Springer-Verlag, New York (1971).

Physical Properties

Common Name: Crotoxyphos

Trade Name: Ciodrin®

Chemical Name: Crotoxyphos has acquired many chemical names in the dozen years of its commercial use. The following is a list of them:

Caswell et al. (1972),1/ Martin (1971),2/ [U.S. designation] and Shell (1962)3/ [alternate]
Dimethyl phosphate of alpha-methylbenzyl 3-hydroxy-cis-crotonate

Caswell et al. (1972) and Fukuto and Sims (1971)4/
Alpha-methylbenzyl 3-hydroxycrotonate dimethyl phosphate

Metcalf (1971)5/
0,0-Dimethyl 0-[1-methyl-2-(1-methyl-2-(1-Phenylcarbethoxy) vinyl]phosphate

Merck Index (1968)6/
3-Hydroxycrotonic acid, α-methylbenzyl ester dimethyl phosphate

Shell (1962) and Beynon et al. (1973) [alternate]
Alpha-methylbenzyl 3-(dimethoxyphosphinyloxy)-cis-crotonate

Chemical Abstract Service
(1971 and earlier) crotonic acid, 3-hydroxy-α-methylbenzyl ester dimethyl phosphate

(1972 and later) 2-butenoic acid, 3-[dimethoxyphosphinyloxy]-1-phenylethyl ester (E)

Beynon et al. (1973)
(IUPAC) dimethyl 2-(α-methylbenzyloxycarbonyl)-1-methylvinyl phosphate (alternate) 1-methylbenzyloxy-1-propen-2-yl dimethyl phosphate

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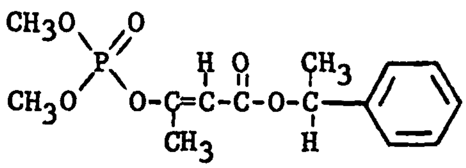
1/ Caswell, R. L., D. E. Johnson, and C. Fleck, Acceptable Common Names and Chemical Names for the Ingredient Statement on Pesticide Labels (2nd ed.), Environmental Protection Agency, Washington, D.C. (June 1972).
2/ Martin, H., Pesticide Manual, British Crop Protection Council, 2nd ed. (1971).
3/ Shell Chemical Company, "Summary of Basic Data for Technical Ciodrin® Insecticide," Technical Bulletin, San Ramon, Calif. (1962).
4/ Fukuto, T. T., and J. J. Sims, "Metabolism of Insecticides and Fungicides," In: R. White Stevens (ed.): Pesticides in the Environment. Marcel Dekker, Inc., New York (1971).
5/ Metcalf, R. L., "Chemistry and Biology of Pesticides," In: R. White Stevens (ed.): Pesticides in the Environment. Marcel Dekker, Inc., New York (1971).
6/ Merck Index, The, P. G. Strecher (ed.), 8th ed., Merck and Co., Rahway, N.J. (1968).

Pesticide Class: Insecticide; organophosphate

Structural Formula:



Empirical Formula: $C_{14}H_{19}O_6P$

Molecular Weight: 314.28

Analysis: C - 53.50%; H - 6.09%; O - 30.55%; P - 30.55%

Data below is for Technical Grade Ciodrin®, approximately 85% pure.

Physical State: light straw colored liquid with mild ester odor

Specific Gravity: 1.2 at 60°F

Density: 10 lb/gal at 68°F

Boiling Point: 135°C at 0.03 mm Hg

Vapor Pressure: (mm Hg)	Temperature (°C)
1.4×10^{-5}	20
3.9×10^{-5}	30
9.8×10^{-5}	40

Refractive Index: $n_D^{25} = 1.50$

Pour Point: Below 0°F

Flash Point: Over 175°F (tag open cup)

Flammability: Nonflammable

Solubility: Slightly soluble in water (0.1% at 25°C). Slightly soluble in kerosene and saturated hydrocarbons. Soluble in acetone, ethanol, isopropanol, chloroform and other highly chlorinated hydrocarbons. Miscible with xylene. Partition coefficient, hexane: water < 0.05.

Corrosive Action: Slightly corrosive to mild steel and bare metals; noncorrosive to stainless steel 316, monel and aluminum 3003. Will not attack rigid PVC, fiberglass, reinforced polyester, or most organic linings.

Stability: Stable when stored in glass, polyethylene, or certain lined containers; stable in presence of hydrocarbon solvents. Formulations are unstable on most solid carriers. See Chemical Properties section for action in water, acids and bases.

Analytical Methods

This subsection reviews analytical methods for crotoxyphos. The review describes multi-residue methods, residue analysis principles, and formulation analysis principles. Information on the sensitivity and selectivity of these methods is also presented.

Multi-Residue Methods - The Association of Official Analytical Chemists methods manual[1/] does not contain multi-residue methods for detecting crotoxyphos. Limited data is available in the Pesticide Analytical Manual, Volume I, (PAM, 1971).[2/]

The multi-residue analytical system used by FDA laboratories (in Kansas City, Missouri) does not detect crotoxyphos since special techniques are required for its detection. Ordinarily, if the FDA does not expect to find a particular pesticide, they do not perform the specific methodology necessary to detect it. However, some multi-residue methods for crotoxyphos have been investigated.

1/ Association of Official Analytical Chemists, Official Methods of Analysis of the Association of Official Analytical Chemists, 11th ed., Washington, D.C. (1970).

2/ U.S. Department of Health, Education, and Welfare, Food and Drug Administration, Pesticide Analytical Manual, Vol. I (1971).

The general PAM multi-residue methods analytical scheme for organophosphate residues is illustrated in Figure 1. According to the manual, no data is available concerning the recovery of crotoxyphos from fatty foods when the Florisil column clean up procedure is used (See Figure 1). The PAM also states that crotoxyphos is not recovered from nonfatty foods; recovery is not achieved by elution of the Florisil column with 6%, 15% or 50% ethyl ether - petroleum ether. However, Beckman and Barber (1969)1/ report an 86% recovery of crotoxyphos from Florisil using acetone as an elutant material.

Watts and Storherr (1969)2/ have provided retention times and response data for over 60 organophosphorus pesticides on three gas chromatograph columns. (This data is cited by Zwieg and Sherma,3/ and by the Pesticide Analytical Manual.) The data is summarized below:

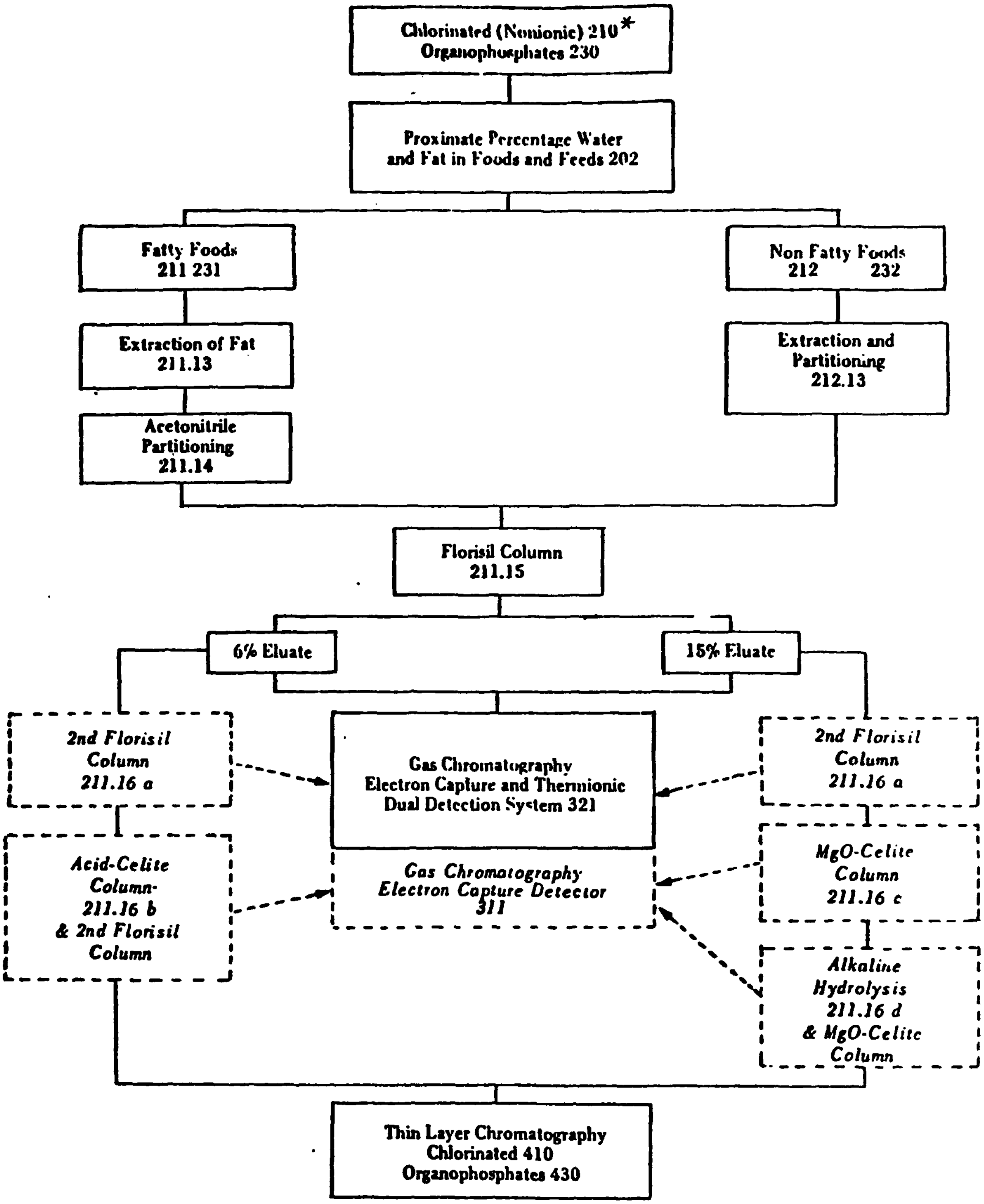
Column packing	Retention time relative to parathion≠	Sensitivity (ng for 1/2 FSD)≢
10% DC-200 or 10% DC-200, 15% QF-1 (1:1 w/w)*	1.36	12
10% DC-200, 15% QF-1*	1.38	35
2% DEGS (stabilized), column temperature 210°C	1.81	10

* At 200°C, nitrogen flowrate 120 ml/min
≠ Potassium Chloride thermionic detector
≢ FSD = Full scale deflection

1/ Beckman, H., and D. Garber, "Recovery of 65 Organophosphorus Pesticides from Florisil with a New Solvent Elution System," J. Assoc. Off. Anal. Chem., 52(2):286-293 (1969).

2/ Watts, R. R., and R. W. Storherr, "Gas Chromatography of Organophosphorus Pesticides; Retention and Response Data on Three Columns," J. Assoc. Off. Anal. Chem., 52(3):513-521 (1969).

3/ Zweig, G. and J. Sherma, Analytical Methods for Pesticides and Plant Growth Regulators, Vol. VI: Gas Chromatographic Analysis, p. 218, Academic Press, Inc., New York (1972).



* The numbers refer to the decimal numbering system of PAM. The primary analytical scheme is in bold type. Additional cleanup and/or quantitation schemes are in italics. (Source: PAM, 1971).

Figure 1
ANALYTICAL SCHEME FOR CHLORINATED (NONIONIC AND ORGANOPHOSPHATE RESIDUES)

Bowman and Beroza (1970)[1/] have provided retention times for crotoxyphos and 137 other pesticides and metabolites. Crotoxyphos data is presented as follows:

Liquid phase	Relative retention time (parathion = 1.00)	
	Isothermal	Temperature programmed
OV-101	1.27	1.14
OV-17	1.44	1.16
OV-210	1.33	1.14
OV-225	1.23	1.07

This data was obtained using a gas chromatograph equipped with a flame photometric detector. Glass columns were packed with 5% w/w of the liquid phases on 80 to 100 mesh Gas Chrom Q and conditioned overnight at 320°C. Nitrogen (carrier) gas flow rate was 160 ml/min. Injection port temperature was 225°C, detector 280°C, column 200°C (isothermal) or programmed to start at 150°C, increase at 10°C/min for 15 min, and then held at 300°C until the last peak emerged.

Residue Analysis Principles - PAM (Vol. II, 1971)[2/] does not contain a specific residue analysis method for crotoxyphos.

Zweig and Sherma (1972) have recommended a gas chromatographic method of residue analysis for crotoxyphos. This is the same method used by Shell.[3/] The method is suitable for residues in animal tissues and milk. The residue is extracted from tissue with acetone or from milk with acetone and sodium sulfate. The extract is concentrated, partitioned into ethyl ether, further concentrated, and then exchanged into ethyl acetate. This solution is analyzed by gas chromatography using a flame photometric or alkali flame ionization detector system. Concentrations as low as 0.03 ppm can be determined, but the accuracy is not stated in the method.

1/ Bowman, M.C., and M. Beroza, "GLC Retention Times of Pesticides and Metabolites Containing Phosphorus and Sulfur on Four Thermally Stable Columns," J. Assoc. Off. Anal. Chem., 53(3):499-508 (1970)

2/ U.S. Department of Health, Education, and Welfare, Food and Drug Administration, Pesticide Analytical Manual, Vol. II (1971).

3/ Shell Development Company, Biological Sciences Research Center, Modesto, Calif., MMS-R-268-1 (April 1971).

The recommended method of Porter (1967) is a cholinesterase-inhibition method, and is the same method used by Shell (1964).[1/] This method has only been tested for the determination of crotoxyphos in animal tissue or animal products. The residue is first extracted with a solvent suitable to the animal product, partitioned into acetonitrile, and then into hexane. A portion is washed to remove water-soluble interferences and then analyzed by a cholinesterase method. The accuracy of the method is not stated.

Porter (1967) commented on three other methods. He reports that experience with gas chromatographic analysis of crotoxyphos has been poor owing to its low volatility and relatively rapid degradation. Another method, thin-layer chromatography, has been used for semiquantitative determination of crotoxyphos. A third satisfactory method has been insect bioassay.

Oehler and Claborn (1970)[2/] have described a gas chromatographic method in the Journal of the AOAC. This method may be used for body tissue or milk. Extraction procedures varied slightly depending upon material, but usually involved hexane or hexane and acetone. The residue was then partitioned into acetonitrile. The gas chromatograph had a flame photometric detector. Recoveries varied from 80 to 98%. Residues as low as 0.003 ppm were detectable.

Another method was described by Westlake et al. (1969a, 1969b)[3,4/]. The two articles give different ways of making the final determination, but both used acid hydrolysis followed by oxidation to convert crotoxyphos to acetophenone. The acetophenone is microdistilled, then extracted into carbon tetrachloride. For the final determination, Westlake et al. (1969a) used a spectrophotometer and measured the carbonyl peak at 1,690 cm^{-1}. Recoveries ranged from 82 to 131% and the lower limit of determination was 20 μg of crotoxyphos.

1/ Shell Development Company, Agricultural Research Division, Analytical Methods MMS-38/64 (July 1964).

2/ Oehler, D. D., and H. V. Claborn, "Determination of Crotoxyphos in Milk and in the Body Tissues of Cattle and Pigs," J. Assoc. Off. Anal. Chem., 53(5):1045-1047 (1970).

3/ Westlake, A., F. A. Gunther, and W. E. Westlake, "Conversion of the Insecticide Ciodrin to Acetophenone for Microdetermination," J. Agr. Food Chem., 17(6):1157-1159 (1969a).

4/ Westlake, A., F. E. Hearth, F. A. Gunther, and W. E. Westlake, "Determination of Ciodrin from Fortified Animal Tissues by Oscillopolarography of Its Conversion Product Acetophenone," J. Agr. Food Chem., 17(6):1160-1163 (1969b).

In a variation of this method, Westlake et al. (1969b) made the final determination using oscillopolarography. In this test they began with animal tissue, milk or eggs containing crotoxyphos as a residue. Recoveries ranged from 40 to 109%, but were more consistent in a specific product category. Polarography cannot be used on residues in liver because of interferring compounds.

Formulation Analysis Principles - Porter (1967) states that the recommended method for formulation analysis employs infrared spectrophotometry. Liquid formulations, such as emulsifiable concentrates or technical grade crotoxyphos, are simply dissolved in carbon disulfide and the absorbance is measured at a characteristic band of 11 µm. Solid formulations are first extracted with chloroform, and the crotoxyphos is then taken into carbon disulfide. The accuracy of the method is not given, but it depends upon the absence of materials which absorb radiation near 11 µm. This method is similar to the method of Czech (1964).1/

Porter (1967) also mentions three other possible methods. The first, which consists of an analysis for total phosphorus, is often used in formulation production. Phosphorus in crotoxyphos is separated from that in degradation products by partitioning between water and chloroform; the quantity of phosphorus in the chloroform phase is then determined. A second method employs gas chromatography with detection by thermal conductivity. A third method consists of measuring cholinesterase inhibition. This method is generally unattractive for macroanalysis because of the high dilutions required and because poor precision is achieved.

Zweig and Sherma (1972) present details of a gas chromatographic method. Emulsifiable concentrates are diluted with chloroform and dust formulations are extracted with chloroform. Any suitable gas chromatograph with a flame ionization or thermal conductivity detector may be used. The precision of the method is estimated to be ± 4% of the mean.

The Shell Development Company (1971)2/ describes a gas chromatographic method for the determination of crotoxyphos in dusts and resin concentrates. It differs from the Porter (1967) method. In the Shell method, the sample is extracted with chloroform, and is subjected to gas chromatographic analysis under conditions which sufficiently separate the E and Z isomers. Crotoxyphos, the E isomer, can then be determined. The accuracy of the method is not stated.

1/ Czech, F. P., "Analysis of Insecticides in Aqueous Emulsions Used in Livestock Dips and Sprays: General Infrared Method," J. Assoc. Off. Agr. Chem., 47(5):829-837 (1964).

2/ Shell Development Company, Biological Sciences Research Center, Modesto, Calif., MMS-C-298-1 (November 1971).

Composition and Formulation

Technical Ciodrin® according to its only domestic manufacturer is over 80% crotoxyphos (Shell, 1962). The remaining percentage is not identified. The concentrations of the more active and less active isomers are also not disclosed.

Crotoxyphos is available in a variety of formulations and strengths. Among those listed by the manufacturer are: 1) emulsifiable concentrates, 1.1, 2.0 and 3.2 lb/gal; 2) solutions, ready-to-use; 1 and 2%; 3) dusts, 3%, ready-to-use; 20% for further formulation.

Technical crotoxyphos is also formulated and used with other insecticides. A "dairy and livestock" spray contains 10% crotoxyphos and 2.3% dichlorvos; no information was available concerning synergistic effects.

According to Porter (1967) the stability of crotoxyphos is poor on most solid carriers and care must be exercised in preparing solid formulations.

No information is available concerning the nature of the degradation products. The manufacturer did not provide the nature of the carriers employed in the various formulations.

Chemical Properties, Degradation Reactions and Decomposition Processes

Crotoxyphos is an ester of phosphoric acid, contains a vinyl phosphate structure and is also an ester of crotonic acid. Its known chemical reactions could be predicted for a compound of this structure.

Most of the available information concerning the chemical reactions of crotoxyphos deals with hydrolysis; no information was found concerning oxidation or photolysis.

Hydrolysis - Like other organophosphate compounds, crotoxyphos readily undergoes hydrolysis. Hydrolysis occurs in acidic or basic solution, but is much more rapid in basic solution. Konrad and Chesters (1969)1/ determined the following half-lives for hydrolysis at various values of pH. The initial pH was adjusted using HCl or NaOH and the solution was not buffered. The temperature was unspecified.

pH	Half-life (hr)
2.0	540
6.0	410
9.0	180

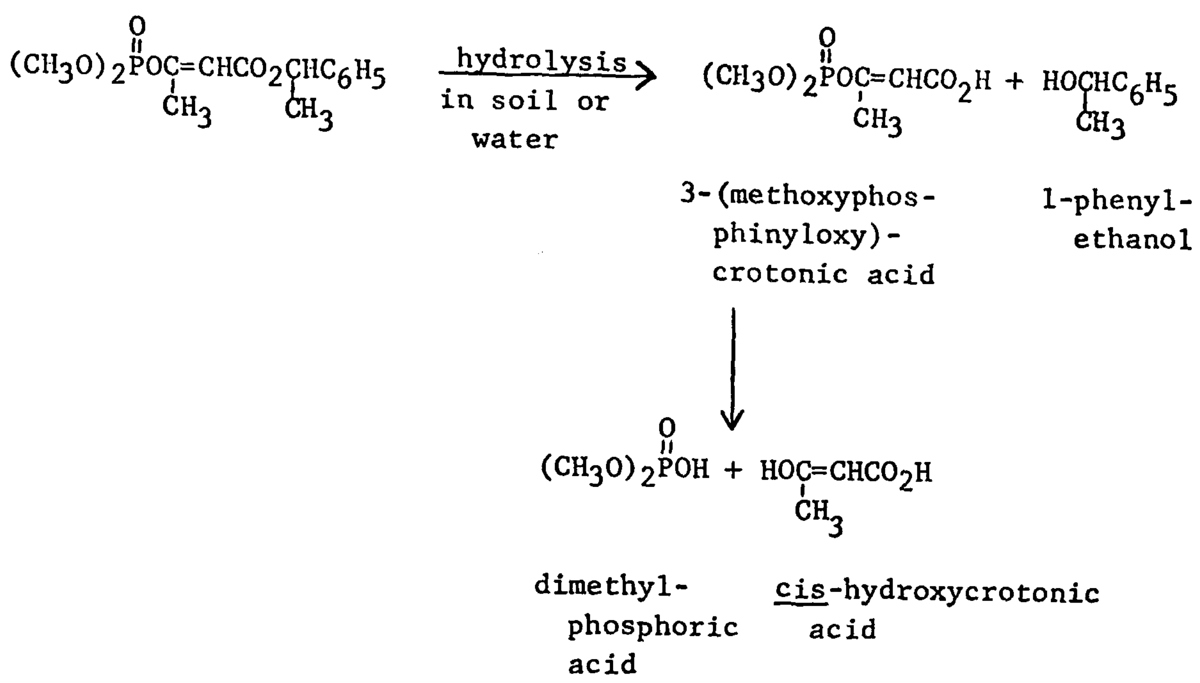
1/ Konrad, J. G., and G. Chesters, "Degradation in Soils of Ciodrin and Organophosphorus Insecticide," J. Agr. Food Chem., 17(2):226-230 (March-April 1969).

The data of Konrad and Chesters (1969) shows a linear relationship between the amount of crotoxyphos remaining and-time progression for each of the pH's indicating that hydrolysis follows first-order kinetics.

Porter (1967) reported the following half-lives in water at 38°C:

pH	Half-life (hr)
1	87
9	35

Konrad and Chesters (1969) listed the hydrolysis products for degradation in soil or water. In their study, no ^{14}C-labeled methanol was detected among the soil-free hydrolysis products. Thus, cleavage of the P-O-CH_3 bonds does not appear to be environmentally significant. This finding is supported by a study (Chamberlain, 1964)1/ using ^{32}P-crotoxyphos in which dimethyl phosphate was detected as the major metabolite. These products and the apparent pathway to them are shown in the following diagram:



1/ Chamberlain, W. F., "The Metabolism of ^{32}P-Labeled Shell SD-4294 in a Lactating Ewe," J. Econ. Entomol., 57:119 (1964).

Porter (1967) states that hydrolysis produces all of the products which can be formed from the cleavage of the P-O-C bonds and the C-O-C bonds of the crotoxyphos molecule. Under alkaline conditions, Porter states that dimethyl phosphate and 1-phenylethyl acetoacetates predominate:

$$\underset{\text{crotoxyphos}}{(CH_3O)_2\overset{O}{\overset{\|}{P}}OC(CH_3){=}CHCO_2CH(CH_3)C_6H_5} \xrightarrow[\text{Hydrolysis}]{\text{Alkaline}} \underset{\text{dimethyl phosphate}}{(CH_3O)_2\overset{O}{\overset{\|}{P}}ONa} + \underset{\text{1-phenylethyl acetoacetate}}{CH_3\overset{O}{\overset{\|}{C}}CH_2CO_2CH(CH_3)C_6H_5}$$

The hyrdolysis of crotoxyphos in aqueous solution is fairly rapid. However, Konrad and Chesters (1969) observed that in soil systems, at pH values near neutrality, the rates of degradation are approximately two orders of magnitude greater than in soil-free, aqueous systems at pH 6.0. (The degradation of crotoxyphos in soils is discussed in the Fate and Significance Section of this report.)

Other Chemical Reactions - Porter (1967) stated that crotoxyphos will undergo the following chemical reactions:

1. Sodium iodide in acetone solution fairly selectively cleaves the P-O-methyl bonds to form the desmethyl derivative:

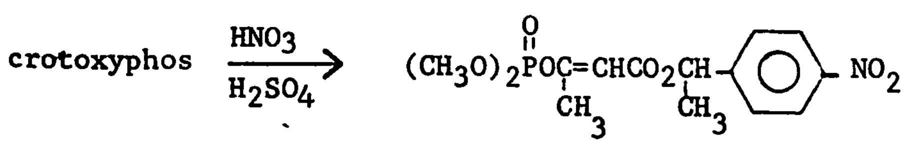
$$\text{crotoxyphos} \xrightarrow[(2)\ H_2O]{(1)\ NaI,\ acetone} 2CH_3I + (HO)_2\overset{O}{\overset{\|}{P}}OCH(CH_3)CH_2CO_2CH(CH_3)C_6H_5$$

2. The double bond is reactive and will easily add bromine or hydrogen:

$$\text{crotoxyphos} \xrightarrow{[H2]} (CH_3O)_2\overset{O}{\overset{\|}{P}}OCH(CH_3)CH_2CO_2CH(CH_3)C_6H_5$$

$$\text{crotoxyphos} \xrightarrow{Br_2} (CH_3O)_2\overset{O}{\overset{\|}{P}}OCBr(CH_3)CHBrCO_2CH(CH_3)C_6H_5$$

3. The benzene ring can be nitrated without destroying the molecule using concentrated nitric acid-concentrated sulfuric acid mixture:



Westlake et al. (1969) suggested a method of analysis for crotoxyphos by acid hydrolysis followed by oxidation to acetophenone, which can then be determined by oscillopolarography. The chemical reactions are as follows:

$$\text{crotoxyphos} \xrightarrow[\text{hydrolysis}]{\text{acid}} \underset{\text{1-phenylethanol}}{HOCH(CH_3)C_6H_5} \xrightarrow{\text{oxidation}} \underset{\text{acetophenone}}{CH_3COC_6H_5}$$

Occurrence of Crotoxyphos in Food and Feed Commodities

The Food and Drug Administration (FDA), Department of Health, Education and Welfare, monitors pesticide residues in the nation's food supply. Much of these data are published and the literature is voluminous. However, a search of the published data has revealed that crotoxyphos has not been reported as a significant residue in any food class.

From conferences with FDA officials, it was learned that the multi-residue analytical system used by the FDA laboratories (in Kansas City) would not detect crotoxyphos. Crotoxyphos is one of the relatively volatile pesticides (an "early eluter" in the gas chromatographic analysis) and special techniques are required for its detection. Ordinarily, if the FDA does not expect to find a particular pesticide, they do not perform the specific methodology necessary to detect it. Thus, the absence of crotoxyphos in the residue data does not mean that it is not present.

Acceptable Daily Intake

The acceptable daily intake (ADI) is defined as the daily intake which, during an entire lifetime, appears to be without appreciable risk on the basis of all known facts at the time of evaluation (Lu, 1973).[1/] It is expressed in milligrams of the chemical per kilogram of body weight (mg/kg).

The Food and Agricultural Organization/World Health Organization (FAO/WHO) establishes ADI levels. An ADI for crotoxyphos, which has only noncrop uses, has not yet been determined by FAO/WHO.

Tolerances

Tolerances for crotoxyphos, established under the purview of the Food, Drug, and Cosmetic Act, as amended, are cited in the Code of Federal Regulations, specifically for "negligible residues" of dimethyl phosphate of α-methylbenzyl 3-hydroxy-*cis*-crotonate in meat, fat and meat by-products of cattle, goats, hogs, and sheep and in milk at 0.02 ppm.[2/]

1/ Lu, F. C., "Toxicological Evaluation of Food Additives and Pesticide Residues and Their 'Acceptable Daily Intakes' for Man: The Role of WHO, in Conjunction with FAO," Residue Rev., 45:81-93 (1973).

2/ Code of Federal Regulations, Title 40, Chapter 1, Subchapter E, Subpart C, Section 180. 280.

References

Association of Official Analytical Chemists, Official Methods of Analysis of the Association of Official Analytical Chemists, 11th ed., Washington, D.C. (1970).

Beckman, H., and D. Garber, "Recovery of 65 Organophosphorus Pesticides from Florisil with a New Solvent Elution System," J. Assoc. Off. Anal. Chem., 52(2):286-293 (1969).

Beynon, K. I., D. H. Hutson, and A. N. Wright, "The Metabolism and Degradation of Vinyl Phosphate Insecticides," Residue Rev., 47:55-142 (1973).

Bowman, M. C., and M. Beroza, "GLC Retention Times of Pesticides and Metabolites Containing Phosphorus and Sulfur on Four Thermally Stable Columns," J. Assoc. Off. Anal. Chem., 53(3):499-508 (1970).

Caswell, R. L., D. E. Johnson, and C. Fleck, Acceptable Common Names and Chemical Names for the Ingredient Statement on Pesticide Labels (2nd ed.), Environmental Protection Agency, Washington, D.C. (June 1972).

Chamberlain, W. F., "The Metabolism of ^{32}P-Labeled Shell SD-4294 in a Lactating Ewe," J. Econ. Entomol., 57:119 (1964).

Code of Federal Regulations, Title 40, Chapter 1, Subchapter E, Subpart C, Section 180. 280.

Czech, F. P., "Analysis of Insecticides in Aqueous Emulsions Used in Livestock Dips and Sprays: General Infrared Method," J. Assoc. Off. Agr. Chem., 47(5):829-837 (1964).

Fukoto, T. R., and J. J. Sims, "Metabolism of Insecticides and Fungicides," In: R. White Stevens (ed.) Pesticides in the Environment, Marcel Dekker, Inc., New York (1971).

Konrad, J. G., and G. Chesters, "Degradation in Soils of Ciodrin and Organophosphorus Insecticide," J. Agr. Food Chem., 17(2):226-230 (March-April 1969).

Lu, F. C., "Toxicological Evaluation of Food Additives and Pesticide Residues and Their 'Acceptable Daily Intakes' for Man: The Role of WHO, in Conjunction with FAO," Residue Rev., 45:81-93 (1973).

Martin, H., Pesticide Manual, British Crop Protection Council, 2nd ed. (1971).

Melnikov, N. N., Chemistry of Pesticides, Vol. 36 of Residue Rev., Springer-Verlag, New York (1971).

Merck Index, The, P. G. Strecher (ed.), 8th ed., Merck and Co., Rahway, N.J., (1968).

Metcalf, R. L., "Chemistry and Biology of Pesticides," In: R. White Stevens (ed.): Pesticides in the Environment, Marcel Dekker, Inc., New York (1971).

Oehler, D. D., and H. V. Claborn, "Determination of Crotoxyphos in Milk and in the Body Tissues of Cattle and Pigs," J. Assoc. Off. Anal. Chem., 53(5):1045-1047 (1970).

Porter, P. E., "Ciodrin® Insecticide," Analytical Methods for Pesticides, Plant Growth Regulators, and Food Additives, Vol. V, Additional Principles and Methods of Analysis, Chap. 11, Academic Press, Inc., New York (1967).

Shell Chemical Company, "Summary of Basic Data for Technical Ciodrin® Insecticide," Technical Bulletin, San Ramon, Calif. (1962).

Shell Development Company, Agricultural Research Division, Analytical Method MMS-38/64 (July 1964).

Shell Development Company, Biological Sciences Research Center, Modesto, Calif., MMS-R-268-1 (April 1971).

Shell Development Company, Biological Sciences Research Center, Modesto, Calif., MMS-C-298-1 (November 1971).

Tieman, C. H., and A. R. Stiles, "Preparation of Vinyl Esters of Phosphorus Acids Useful as Insecticides," U.S. Patent No. 3,068,268 (to Shell Oil Company, 11 December 1962).

U.S. Department of Health, Education and Welfare, Food and Drug Administration, Pesticide Analytical Manual, 2 vols. (1971).

Watts, R. R., and R. W. Storherr, "Gas Chromatography of Organophosphorus Pesticides; Retention and Response Data on Three Columns," J. Assoc. Off. Anal. Chem., 52(3):513-521 (1969).

Westlake, A., F. E. Hearth, F. A. Gunther, and W. E. Westlake, "Determination of Ciodrin from Fortified Animal Tissues by Oscillopolarography of Its Conversion Product Acetophenone," J. Agr. Food Chem., 17(6):1160-1163 (1969).

Westlake, A., F. A. Gunther, and W. E. Westlake, "Conversion of the Insecticide Ciodrin to Acetophenone for Microdetermination," J. Agr. Food Chem., 17(6):1157-1159 (1969).

Whetstone, R., and D. Harman, "Insecticidally Active Esters of Phosphorus Acids and Preparation of the Same," U.S. Patent No. 2,956,073 (to Shell Oil Company, 11 October 1960).

Whetstone, R., and D. Harman, "Organo-Phosphorus Insecticide" U.S. Patent No. 3,116,201 (to Shell Oil Company, 31 December 1963).

Whetstone, R., and A. R. Stiles, "Arylphosphate Compounds," U.S. Patent No. 2,982,686 (to Shell Oil Company, 2 May 1961).

Zweig, G., and J. Sherma, Analytical Methods for Pesticides and Plant Growth Regulators, Vol. VI; Gas Chromatographic Analysis, Academic Press, Inc., New York (1972).

PART II. INITIAL SCIENTIFIC REVIEW

SUBPART B. PHARMACOLOGY AND TOXICOLOGY

CONTENTS

This section reviews pharmacological and toxicological data on crotoxyphos. The acute, subacute and chronic toxicity data for a number of species by various routes of administration is discussed. Data is presented on metabolism, effects on reproduction, and mutagenic and oncogenic effects. Data is also included on human exposure to crotoxyphos. This section summarizes rather than interprets scientific data reviewed.

Acute, Subacute and Chronic Toxicity

Toxicity to Laboratory Animals -

Acute oral toxicity - rats - The results of a number of tests for the acute oral toxicity of crotoxyphos to rats are shown in Table 1. There is a large variation in the acute toxicity as reported by several investigators for the technical compound. The acute oral LD_{50} ranges from 38.4 (Vorobieva and Lapchenko, 1973)[1/] to 125 mg/kg (Simelskii, 1970).[2/] The variation in acute LD_{50} values is evidently due to differences in experimental techniques such as choice of vehicle and whether animals are fasted. As shown in Table 1, female rats appear to be slightly more susceptible to this compound than male rats (Gaines, 1969).[3/]

Symptoms of toxicity of rats exposed to crotoxyphos are due to cholinesterase inhibition. The symptoms include: excessive salivation, tremors, convulsions, lacrimation and diarrhea (Shellenberger and Newell, 1961).[4/]

Acute toxicity - rats (routes other than oral) - The toxicity of crotoxyphos for rats by routes of exposure other than oral is shown in Table 2. The dermal LD_{50} indicates that the compound is absorbed fairly well from the skin. A dermal LD_{50} of 202 mg/kg for the female rat is reported by both Ben-Dyke, et al. (1970)[5/] and Gaines (1969).

1/ Vorobieva, N. M., and V. S. Lapchenko, "Toxicity and Hygienic Standardization of Ciodrin Pesticide," Gigiyena I Santariya, Moscow, 38(6):30-33 (1973).

2/ Simelskii, M. A., "The Toxicity of Ciodrin for Warm-blooded Animals and Arthropods," Tr. Vses. Nauchno-Issled. Inst. Vet. Sanit. (1970).

3/ Gaines, Thomas B., "Acute Toxicity of Pesticides," Toxicol. Appl. Pharmacol., 14(3):515-534 (1969).

4/ Shellenberger and Newell, Stanford Research Institute, EPA Pesticide Petition No. 9F0770 (1961).

5/ Ben-Dyke, R., D. M. Sanderson, and D. Noakes, "Acute Toxicity Data for Pesticides," World Review of Pest Control, 9(3):119-127 (1970).

Table 1. ACUTE ORAL TOXICITY OF CROTOXYPHOS TO RATS

Formulation	Measurement	Results (mg/kg) Male	Results (mg/kg) Female	References
Technical	LD_{50}	74-125		a/
Technical	LD_{50}	110 (95-128)***	74 (65-84)	b/
Technical*	LD_{50}	125 (100-147)		c/
Technical	LD_{50}	21-112		d/
Technical	LD_{50} (ml/kg)	0.0584 (0.0476-0.0716)		e/
Technical	LD_{50}		125	f/
	LD_{50}	38.4±7.8		g/
Technical*	LD_1	55	42	b/
Technical*	Lowest lethal dose	100	63	b/
Wettable powder 25%≠	LD_{50}	288≠ 236-356		c/

Table 1 (Continued)

Formulation	Measurement	Results (mg/kg) Male	Female	References
Emulsible concentrate 3.2 (lb/gal)	LD_{50}		0.213 ml** (0.195-0.234)	c/
			21.3±4.3	d/

---

* Dissolved or suspended in peanut oil.

ƚ Dissolved in water.

ǂ LD_{50} formulation 1 kg = 72 mg crotoxyphos per kilogram (59-89)

** LD_{50} formulation 1 kg = 81 mg crotoxyphos per kilogram (74-89).

*** Data in parentheses represent 95% confidence limits.

a/ Ben-Dyke, et al., op. cit. (1970).

b/ Gaines, op. cit. (1969).

c/ Shellenberger and Newell, op. cit. (1961).

d/ Witherup and Schlecht, Kettering Laboratory, EPA Pesticide Petition 9F0770, Vol. 1. (1964).

e/ Doyle and Elsea, Hilltop Research, EPA Pesticide Petition 9F0770 (1966).

f/ Simelskii, op. cit. (1970).

g/ Vorobieva and Lapchenko, op. cit. (1973).

Table 2. ACUTE TOXICITY OF CROTOXYPHOS FOR RATS VIA ROUTES OTHER THAN ORAL

Measurement	Results (mg/kg) Male	Female	Reference
Subcutaneous LD_{10}		106 (62.9-126.1)*	a/
Subcutaneous LD_{50}		148.8 (124.5-179.4)	a/
Subcutaneous LD_{90}		208.9 (174.8-360.1)	a/
Dermal LD_{50}		202	b/
Dermal LD_{1}	200	130	c/
Lowest dose to kill	300	150	c/
Dermal LD_{50}	375 (323-435)	202 (177-230)	c/

* Data in parentheses represent 95% confidence limits.

a/ Natoff, I. L., and B. Reiff, "Quantitative Studies of the Effect of Antagonists on the Acute Toxicity of Organophosphates in Rats," Brit. J. Pharmac., 40:124-134 (1970).

b/ Ben-Dyke, et al., op. cit. (1970).

c/ Gaines, op. cit. (1969).

Crotoxyphos is readily absorbed from the lungs. The inhalation toxicity of both the technical and 3.2 lb/gal formulation is such that both are in the highly toxic category (defined as LC_{50} < 2 mg/l for a 1 hr exposure).[1/]

The subacute oral toxicity to rats is summarized in Tables 4 & 5. Feeding crotoxyphos in the diet of rats for 10 months at 0.01 mg/kg caused no adverse effects. Higher doses caused inhibition of cholinesterase activity, increase in vitamin C levels in liver and kidney, and reduced rate of hippuric acid synthesis (Vorobieva and Lapchenko, 1973).

Demyelination - Crotoxyphos does not induce demyelination of peripheral nerves of chicken (Witherup and Ushry, 1965).

Acute oral toxicity - mice - A summary of the acute oral toxicity of crotoxyphos to mice is shown in Table 6. When formulated as a wettable powder, crotoxyphos remains as toxic as its technical form. (Shellenberger and Newell, 1961).

Acute oral toxicity - chicks - A summary of the acute oral toxicity of crotoxyphos to chicks is given in Table 7. A LD_{50} of 111 mg/kg is reported by Sherman et al. (1965)[2/] and an LD_{50} of 147 mg/kg is reported by Witherup and Ushry (1965).

Subacute oral toxicity - chichens - A 1-week feeding study to chickens at levels of 50, 100, 200, 400 and 800 ppm in the diet showed that 800 ppm caused a 50% inhibition of plasma cholinesterase (Sherman et al., 1965). This data is summarized in Table 8.

Subacute oral toxicity - dogs - The subacute oral toxicity of crotoxyphos to dogs is summarized in Table 9. Feeding crotoxyphos in the diet of dogs for 12 weeks at levels of 5, 15, and 45 ppm caused no effect on growth or organ weights at any level of exposure. However, 15 and 45 ppm caused a depression of plasma and RBC cholinesterase activity. When 135 ppm were fed for 2 weeks, brain cholinesterase was not affected. Microscopic examination of tissues at all dose levels in the 12 week study revealed no pathological changes that could be attributed to the compound (Shellenberger and Newell, 1961). The cholinesterase no-effect level in dogs appears to be 5 ppm.

Acute toxicity - cats - The acute oral LD_{50} of crotoxyphos to cats is 802 $\pm$ 9.02 mg/kg (Vorobieva and Lapchenko, 1973).

1/ Witherup and Ushry, Kettering Laboratory, EPA Pesticide Petition No. 9F0770 (1965).

2/ Sherman, M., E. Ross, and M. T. Y. Chang, "Acute and Subacute Toxicity of Several Insecticides to Chicks," Toxicol. Appl. Pharmacol., 7: 606-608 (1965).

Table 3. ACUTE INHALATION TOXICITY OF CROTOXYPHOS TO RATS

Method of exposure	Exposure formulation time	Percent mortality	Chamber concentration mg/ℓ
Dynamic Flow	45 min	100	1.67
(Technical	64 min	40	0.67
Material)	120 min	60	0.61
	240 min	0	0.34
Dynamic Flow	60 min	70	0.94
3.2 lb/gal	60 min	0	0.78 *
(38.2%)	140 min	0	0.42 *

Source: Witherup and Ushry, op. cit. (1965).

* Active ingredient = formulation concentrations approximately 2.04 and 1.10 mg/1.

Table 4. SUBACUTE ORAL TOXICITY TEST IN RATS

Concentration of Ciodrin® in feed (ppm)	Duration of test	Comments
0, 100, 300, 900	12 weeks	Growth of female rats significantly less than controls at 900 ppm. Hematology of males and females not effected at any level.
0. 7, 20, and 60	12 weeks	Slight inhibitory effect on whole blood cholinesterase at 20 ppm. 600 caused marked influence.
0, 10, 30, 100, 250, 750, 2000, 4000, 6000	2 weeks	No effect on rat brain cholinesterase at 250 ppm; marked depression at 750 ppm. In males, no blood cholinesterase inhibition occurred with 10 ppm, while in females this level caused inhibition. Microscopic examination of tissues of animals exposed to all dose levels revealed no pathological changes attributed to the compound.

Source: Shellenberger and Newell, op. cit. (1961).

Table 5. SUBACUTE TOXICITY OF CROTOXYPHOS TO RATS

Daily Dose mg/kg	Duration of Test	Percent Mortality	Comments
0.01	10 months	0	No effect on cholinesterase activity, no gross signs of toxicity.
0.05 and 0.25	10 months	0	Reduced eosinophilic cell count in hypophysis and adrenal cortex. Increased Vit C content in adrenal glands and elevated blood sugar levels. No gross signs of toxicity.
0.77, 1.92 and 3.84	10 months	0	Inhibition of cholinesterase activity, increased Vit C levels in liver and kidney. Reduced rate of hippuric acid synthesis.

Source: Vorobieva and Lapchenko, op. cit. (1973).

Table 6. ACUTE ORAL TOXICITY OF CROTOXYPHOS TO MICE

Formulation tested	LD_{50} of formulation	LD_{50} of crotoxyphos equivalent	Reference
--	39.8 ± 10.6 mg/kg	--	a/
3.2 lb/gal	0.16 ml/kg (0.14-0.187)	61 mg/kg (53-71)	b/
25% Wettable Powder	288 mg/kg (232-256)	72 mg/kg (58-89)	b/
Technical 83%	--	89 mg/kg (76-103)	b/

a/ Vorobieva and Lapchenko, op. cit. (1973).
b/ Shellenberger and Newell, op. cit. (1961).

Acute toxicity - rabbits - The dermal toxicity of crotoxyphos to rabbits is summarized in Table 10. Crotoxyphos appears to be fairly well absorbed from the skin of the animal. There are wide variations in the acute dermal toxicity as determined by several investigators. This is most likely due to differences in experimental techniques.

Toxicity to Domestic Animals - Numerous studies have been undertaken to determine the safety of crotoxyphos to a variety of domestic animals. Weidenbach and Younger (1962)[1/] dipped sheep and goats in 1% emulsion of crotoxyphos and sprayed swine and young dairy calves with 0.5 and 2% emulsions to run-off. The only signs of toxicity were diarrhea and muscular weakness to some dairy calves when sprayed with the 2% emulsion. These findings are summarized in Table 11.

The effects of crotoxyphos applied to Brahman calves, and Brahman and crossbred steers were also studied by Greer, et al. (1973).[2/] Animal toxicosis was determined by clinical symptoms such as cholinesterase inhibition, dyspnea, constriction of pupils, diarrhea, profuse salivation, inability to stand, and clonic convulsion.

The crotoxyphos formulations used were an emulsifiable concentrate (132 g/liter) and a 3% dusting powder.

The experimental groups of Brahman calves for 21-day tests were (1) controls, (2) a 3% dust group, (3) a 0.5% spray group and (4) a 1% spray group. The dust was applied at 57 g/head/day. The sprays were applied weekly at 946 ml/head.

The Brahman calves treated with 946 ml of 1% spray per head exhibited inhibition in whole blood and red cell cholinesterase. Two of four calves exhibited severe toxicosis and one developed skin lesions.

Calves treated with 946 ml of 0.5% spray or 57 g of 3% dust exhibited cholinesterase inhibition but other signs of toxicosis were not observed.

Whole blood and red cell cholinesterase of Brahman and crossbred steers were inhibited when treated with 1.9 liter of 0.5% crotoxyphos spray per head at weekly intervals for 11 weeks. Brahman steers exhibited a greater reduction than crossbred steers.

In another acute dermal study, it was shown that Brahman cattle were more sensitive to crotoxyphos than European-crossbreed when the dermal toxicities were compared (Palmer and Danz, 1964).[3/] This is shown in Table 12.

1/ Weidenbach, Carl P., and R. L. Younger, "The Toxicity of Dimethyl 2-(alpha-methylbenzyloxycarbonyl)-1-methylvinyl phosphate (Shell Compound 4294) to Livestock" J. Econ. Entomol., 55(5):793 (1962).

2/ Greer, N. I., M. J. Janes, and D. W. Beardsley, "Toxicity of Crotoxyphos Insecticide to Brahman and Crossbred Yearling Steers," Fla. Ent. 56: 243-250 (1973).

3/ Palmer, J. S., and J. W. Danz, "Tolerance of Brahman Cattle of Organic Phosphorus Insecticides," J. Amer. Vet. Med. Assoc., 1944(2):143-145 (1964).

Table 7. ACUTE ORAL TOXICITY OF CROTOXYPHOS TO CHICKS

Formulation	Measurement	Results (mg/kg) Male	Female	References
Technical	LD_{50}	111 (101-122)*		a/
Technical	LD_{50}	147 ± 8		b/
Technical	LD_{50}	147		c/

* Data in parentheses represent 95% confidence limits.
a/ Sherman et al., op. cit. (1965).
b/ Witherup and Schlect, op. cit. (1964).
c/ Witherup and Ushry, op. cit. (1965).

Table 8. SUBACUTE ORAL TOXICITY TEST IN WHITE LEGHORN COCKERELS

Ciodrin in feed-ppm	Duration of test	Percent mortality	Comments
50	1 week	0	The concentration of Ciodrin in the feed which resulted in approximately 50% inhibition of the cholinesterase of blood plasma at the end of 1 week is 800 ppm.
100	1 week	0	
200	1 week	0	
400	1 week	0	
800	1 week	0	

Source: Sherman et al., op. cit. (1965).

Table 9. SUBACUTE ORAL TOXICITY TEST IN DOGS

Concentration of crotoxyphos in feed (ppm)	Duration of test	Percent mortality	Comments
5, 15, and 45	12 weeks	0	No effect on growth or organ weights. In male dogs plasma cholinesterase activity inhibited at 15 and 45 ppm. In females cholinesterase activity markedly reduced at 45 ppm. RBC cholinesterase activity of male dogs slightly effected at 15 ppm and significantly at 45 ppm. In females 5 and 15 ppm exposure did not inhibit RBC cholinesterase activity, but inhibition occurred at 45 ppm. Inhibition returned to normal levels after 2-3 weeks. Brain cholinesterase activity not affected at 5, 15, and 45 ppm.
135	2 weeks	0	Brain cholinesterase activity not affected. Microscopic examination of tissues at all dose levels revealed no pathological changes attribted to the compound.

Source: Shellenberger and Newell, _op. cit_. (1961).

Table 10. ACUTE DERMAL TOXICITY TO RABBITS

Formulation	Measurement	Results (mg/kg) Male	Female	References
Technical	LD_{50}	742±102		a/
	LD_{50}	1780(1210-2610)*		
Technical	LD_{50}	384 (295-500)		b/
3.2 lb/gal	LD_{50}	> 200		c/
Emulsible concentrate		338(152-750)		b/
25% wettable powder	LD_{50}	> 1,250		

* Data in parentheses represent 95% confidence limits.

a/ Witherup and Schlect, Kettering Laboratory, EPA Pesticide Petition No. 9F0770 (1962).

b/ Shellenberger and Newell, op. cit. (1961).

c/ Palazzolo, R., Industrial Bio-Test Laboratories, EPA Pesticide Petition No. 9F0770 (1963).

Table 11. ACUTE DERMAL TOXICITY OF CROTOXYPHOS TO SOME DOMESTIC SPECIES

Animal species	Emulsion concentration	Volume applied	Comments
Young dairy calves	0.5% emulsions 2.0% emulsion	Thoroughly wetted with 4 liters of solution as a spray.	Not affected by treatment at 0.5%. Diarrhea and muscular weakness in 7 of 11 animals treated at 2%.
Angora Goats	0.5% and 1%	Thoroughly wetted by dipping.	No visible harmful effects.
Sheep	0.5% and 1%	Thoroughly wetted by dipping.	No visible harmful effects.
Swine	2%	Sprayed with 1.25 liters per head.	No visible harmful effects.

Source: Weidenbach and Younger, op. cit. (1962).

Table 12. COMPARATIVE DERMAL TOXICITY TO CATTLE

Animal	Emulsion concentration	Volume of emulsion (gal/head)	Comments
Brahman cross	0.6%*	1.25-2.0	Absence of gross signs of toxicity or cholinesterase activity depression.
European δ	0.6%*	1.25-2.0	No gross signs of toxicity or cholinesterase activity depression.
Brahman	1.0%†	1.25-2.0	Cholinesterase activity depressed 13% of normal. Moderate gross signs of toxicity.
European cross	1.0%†	1.25-2.0	Gross signs of toxicity evident in some animals. Cholinesterase activity 63% of normal.
Brahman	1.0%‡	1.25-2.0	Most animals exhibited gross symptoms of toxicity. Cholinesterase activity 45% normal.
European cross	1.0%‡	1.25-2.0	No evidence of gross toxic signs. Cholinesterase 66% normal.
Brahman	1.0%**	1.25-2.0	Moderate to severe toxic symptoms in majority of animals. Cholinesterase activity 34% normal.

* Diluted from 3 lb/gal E.C.

† Diluted from 25% wettable powder.

‡ Diluted from 14.4% E.C.

** Diluted from 4 lb/gal E.C.

Source: Palmer and Danz, op. cit. (1964).

In subacute dermal studies, pigs (Palmer and Schlinke, 1971)1/ yearling cattle (Weidenbach and Younger, 1962), adult cattle (Singh and Fireoved, 1964)2/ and horses (Knapp et al., 1967)3/ have been exposed to various concentrations of emulsions for varying lengths of time. Pigs, horses, and adult cattle exhibited cholinesterase depression during treatment or post-treatment period. This data is summarized in Tables 12, 13, and 14.

Metabolism

Absorption - Chamberlain (1964)4/ demonstrated that ^{32}P-crotoxyphos given orally to lactating sheep or dermally to lactating goats was absorbed by both routes. Ivie et al. (1967)5/ demonstrated that crotoxyphos inhibited acetylcholinesterase. Using this as a criterion for absorption, Vorobieva and Lapchenko (1973) reported that 0.01 mg/kg of crotoxyphos administered orally on a chronic basis to mice, rats, and cats produced a depression of liver cholinesterase activity.

Distribution - Chamberlain (1964) found ^{32}P-crotoxyphos in sheep blood 6 hr after an oral dose given in capsule form.

Excretion - Chamberlain (1964) reported that the peak urinary excretion of orally administered ^{32}P-crotoxyphos in lactating sheep was 6 hr after dosing. After 48 hr, 78.7% of the dose was present in the urine and 7.25% in the feces. Chamberlain (1964) treated lactating goats dermally with ^{32}P-crotoxyphos and recovered 11% of the radioactivity in the urine. The highest milk concentration was 0.2 ppb. Beynon et al. (1973)6/ reported that cows sprayed with 0.03% crotoxyphos had a maximum milk concentration of 0.007 ppm. After 2 days, this decreased to 0.001 ppm and was undetectable thereafter.

1/ Palmer, J. S., and J. C. Schlinke, "Toxicologic Effects of Two Crotoxyphos Formulations on Pigs," J. Econ. Entomol., 64(3):1971 (1971).
2/ Singh and Fireoved, Report on Crotoxyphos, Bio-Toxicological Research Associated, EPA Pesticide Petition No. 9F0770 (1964).
3/ Knapp, F. W., J. H. Drudge, and Eugene Lyons, "Toxic Effect of Ciodrin and Dichlorvos Applied Topically to Horses and Their Efficacy Against Internal Parasites," J. Econ. Entomol., 60(2):330-332 (April 1967).
4/ Chamberlain, W. F., "The Metabolism of ^{32}P-Labelled Shell SD-4294 in a Lactating Ewe," J. Econ. Entomol., 57:119 (1964).
5/ Ivie, G. W., L. R. Green, and H. W. Dorough, "The Use of Sodium Bicarbonate - C14 to Determine Cholinesterase Activity," Bull. Environ. Contam. Toxicol., 2(1):34-40 (1967).
6/ Beynon, K. I., D. H. Hutson, and A. N. Wright, "The Metabolism and Degradation of Vinyl Phosphate Insecticides," Residue Rev., 45:96-101 (1973).

Table 13. SUBACUTE DERMAL TOXICITY OF CROTOXYPHOS TO PIGS AND CATTLE

Animal	Duration of test	Percent mortality	Comments	References
Pig	3 weeks	0	One liter of a 1% emulsion was applied dermally to pigs for 3 weeks. Signs of toxicosis were seen after first spray application. These were area of skin erythema accompanied by squealing, salivating, and rubbing. Cholinesterase markedly depressed in one animal on second day of the first exposure.	a/
Pig	3 weeks	0	0.5 and 1 liters of a 1% emulsion of a 240 g/liter EC and 1 liter 120 g/liter formulation were applied dermally at weekly intervals for 3 weeks to 3 groups of animals to evaluate influence on cholinesterase activity. There were neither overt signs of toxicosis nor dermatosis in any group. However cholinesterase inhibition was exhibited by all groups 1 day after treatment and continuing throughout the experiment.	a/
Yearling cattle	16 weeks	0	1.5 gal. of a 0.5% or 2% emulsion were sprayed to each head of cattle without visible harmful effects.	b/

Table 13 (Continued)

Animal	Duration of test	Percent mortality	Comments	References
Cattle	3 days	0	Whole blood cholinesterase activity depressed. Activity returns to normal 7-8 weeks after treatment stopped. Growth and well being not affected.	c/

a/ Palmer and Schlinke, *op. cit*. (1971).
b/ Weidenbach, and Younger, *op. cit*. (1962).
c/ Singh and Fireoved, *op. cit*. (1964).

Table 14. SUBACUTE DERMAL TOXICITY TO HORSES

Animal	Duration of test	Percent mortality	Comments	References
Horse	12 days	0	1 pt 2% crotoxyphos EC in water poured on 5 times at 3-day interval (22.3 mg/kg each treatment) caused depression of cholinesterase activity of plasma for 8 days after last treatment. No signs of toxicity were observed.	a/
Horse	7 days	0	4 oz of 2% crotoxyphos in oil sprayed daily for 7 days (9 mg/kg) caused inhibition of plasma cholinesterase activity. No clinical signs of toxicity were observed.	a/

a/ Knapp et al., op. cit. (1967).

Biodegradation - Oehler and Claborn (1970)[1/] attempted to recover crotoxyphos from several cattle and pig tissures *in vitro*. Recovery was 80 to 95% from all tissues tested except blood. Recovery from beef blood was 82% immediately after mixing but only 25% after standing for 1 hr. In pig blood, these figures were 79 and 42%, respectively.

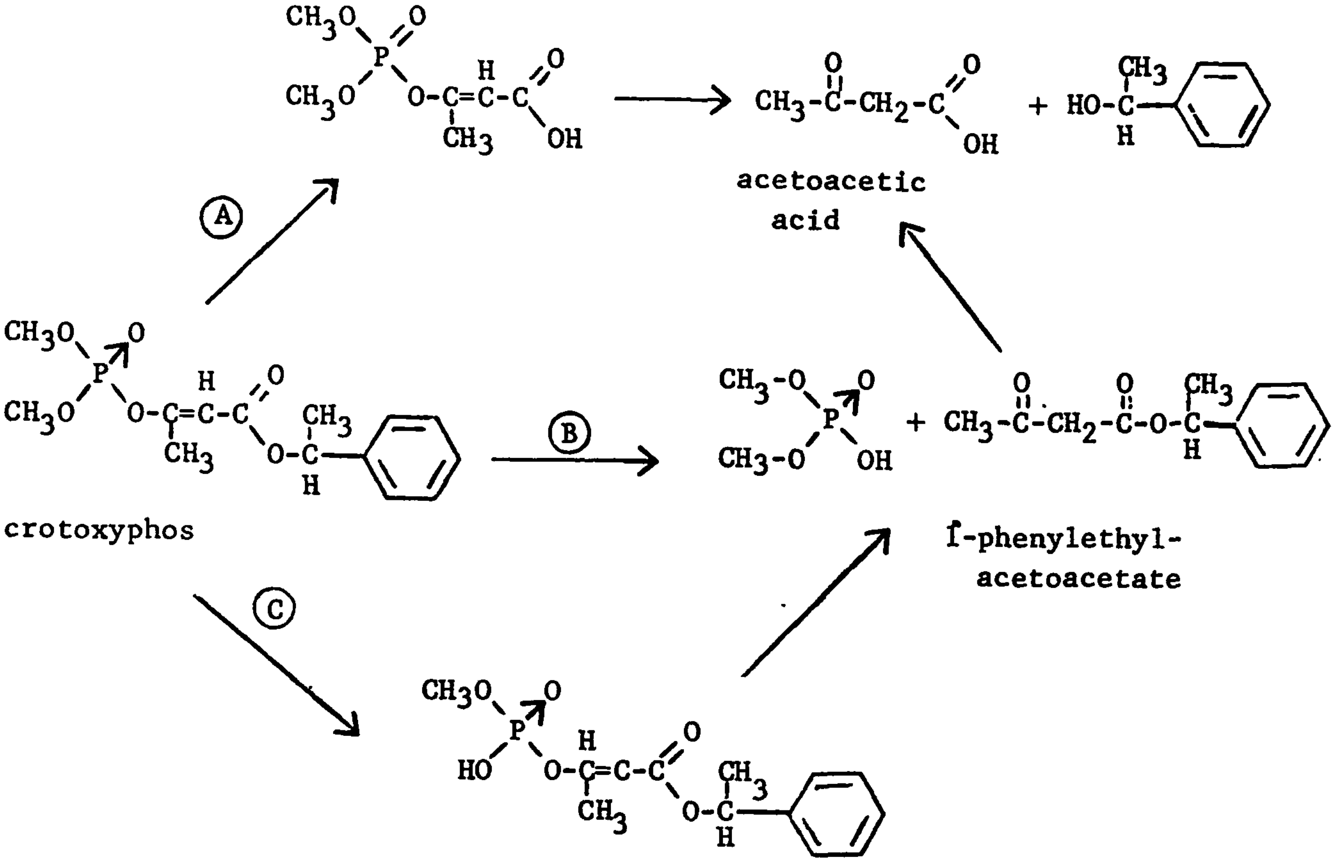
Chamberlain (1964) studied the metabolism of ^{32}P-crotoxyphos in lactating sheep. The major urinary metabolite was dimethylphosphoric acid (84% in 6 hr). After 3 hr 10% of the urinary metabolites was 3-(dimethoxy phosphinyloxy) crotonic acid. Seven other minor metabolites were found but not identified. Sheep may respond differentially to the α- and β-isomers of crotoxyphos since only β-crotoxyphos could be found in milk 5 hr after treatment. The peak radioactivity in the blood occurred 6 hr after treatment. The chloroform-exactable radioactivity in the 6 hr blood samples contained 66% α-isomers and 31% β-isomers.

Chamberlain (1964) found that 80 to 91% of ^{32}P-crotoxyphos excreted in the urine of lactating goats after dermal treatment was in the form of dimethylphosphoric acid.

Beynon et al. (1973) reported that the carboxylic acid that resulted from the de-esterification of crotoxyphos was also a weak cholinesterase inhibitor but of minor importance. They reported that the metabolic pathways of crotoxyphos in mammals and soil were essentially the same.

1/ Oehler, D. D., and H. V. Claborn, "Determination of Crotoxyphos in Milk and in Body Tissues of Cattle and Pigs," J. Assoc. Official Agr. Chem., 53:1045 (1970).

They proposed the following three pathways for the metabolic degradation of crotoxyphos:



Pathway B is probably the main pathway in mammals, while A produces the minor acid metabolite which is the weak cholinesterase inhibitor.

Tissue Residues - The relatively rapid excretion of ^{32}P-crotoxyphos by sheep (Chamberlain, 1964), goats (Chamberlain, 1964) and cows (Benynon et al., 1973) and its disappearance from milk after a few days suggests little or no accumulation in animal tissues. However, Vorobieva and Lapchenko (1973) found that chronic administration of crotoxyphos at 0.01 mg/kg/day in rats, mice, and cats depressed liver cholinesterase, increased liver and kidney vitamin C and decreased hipuric acid synthesis.

Effects on Reproduction

Macklin and Ribelin (1971)[1/] showed that feeding crotoxyphos to pregnant cattle failed to produce abortions.

Mutagenic Effects

Dean (1972)[2/] showed that crotoxyphos failed to induce a reverse mutation in Escherichia coli WP_2 on solid medium.

Teratogenic Effects

Crotoxyphos did not cause any teratogenic effects in embryos when hen's eggs were injected on day 4 of incubation (Roger et al., 1968)[3/] or when eggs were injected on day 5 of incubation (Flockhart and Casida, 1972).[4/]

Symptomology - Acute intoxication of animals by crotoxyphos is indicated by cholinesterase inhibition. Other symptoms are of rapid onset at toxic doses and appear within 30 min when crotoxyphos is administered orally to rats. These symptoms include tremors, clonic convulsions, lacrimation, salivation and diarrhea (Shellenberger and Newell, 1971; Doyle and Elsea, 1965). Within 2-1/2 hr following administration, most of the signs of acute intoxication in surviving animals have subsided. Death usually occurs within 1 hr after a lethal dose (Palazzolo, 1963).

1/ Macklin, A. W., and W. E. Ribelin, "Relation of Pesticides to Abortion in Dairy Cattle," J. Amer. Vet. Med. Assoc., 159(12):1743-48 (1971).

2/ Dean, B.J., "The Mutagenic Effects of Organophosphorus Pesticides on Micro-Organisms," Arch. Toxicol., 30:67-74 (1972).

3/ Roger, Jean-Claude, G. David Upshall, and J.E. Casida, "Structure-Activity and Metabolism Studies on Organophosphate Teratogens and Their Alleviating Agents in Developing Hen Eggs with Special Emphasis on Bidrin," Biochem. Pharmacol., 18:373-392 (1968).

4/ Flockhart, Jan R., and J.E. Casida, "Relationship of the Acylation of Membrane Esterases and Protein to the Teratogenic Action of Organophosphorus Insecticides and Eserin in Developing Hen Eggs," Biochem. Pharmacol., 21:2591-2603 (1972).

Signs of toxicity in mallard ducks are similar to those seen in rats. Ducks exhibit leg weakness, ataxia, wings crossed high over back, and opisthotonos. Signs appear about 1 hr post-treatment and persist in most survivors for only a few hours. Death occurs approximately 1 hr after treatment (Tucker, 1968).1/

Antidote - In rats atropine alone or in combination with N-methylpyridine-2-aldoxime methane-sulphonate (P25) or (bis-(4 hydroxyiminomethyl pyridinium-1-methyl) ether dichloride (obidoxime) is antidotal. (Natoff and Reiff, 1970).

Accidents

Crotoxyphos has not been associated with accidental exposure to man or the environment to any significant degree. Preliminary data from the EPA Pesticide Episode Review System (PERS) reported in 1973 that crotoxyphos was not cited in episodes involving humans, animals, plants and area contamination. The computerized PERS data base, which generally includes data for 1972 through early 1974, lists a total of three episodes involving crotoxyphos. One of these episodes involved potential human exposures to three pesticides (including crotoxyphos); the other two were associated with warehouses in flooded areas.

1/ Tucker, R., "Ciodrin," Internal Report Series in Pharmacology, Denver Wildlife Research Center, Division of Environmental Research, (Nov. 15, 1968).

References

Ben-Dyke, R., D. M. Sanderson, and D. Noakes, "Acute Toxicity Data for Pesticides," World Review of Pest Control, 9(3):119-127 (1970).

Beynon, K. I., D. H. Hutson, and A. N. Wright, "The Metabolism and Degradation of Vinyl Phosphate Insecticides," Residue Rev., 47:96-101 (1973).

Chamberlain, W. F., "The Metabolism of ^{32}P Labelled Shell SD-4294 in a Lactating Ewe," J. Econ. Entomol., 57:119 (1964).

Dean, B. J., "The Mutagenic Effects of Organophosphorus Pesticides on Micro-Organisms," Arch. Toxicol., 30:67-74 (1972).

Doyle and Elsea, Hilltop Research, EPA Pesticide Petition No. 9F0770 (1966).

Flockhart, Jan R., and J. E. Casida, "Relationship of the Acylation of Membrane Esterases and Protein to the Teratogenic Action of Organophosphorus Insecticides and Eserine in Developing Hen Eggs," Biochem. Pharmacol., 21:2591-2603 (1972).

Gaines, Thomas B., "Acute Toxicity of Pesticides," Toxicol. Appl. Pharmacol., 14(3):515-534 (1969).

Greer, N. I., M. J. Janes, and D. W. Beardsley, "Toxicity of Crotoxyphos Insecticide to Brahman and Crossbred Yearling Steers," Fla. Ent., 56:243-250 (1973).

Ivie, G. W., L. R. Green, and H. W. Dorough, "The Use of Sodium Bicarbonate - C14 to Determine Cholinesterase Activity," Bull. Environ. Contam. Toxicol., 2(1):34-40 (1967).

Knapp, F. W., J. H. Drudge, and Eugene Lyons, "Toxic Effect of Ciodrin and Dichorvos Applied Topically to Horses and Their Efficacy Against Internal Parasites," J. Econ. Entomol., 60(2):330-332 (April 1967).

Macklin, A. W., and W. E. Ribelin, "Relation of Pesticides to Abortion in Dairy Cattle," J. Amer. Vet. Med. Assoc., 159:1743-48.

Natoff, I. L., and B. Reiff, "Quantitative Studies of the Effect of Antagonists on the Acute Toxicity of Organophosphates in Rats," Brit. J. Pharmac., 40:124-134 (1970).

Oehler, D. D., and H. V. Claborn, "Determination of Crotoxyphos in Milk and in Body Tissues of Cattle and Pigs," J. Assoc. Official Agr. Chem., 53:1045 (1970).

Palmer, J. S., and J. W. Danz, "Tolerance of Brahman Cattle of Organic Phosphorus Insecticides," J. Amer. Vet. Med. Assoc., 144(2):145 (1964).

Palmer, J. S., and J. C. Schlinke, "Toxicologic Effects of Two Crotoxyphos Formulations on Pigs," J. Econ. Entomol., 64(3):1971 (1971).

Palazzolo, R., Industrial Bio-Test Laboratories, EPA Petition No. 9F0770 (1963).

Roger, Jean-Claude, G. David Upshall, and J. E. Casida, "Structure-Activity and Metabolism Studies on Organophosphate Teratogens and Their Alleviating Agents in Developing Hen Eggs With Special Emphasis on Bidrin," Biochem. Pharmacol., 18:373-392 (1968).

Sherman, M., E. Ross, and M. T. Y. Chang, "Acute and Subacute Toxicity of Several Insecticides to Chicks," Toxicol. Appl. Pharmacol., 7:606-608 (1965).

Shellenberger and Newell, Stanford Research Institute, EPA Pesticide Petition No. 9F0770 (1961).

Simelskii, M. A., "The Toxicity of Ciodrin for Warmblooded Animals and Arthropods," TR Vses. Nauchno-Issled. Inst. Vet. Sanit. (1970).

Singh and Fireoved, Bio-Toxicological Research Associates, EPA Pesticide Petition No. 9F0770 (1964).

Tucker, R., "Ciodrin," Internal Report Series in Pharmacology, Denver Wildlife Research Center, Division of Environmental Research, (Nov. 15, 1968).

Vorobieva, N. M., and V. S. Lapchenko, "Toxicity and Hygienic Standardization of Ciodrin Pesticide," Gigiyena I Santariya, Moscow, 38(6):30-33 (1973).

Weidenbach, Carl P., and R. L. Younger, "The Toxicity of Dimethyl 2-(alpha-methylbenzyloxycarbonyl)-1-methylvinyl phosphate (Shell Compound 4294) to Livestock," J. Econ. Entomol., 55(5):793 (1962).

Witherup and Schlecht, Kettering Laboratory, EPA Pesticide Petition No. 9F0770 (1964, 1962).

Witherup and Ushry, Kettering Laboratory, EPA Pesticide Petition No. 9F0770 (1965).

PART II. INITIAL SCIENTIFIC REVIEW

SUBPART C. FATE AND SIGNIFICANCE IN THE ENVIRONMENT

CONTENTS

This section contains data on the environmental effects of crotoxyphos, including effects on aquatic species, wildlife and beneficial insects, interactions with lower terrestrial organisms and effects on residues in soil, water and air. The section summarizes rather than interprets scientific data reviewed.

Effects on Aquatic Species

Fish -

Laboratory Studies - The toxicity of crotoxyphos to fish has been evaluated and the results are summarized in Table 15.

Field Studies - Reports were not found on the effects of crotoxyphos on fish under field conditions.

Commercial labels of crotoxyphos-containing formulations state that the product is toxic to fish and warn against contaminating water by runoff, cleaning of equipment, disposal of wastes, or other means.

Lower Aquatic Organisms - The toxicity of crotoxyphos to estuarine animals was studied in 1966 at the biological laboratory at Gulf Breeze, Florida, which at that time belonged to the U.S. Bureau of Commercial Fisheries (Lowe, 1966).1/ Brown shrimp (*Penaeus aztecus*) were exposed for 48 hr to crotoxyphos concentrations ranging from 0.001 to 1.0 ppm in natural flowing seawater at a temperature of 68°F, salinity of 31%. The EC_{50} in ppm was determined by percent mortality or paralysis of the shrimp at the end of the observation period. Under these experimental conditions, the following EC_{50} levels were determined for crotoxyphos:

24 hr exposure - 0.20 ppm
48 hr exposure - 0.032 ppm

In 1965 at the same laboratory, the effects of crotoxyphos on the Eastern oyster, (*Crassostrea virginica*), were tested at a temperature of 82°F and salinity of 28%. Possible decrease in shell deposition during a 96-hr exposure period was observed as an indicator of adverse effects. At the highest rate tested, 1.0 ppm, crotoxyphos did not aversely affect the Eastern oyster under these experimental conditions.

1/ Lowe, J. I., "Bioassay Screening Test-Ciodrin," Bureau of Commercial Fisheries Biological Laboratory, Gulf Breeze, Florida (unpublished data, 1966).

Table 15. ACUTE AND SUBACUTE TOXICITY OF TECHNICAL CROTOXYPHOS TO FISH

Specie	Exposure time (hr)	Toxicity measure	Toxicity value (ppb)	References
Sheepshead minnow	24	EC_{50}	> 1 ppm	a/
(*Cyprinodon variegatus*)	48	EC_{50}	> 1 ppm	
Bluegill (1.1 g)	24	LC_{50}*	390	b/
(*Lepomis macrochirus*)			(338-450)	
	96	LC_{50}	152	
			(126-183)	
Channel catfish (1.1 g)	24	LC_{50} ≠	3,700	b/
(*Ictalurus punctatus*)	96	LC_{50}	2,600	
Cutthroat trout (1.0 g)	24	LC_{50} ≠	92	b/
(*Salmo clarki*)			(49-170)	
	96	LC_{50}	51	b/
			(28-94)	
Rainbow trout (1.0 g)	24	LC_{50}*	101	b/
(*Salmo gairdneri*)			(82.4-124)	
	96	LC_{50}	72.4	b/
			(60.0-87.4)	
Fathead minnow (1.03 g)	24	LC_{50}*	15,500	b/
(*Pimephales promelas*)			(12,800-18,700)	
	96	LC_{50}	11,900	b/
			(9,830-14,400)	
Largemouth bass (0.65 g)	24	LC_{50}**	1,800	b/
(*Micropterus salmoides*)	96	LC_{50}	1,100	

* At 17°C, pH 7.1.
≠ At 18°C, pH 7.1.
≠ At 13°C, pH 7.1.
** At 18°C, pH 7.75.
a/ Lowe, *op. cit.* (1966).

b/ Johnson, W. W., "Toxicity of Ciodrin to Select Species of Fish and Invertebrates," unpublished data, Fish-Pesticide Research Laboratory, Fish and Wildlife Service, U.S. Department of the Interior, Columbia, Missouri (undated).

The Fish-Pesticide Research Laboratory, Bureau of Sport Fisheries and Wildlife, (1974),[1/] studied the effects of crotoxyphos on the scud (Gammarus spp.), and the stonefly (Pteronarcys spp.). Scuds were exposed for 48 hr at 60.8°F, pH 7.4, 35 mg/liter alkalinity, and 40 mg/liter hardness. Under these conditions, the reported LC_{50} was 10 to 100 μg/liter at 24 as well as at 48 hr. Stoneflies were exposed for 96 hr under the same test conditions as in the Gammarus studies. The LC_{50} was 1.0 to 10.0 μg/liter at 24 hr and at 96 hr.

Additional observations on the toxicity of crotoxyphos to scuds, (Gammarus lacustris), were reported by Sanders (1969).[2/] In static bioassay tests, mature scuds were exposed for 96 hr at 70°F in test water at pH 7.1, containing 88.0 ppm total dissolved solids, 30.0 ppm total alkalinity, 7.1 ppm calcium, and 3.1 ppm magnesium. The LC_{50} of crotoxyphos was 49 μg/liter at 24 hr, 29 μg/liter at 48 hr, and 15 μg/liter at 96 hr. The corresponding 95% confidence limits were 36 to 67, 21 to 41, and 14 to 20 μg/liter, respectively.

Butler (1964)[3/] reported that there was decrease in productivity of natural phytophlankton communities during a 4-hr exposure to a concentration of 1.0 ppm of Ciodrin.

Effects on Wildlife

The oral LD_{50} for 3-to-4 month old mallard drakes (Anas platyrhynchos) is 790 mg/kg with 95% confidence limits of 411-1520 mg/kg (Tucker and Crabtree, 1970).[4/]

Commercial labels of insecticides containing crotoxyphos as active ingredient contain the caution statement: "This product is toxic to fish and wildlife. Apply this product only as specified on this label."

1/ Fish-Pesticide Research Laboratory, Bureau of Sport Fisheries and Wildlife, U.S. Department of the Interior, Columbia, Missouri. Unpublished Laboratory Bioassay Screening Test Data (1974).

2/ Sanders, H. O., "Toxicity of Pesticides to the Crustacean Gammarus lacustris," Technical Paper No. 25, pp. 18, U.S. Department of the Interior, Fish and Wildlife Service (1969).

3/ Butler, P. A., "Fishery Investigation," Pesticide-Wildlife Studies, 1963, U.S. Fish Wildl. Serv. Circ., 199:5-28 (1964).

4/ Tucker, R. K., and D. G. Crabtree, Handbook of Toxicity of Pesticides to Wildlife, Bureau of Sport Fisheries and Wildlife, Denver Wildlife Research Center, Resource Publication No. 84 (1970).

Effects on Beneficial Insects

Atkins et al. (1973)1/ summarized the results of toxicity tests in which a large number of pesticides and other agricultural chemicals were studied in regard to their effects on the honeybee, (*Apis mellifera*). In a laboratory procedure which primarily measures a chemical's contact effect, pesticides were applied in dust form to groups of 25 bees per test dose, three replicates per each of three colonies, for a total of nine replicates per test dose. The procedure permits determination of an LD_{50} value for each pesticide in micrograms of chemical per bee.

Honeybees were exposed to crotoxyphos for 48 hr at 80°F and 65% relative humidity. Under these test conditions, the LD_{50} of crotoxyphos was 2.26 µg per bee, placing it into Group II, "Moderately Toxic to Honeybees." Anderson et al. (1971)2/ define moderate honeybee toxicity as "able to be used around bees if dosage timing, and method of application are correct; direct application should not be made to exposed bees in the field or at the colonies."

In their test procedure, Atkins et al. (1973) also determined the slope of the dosage-mortality curve for each pesticide tested and recorded it as a "slope value" in terms of probit units. Pesticides with a slope value of four probits or higher can often be made safer to honeybees by lowering the dosage only slightly. Conversely, by increasing the dosage only slightly, the pesticide can become highly hazardous to bees. Crotoxyphos rated an unusually high "slope value" of 17.10, indicating that small changes in dosage rate would produce large changes in bee toxicity.

However, since honeybees do not usually search on or near livestock, the only environment where crotoxyphos is registered for use, its toxicity to honeybees (or lack thereof) is of limited significance.

Axtell (1966)3/ studied the toxicities of several insecticides including crotoxyphos to housefly (*Musca domestica*) larvae and to a mite predator of the housefly (*Macrocheles muscaedomestica*).

1/ Atkins, E. L., E. A. Greywood, and R. L. Macdonald, *Toxicity of Pesticides and Other Agricultural Chemicals to Honeybees*, University of California, Agricultural Extension Report M-16, 37 pp. (1973).

2/ Anderson, L. D., E. L. Atkins, Jr., H. Nakakihara, and E. A. Greywood, *Toxicity of Pesticides and Other Agricultural Chemicals to Honey Bees*, University of California, Agricultural Extension Service, Riverside, Calif. (1971).

3/ Axtell, R. C., "Comparative Toxicity of Insecticides to Housefly Larvae and *Macrocheles muscaedomestica*, a Mite Predator of the Housefly," *J. Econ. Entomol.*, 59(5):1128-1130 (1966).

Predaceous mites of the family Macrochelidae are common in the manure of dairy cattle and poultry where the housefly often breeds. The mites prey on the eggs and first-instar larvae of the housefly and are important biological agents in suppressing fly populations. Thus, they are important elements in the development of integrated housefly management programs.

Adult female Macrocheles muscaedomestic and third-instar larvae of the housefly were exposed to the test insecticides incorporated into CSMA fly rearing medium. Crotoxyphos was used in the form of an emulsifiable concentrate. Three replications of each of five or six concentrations of an insecticide were tested on day 1. This procedure was repeated on given days. Each concentration-mortality curve is based on the combined results of 9 to 12 replications. Concentrations are expressed in wt/wt percent. Dosage-mortality regression lines were determined by probit analysis with the maximum likelihood procedure.

Results obtained for crotoxyphos were as follows:

	LC_{50}	95% Confidence limits	Slope
Fly larvae	0.018%	0.014-0.022%	1.045
Mites	0.016%	0.015-0.018%	3.125

Ratio of fly: mite LC_{50} 1:1; LC_{95} 12:1.

Thus, crotoxyphos was relatively more toxic to the mites than to the fly larvae. Axtell points out that extrapolation from the laboratory results to the field is complicated by several factors, including longer exposure periods, exposure of additional stages of the mites and flies, interactions between the manure and the insecticide, and fluctuating environmental conditions.

In a follow-up experiment, Axtell (1968)[1/] studied the populations of housefly larvae and predaceous mites in poultry manure after larvicide treatment under field conditions, i.e., after application of 12 insecticides (including crotoxyphos) to the manure under caged laying hens.

1/ Axtell, R. C., "Integrated Housefly Control: Populations of Fly Larvae and Predaceous Mites, Macrocheles muscaedomesticae, in Poultry Manure After Larvicide Treatment," J. Econ. Entomol., 61(1):245-249 (1968).

Each treatment was replicated four to six times. The numbers of adult mites and third-instar housefly larvae were counted before and at intervals after treatment.

Crotoxyphos was applied at a concentration of 1.0% by sprinkling can at the rate of 0.5 liter/m^2 to manure 60 cm deep. Mean numbers of mites and fly larvae per sample were as follows:

	Pretreatment	Days after treatment	
		5	13
Mites	37.1	38.3	25.6
Fly larvae	32.3	70.6	2.8

As indicated by these data, crotoxyphos had little effect on the mite population, and no adverse effect on the fly population 5 days after treatment. According to the Axtell, the decline in fly larvae 13 days after treatment was probably due to causes other than the insecticide treatment.

In a second experiment, crotoxyphos was again applied at a concentration of 1.0% by sprinkling can at the rate of 0.5 liter/m^2 this time to manure 5 cm deep. Numbers of mites and fly larvae were determined at intervals of 5 to 30 days after treatment. Results in this test (mean numbers of mites or fly larvae per sample) were as follows:

	Pretreatment	Days after treatment			
		5	14	21	30
Mites	143.0	60.3	109.9	32.4	66.8
Fly larvae	137.0	115.0	90.4	114.0	131.0

Interactions with Lower Terrestrial Organisms

Reports were not found on the effects of crotoxyphos on lower terrestrial organisms, or on the effects of such organisms on the insecticide.

Residues in Soil

Laboratory Studies - Konrad and Chesters (1969)1/ studied the degradation of crotoxyphos in three different soils, Poygan silty clay loam (33.6% clay; 10.0% organic matter; pH 7.2); Kewaunee clay (48.7% clay, 3.8% organic matter; pH 6.4); and Ella loamy sand (5.2% clay; 1.6% organic matter; pH 3.8). Analytical grade and ^{14}C-labeled crotoxyphos were used. Samples were extracted with benzene. Gas chromatography was used to verify that the ^{14}C-activity extracted arose entirely from crotoxyphos. Presence of water-soluble degradation products was determined as the difference between total and benzene-extractable ^{14}C-activity.

The half-lives of crotoxyphos in hours were as follows:

	Nonsterile	Sterile
Poygan silty clay loam	2.00	3.75
Kewaunee clay	5.50	6.00
Ella loamy sand	71.0	77.0

The degradation rates followed first-order kinetics and were related to the extent of initial insecticide adsorption by the soils. In each of the three soils, the degradation rate was somewhat slower in the electron beam-sterilized soils but this was due to decreased crotoxyphos adsorption resulting from the irradiation treatment, rather than from retardation of microbial degradation processes. The first-order rate constants for degradation of crotoxyphos were directly related to adsorption and were the same for sterile and nonsterile soils for constant adsorption in a given soil. Between soils, even at constant adsorption, the rates

1/ Konrad, J. G., and G. Chesters, "Degradation in Soils of Ciodrin, an Organophosphate Insecticide," J. Agr. Food Chem., 17(2):226-230 (1969).

of crotoxyphos degradation were variable. The high acidity of the Ella soil may have retarded the rate of degradation.

Further studies by Konrad and Chesters (1969) concerning the pathways of chemical breakdown of crotoxyphos indicated that dimethylphosphorice acid, cis-hydroxycrotonic acid, and 1-phenylethanol are the major degradation products of crotoxyphos breakdown in soils.

Getzin and Rosefield (1968)1/ studied the effects of a heat-labile substance in soil on the degradation of crotoxyphos and several other organophosphate insecticides. Chehalis clay loam was sterilized by gamma radiation, heat, or a combination of the two methods, in 4-oz prescription bottles, each containing 10 cc of moist soil. Crotoxyphos was then applied at rates of 15 to 25 μg/cc of soil with sufficient water to maintain the soil samples at their moisture equivalent. The bottles were then capped and agitated to distribute the insecticide throughout the soil, and samples were kept at 25°C for the desired periods of time before extracting the pesticide residues. After extraction by appropriate solvents and procedures, insecticide residues were measured by GLC.

Crotoxyphos, along with two other insecticides, was among the least stable compounds tested. After an incubation period of 1 day, 4% of the initial quantity of crotoxyphos were degraded in the autoclaved soil; 34% in the irradiated soil; and 87% in the nonsterile soil. All insecticides studied degraded more rapidly in nonsterile than in the heat- or irradiation-sterilized soils, suggesting that microorganisms were partlv responsible for degradation. With only one exception, all insecticides studied, including crotoxyphos, degraded more rapidly in the irradiated than in the heat-sterilized soil. The authors suggest that this may be due to the action of a heat-labile, nonviable, water-soluble substance. Further studies were performed to characterize this substance, and it was determined that it was destroyed by heating soil suspensions for 10 min at 90°C but most of its activity was retained in soils held at 25°C for 2 to 3 months after radiation sterilization.

1/ Getzin, L. W., and I. Rosefield, "Organophosphorus Insecticide Degradation by Heat-Labile Substances in Soil," J. Agr. Food Chem., 16(4):598-601 (1968).

Helling et al. (1971)[1] offer an interesting alternate explanation for the observations reported by Getzin and Rosefield (1968). They point out that there exists yet another mechanism of pesticide degradation in soils which may be influenced by different soil sterilization techniques, i.e., the reaction of pesticides with free radicals in the soil. Free radical content in the soil is reduced by autoclaving, but increased by gamma irradiation. Thus, the results reported by Getzin and Rosefield might have been due to the creation of more highly reactive free radicals by soil irradiation. These radicals would be destroyed by high temperature and therefore appear to be "heat-labile." According to Helling et al. (1971), Konrad and Chesters (1969) did not compare the degradation of crotoxyphos in autoclaved versus irradiation-sterilized soils, but the rates of crotoxyphos degradation which they reported for the sterile soils may also have been promoted by the free radical process.

Field Studies -

Reports were not found on field studies dealing with crotoxyphos residues in soil.

1/ Helling, C. S., P. C. Kearney, and M. Alexander, "Behavior of Pesticides in Soils," Advances in Agronomy, 23:147-240 (1971).

Monitoring Studies -

Since the results of the 1972 National Monitoring Program for pesticides has not yet been published, data from this source could not be included. No other monitoring studies of crotoxyphos were found.

Residues in Water

Konrad and Chesters (1969) reported the following half-life values for the hydrolysis of crotoxyphos in water: 540 hr at pH 2.0; 410 hr at pH 6.0; 180 hr at pH 9.0. This data shows that hydrolysis is faster in alkali than in near-neutral solution and/or acid solutions. (Temperature was not specified.) The solution pH values were adjusted with hydrochloric acid or sodium hydroxide, and apparently were not buffered. Beynon et al. (1973)[1/] point out that these half-lives are considerably longer than those found in contact with soil. Porter (1967)[2/] studied the hydrolysis of crotoxyphos at 38°C and found that hydrolysis was moderately rapid under alkaline or strongly acid conditions.

Shell Chemical Company (1972)[3/] states that crotoxyphos decomposes moderately fast in the presence of water, and that its half-life in aqueous solution at 100°F ranged from 35 hr at pH 9 to 87 hr at pH 1 (these values are apparently taken from Porter, 1967).

Residues in Air

No other data on the presence, fate, or persistence of crotoxyphos in air was found.

Residues in Nontarget Plants

Reports were not found on the possible effects of crotoxyphos on nontarget plants or on the occurrence of residues in such plants.

Bioaccumulation, Biomagnification

Reports were not found on the possible bioaccumulation or biomagnification of crotoxyphos.

1/ Beynon, K. I., D. H. Hutson, and A. N. Wright, "The Metabolism and Degradation of Vinyl Phosphate Insecticides," Residue Rev. 47:55-142 (1973).

2/ Porter, P. E., "Ciodrin® Insecticide," In: G. Zweig (ed.): Analytical Methods for Pesticides, Plant Growth Regulators, and Food Additives, Vol. V, p. 243. Academic Press, Inc., New York (1967).

3/ Shell Chemical Company, "Summary of Basic Data for Technical Ciodrin Insecticide," Agr. Division, Technical Data Bulletin ACD:62-1, San Ramon, Calif. (1972).

Environmental Transport Mechanisms

No data was found on environmental transport mechanisms of crotoxyphos.

However, there is one related report in this area. Sun (1971)[1/] suggested relationships between the speed of action of insecticides on the housefly (Musca domestica), and the occurrence of residues in fat and milk. Organophosphate insecticides generally act faster than organochlorine insecticides on insects and other animals. Differences in respective rates of penetration and detoxication determine the speed of action. Sun points out that an unstable, quick-penetrating insecticide would show little difference in LC_{50} values between short-and long-time exposures. He used the ratio of the LC_{50} values between 3 hr and 22 hr exposure as an index for the speed of action. When crotoxyphos was tested on houseflies by a residue-file method, its LC_{50} (μg/jar) was 5.5 for an exposure period of 3 hr; 4.6 for 22-hr exposure, resulting in a "speed index" of 1.2. This value is at the lower end of the scale for organophosphate insecticides. The "speed indices" of the 36 organophosphates insecticides tested in this manner ranged from 0.93 to 3.5.

1/ Sun, Y. P., "Speed of Action of Insecticides and Its Correlation with Accumulation in Fat and Excretion in Milk," J. Econ. Entomol., 64(3):624-630 (1971).

References

Anderson, L. D., E. L. Atkins, Jr., H. Nakakihara, and E. A. Greywood, Toxicity of Pesticides and Other Agricultural Chemicals to Honeybees, University of California, Agricultural Extension Service, Riverside, Calif. (1971).

Atkins, E. L., E. A. Greywood, and R. L. Macdonald, Toxicity of Pesticides and Other Agricultural Chemicals to Honeybees, University of California, Agricultural Extension Report M-16, 37 pp. (1973).

Axtell, R. C., "Comparative Toxicity of Insecticides to Housefly Larvae and Macrocheles muscaedomestica, a Mite Predator of the Housefly," J. Econ. Entomol., 59(5):1128-1130 (1966).

Axtell, R. C., "Integrated Housefly Control: Populations of Fly Larvae and Predaceous Mites, Macrocheles muscaedomesticae, in Poultry Manure After Larvicide Treatment," J. Econ. Entomol., 61(1):245-249 (1968).

Beynon, K. I., D. H. Hutson, and A. N. Wright, "The Metabolism and Degradation of Vinyl Phosphate Insecticides," Residue Rev. 47:55-142 (1973).

Butler, P. A., "Fishery Investigations," Pesticide - Wildlife Studies, 1963, U.S. Fish. Wildl. Serv. Circ., 199:5-28 (1964).

Fish-Pesticide Research Laboratory, Bureau of Sport Fisheries and Wildlife U.S. Department of the Interior, Columbia, Missouri. Unpublished Laboratory Bioassay Screening Test Data (1974).

Getzin, L. W., and I. Rosefield, "Organophosphorus Insecticide Degradation by Heat-Labile Substances in Soil," J. Agr. Food Chem., 16(4):598-601 (1968).

Helling, C. S., P. C. Kearney, and M. Alexander, "Behavior of Pesticides in Soils," Advances in Agronomy, 23:147-240 (1971).

Johnson, W. W., "Toxicity of Ciodrin to Select Species of Fish and Invertebrates," unpublished data, Fish-Pesticide Research Laboratory, Fish and Wildlife Service, U.S. Department of the Interior, Columbia, Missouri (undated).

Konrad, J. G., and G. Chesters, "Degradation in Soils of Ciodrin, an Organophosphate Insecticide," J. Agr. Food Chem., 17(2):226-230 (1969).

Lowe, J. I., "Bioassay Screening Test-Ciodrin," Bureau of Commercial Fisheries Biological Laboratory, Gulf Breeze, Florida (unpublished data, 1966).

Porter, P. R., "Ciodrin® Insecticide," In: G. Zweig (ed.): Analytical Methods for Pesticides, Plant Growth Regulators, and Food Additives, Vol. V, p. 243. Academic Press, Inc., New York (1967).

Sanders, H. O., "Toxicity of Pesticides to the Crustacean Gammarus lacustris," Technical Paper No. 25, pp. 18, U.S. Department of the Interior, Fish and Wildlife Service (1969).

Shell Chemical Company, "Summary of Basic Data for Technical Ciodrin Insecticide," Agr. Division, Technical Data Bulletin ACD:62-1, San Ramon, California (1972).

Sun, Y. P., "Speed of Action of Insecticides and Its Correlation with Accumulation in Fat and Excretion in Milk," J. Econ. Entomol., 64(3):624-630 (1971).

Tucker, R. K., and D. G. Crabtree, Handbook of Toxicity of Pesticides to Wildlife, Bureau of Sport Fisheries and Wildlife, Denver Wildlife Research Center, Resource Publication No. 84 (1970).

PART II. INITIAL SCIENTIFIC REVIEW

SUBPART D. PRODUCTION AND USE

CONTENTS

This section contains information on the registration status, and on the production and uses of crotoxyphos. The section summarizes rather than interprets data reviewed.

Registered Uses of Crotoxyphos

Federally Registered Uses - Crotoxyphos is an organic phosphate insecticide that acts as a contact and stomach poison. By virtue of its spectrum of insecticidal effectiveness and relatively "moderate" mammalian toxicity, it is useful for the control of external parasites on livestock, including flies, lice, and ticks. The chemical's potential as an insecticide was first recognized about 1960 by the Shell Chemical Company. It progressed through various research and development stages and has been commercially available as a livestock insecticide since the mid-1960's.

The registered uses of crotoxyphos by principal formulations, animal species, established tolerances, dosage rates, and use limitations are outlined below.[1/]

Crotoxyphos is registered and recommended for use on beef cattle, dairy cattle, goats, sheep, and swine, and for the treatment of agricultural premises including barns, dairy barns, fences, fly breeding areas, and other farm buildings except poultry houses. The product is available in a number of different formulations, as outlined in greater detail in the subsection on formulations (page 23). Crotoxyphos is used on animals as a spray or fog in water or in oil, or as a dust.

On beef and dairy cattle, crotoxyphos may be used as follows:

1. 1.0% active ingredient in water at the rate of 1 to 2 pints per adult animal (proportionately less for smaller animals); may be repeated, but not more often than every 7 days. Concentration and volume per animal may be varied inversely; for instance, 0.5% active ingredient may be applied at the rate of 1 to 2 quarts per animal; 0.25% active ingredient at up to 1 gal per animal; 0.1% active ingredient at up to 2 gal per animal.

1/ U.S. Environmental Protection Agency, EPA Compendium of Registered Pesticides, Vol. III, p. D 46.1-D 46.3.

2. 2.0% active ingredient in water may be applied daily at the rate of 1 to 2 oz per animal.

3. 1.0% active ingredient in water may be applied up to three times per week at the rate of 15 teaspoonfuls sprayed to face and a total of 5-10 teaspoonfuls sprayed to back and sides of animal.

4. 1.0% active ingredient in oil may be applied as a spray at the rate of 3.5 fluid ounce per animal, two applications at 14-day intervals; as a spray at the rate of 2 fluid ounce per animal daily; or by back rubbers, without time limitations.

5. Dust containing 3% active ingredient may be used at the rate of one to two heaping tablespoonfuls per animal on poll, back and upper portions of sides, not more often than every 2 weeks; or as a thorough treatment of the entire animal (for louse control), not to be repeated within less than 3-to-4 weeks (this treatment not permitted on calves under 6 months of age); or by way of dust bags suspended in livestock holding pens, feedlots, loafing sheds, near mineral or salt licks, and in alleyways leading to and from animal buildings or dairy farms; without time limitations.

The following use patterns are registered for use on goats, sheep, and swine:

1. 1.0% active ingredient in water at the rate of 1 pint per animal per application, not to be repeated in less than 7 days. For this use pattern, concentration and volume of spray per animal are somewhat interchangeable; 0.5% active ingredient in water may be applied at the rate of 1 quart per animal per application; or 0.25% at up to 1 gal. of spray per animal; or up to 2 gal. per animal of 0.1% spray.

2. 1.0% active ingredient in water may be applied at the rate of 15 teaspoonfuls to the face and a total of 5 to 10 teaspoonfuls to back and sides of animals, to be repeated not more than three times per week.

3. 0.25% active ingredient in oil may be applied (to swine only) at the rate of 1 fluid ounce per animal, without time limitations.

4. Dusts containing 3% active ingredient may be applied to swine at the rate of 1 to 2 oz as thoroughly as possible, especially to the neck and area around the ears, to be repeated in 3 to 4 weeks if necessary.

For the control of pest insects in and around agricultural premises, crotoxyphos is registered and recommended as follows:

1. 1.0% active ingredient as an aqueous spray at the rate of 1 gal per 1,000 ft^2 of surface area.

2. 0.25% in oil as a fog, at the rate of about 2 fluid ounces per 1,000 ft^2 (not to be applied in areas where animals have been directly treated with DDVP within the last 8 hr).

Crotoxyphos by itself is not registered for use as a livestock dip, for use on poultry, in poultry houses, nor for use on pets, based on information provided by the basic producer, Shell Chemical Company. For an overview of the economically and ecologically most important registrations, including dosage rates, general and specific directions for use, types of equipment, use limitations, caution statements, and other details pertinent to commercial use, specimen labels for two typical crotoxyphos liquid formulations are included in this section, i.e., a dairy spray concentrate containing 21.5% crotoxyphos for dilution with water, as illustrated in Table 16, and a ready-to-use oil base dairy spray containing 1.0% crotoxyphos and a 0.23% DDVP (dichlorvos), as illustrated in Table 17.

Tolerances established for residues of crotoxyphos are recorded in the Code of Federal Regulations, Title 40, Part 180.280. Tolerances have been established for meat, fat and meat by-products of cattle, goats, hogs, and sheep, and for milk.

Several regional formulators combine crotoxyphos with other insecticides. Among these combinations, crotoxyphos with DDVP at the ratio of four parts of crotoxyphos to one part of DDVP is most widely used. Crotoxyphos-DDVP combination formulations are generally registered and recommended for the same insect control purposes as crotoxyphos by itself. The DDVP component provides more rapid extermination of target insects.

At least one brand label of an emulsifiable concentrate formulation of crotoxyphos containing 14.4% of active ingredient includes recommendations for the control of stable flies on horses (Roberts Laboratories, Inc., Rockford, Illinois 61101).

At least one ready-to-use crotoxyphos (1.0%)-DDVP (0.25%) combination formulation in oil is recommended not only for use on dairy and beef cattle, but also for the control of flies, gnats, mosquitoes, fleas, and brown dog ticks in kennels; as a spray to be applied outside of dog runways, window sills and ledges (but not on dogs directly); and against maggots breeding in garbage dumps, manure piles, and other breeding areas.

Table 16. CROTOXYPHOS 21.5% SPRAY CONCENTRATE LABEL

HOW TO USE PURINA DAIRY SPRAY CONCENTRATE

For Dairy Cattle—Beef Cattle—Sheep—Goats—Hogs

For Control of Stable Flies, House Flies, Horn Flies, and Face Flies on Dairy and Beef Cattle:
Using low pressure equipment (compression sprayer, knapsack sprayer)—Mix 1 pint of Dairy Spray Concentrate in 2½ gallons of water (½ oz. per gallon). Spray to thoroughly cover all parts of the animal, including the legs, using 1 to 2 pints of spray per large animal and proportionately less for small animals.
Using high pressure equipment (hydraulic sprayer for pen or corral operations)—Mix 1 pint of Dairy Spray Concentrate in 5 gallons of water. Spray to thoroughly cover the animal's body and legs (avoid excessive spraying of the head) using 1 to 2 quarts of spray per large animal and proportionately less for smaller animals.
Repeat above application as necessary to maintain control, but not more often than once every 7 days for either low or high pressure equipment.
To improve face fly control, add ½ pound of sugar per 5 gallons of spray.
Using hand atomizer sprayer—Mix 3 oz. (6 tablespoonfuls) of Dairy Spray Concentrate per quart of water. Spray to thoroughly cover all parts of the animal, including the legs. Use 1-2 fluid ounces of spray per animal daily. To improve face fly control, add 2 level tablespoons of sugar per quart of spray.
For Control of Lice, Lone Star Ticks, and Winter Ticks on Dairy Cattle, Beef Cattle, Sheep, Goats and Hogs: Mix 1 pint of Dairy Spray Concentrate in 10 gallons of water. Spray animals thoroughly using up to 1 gallon of spray per large animal and proportionately less for smaller animals. Apply a second application 14 days later. Repeat applications as necessary to maintain control.
For Cattle Rubbing Devices: For the control of horn flies and face flies: Mix 1 pint of Dairy Spray Concentrate in 3 gallons of #2 fuel oil or diesel fuel oil. Install rubbing devices in areas where the animals loaf, feed, or water.
WARNING: HAZARDOUS IF SWALLOWED, INHALED, OR ABSORBED THROUGH SKIN. Hazardous or fatal if swallowed. If swallowed, induce vomiting. Call a physician immediately. Vapor harmful. Hazardous if absorbed through the skin. Atropine is antidotal.

Wash thoroughly with soap and water after handling and before eating and smoking. Wear clean clothing. In case of spillage on person or clothing, immediately remove clothing and flush skin or eyes with plenty of water; for eyes get medical attention. Keep away from heat and open flame.

Do not apply regularly to calves under 6 months of age. Brahman cattle should not be treated as they may show hypersensitivity to organic phosphate. Do not contaminate feed, foodstuffs, or drinking water. During commercial or prolonged exposure in spray-mixing and loading operations, wear clean synthetic rubber gloves and a mask or respirator of a type approved by the U. S. Bureau of Mines for protection against Ciodrin* Insecticide. Use this material only for recommended purposes and at recommended dosages.

This product is toxic to fish and wildlife. Apply this product only as specified on this label.

Rinse equipment and containers and dispose of wastes and soil contaminated by spillage by burying in non-crop lands away from water supplies. Containers should be disposed by punching holes in them and burying with wastes.

DO NOT USE, POUR, SPILL OR STORE NEAR HEAT OR OPEN FLAME

7110H D-2532 EPA Est. 602—MO-1 Printed in U.S.A.

QUALITY CONTROLLED BY PURINA RESEARCH

NET CONTENTS: 16 FL. OZ. (1 PT.) E.P.A. Reg. No. 602-101-AA

CONTAINS "CIODRIN"* INSECTICIDE

NEW FORMULA

PURINA® DAIRY SPRAY Concentrate®

1 PINT MAKES UP TO 10 GALLONS OF SPRAY

FOR CONTROL OF: FACE FLIES—STABLE FLIES—HORN FLIES—HOUSE FLIES—LICE—LONE STAR TICKS—WINTER TICKS

Active Ingredients:	
Dimethyl phosphate of alpha-methylbenzyl 3-hydroxy-cis-crotonate	21.5%
Xylene	67.4%
Inert Ingredients	11.1%
	100.0%

*Reg. T. M. Shell Chemical Company

WARNING: KEEP OUT OF REACH OF CHILDREN
SEE OTHER WARNINGS ON BACK PANEL

Manufactured by **RALSTON PURINA COMPANY**
GENERAL OFFICES • CHECKERBOARD SQUARE • ST. LOUIS, MO. 63188

Source: Label for "Purina Dairy Spray Concentrate"
EPA Reg. No. 602-101-AA (1 pint container)
Ralston Purina Company, St. Louis, Missouri

Table 17. CROTOXYPHOS 1% + DICHLORVOS 0.23% FLY SPRAY LABEL

Net Contents: 30 Gallon

E P A Reg. No. 602-186-AA

CONTAINS
Ciodrin®
AND
Vapona®
INSECTICIDES

PURINA®
DAIRY SPRAY SPECIAL

D-2568

CAUTION: KEEP OUT OF REACH OF CHILDREN
See Other Cautions on Back Panel

READY-TO-USE OIL BASE FLY SPRAY

TAKE TIME
OBSERVE LABEL DIRECTIONS

Kills House Flies, Stable Flies, Face Flies, Horn Flies, Lice on Dairy or Beef Cattle.

Active Ingredients:

Dimethyl Phosphate of Alpha methylbenzyl-3 Hydroxy-cis-Crotonate	1.00%
2,2-Dichlorovinyl Dimethyl Phosphate**	0.23%
Related Compounds**	0.02%
Petroleum Oils	98.50%
Inert Ingredients	0.25%
	100.00%

**Equivalent to 0.25% Vapona Insecticide

Manufactured by
RALSTON PURINA COMPANY
General Offices • St. Louis, Missouri 63188

Table 17. (Continued)

HOW TO USE PURINA DAIRY SPRAY SPECIAL

Purina Dairy Spray Special is a ready-to-use oil base spray for use in hand sprayers, misting equipment, and back or face rubbers. Contains Ciodrin* and Vapona* Insecticides for effective knock-down, kill and residual protection against flies and lice on dairy or beef cattle. Do not apply on horses.

For Control of House Flies, Stable Flies, Horn Flies, and Face Flies: Apply Dairy Spray Special as a mist to the hair coat by using a hand atomizer-type sprayer or mechanical misting equipment. Spray once daily using 1 to 2 ounces over the entire animal. Spray calves more sparingly. Do not wet the skin.

For stable flies, spray legs and flanks; for face flies spray face and head areas. Repeat once daily as necessary.

Back Rubbers and Face Rubbers: For the control of horn flies and face flies on lactating dairy and beef animals:

Use 1 gallon of Dairy Spray Special for each 20 linear feet of burlap back rubber. For automatic back rubbers recharge the reservoir as needed. Animals must rub face on rubbers for best face fly control.

For Control of Lice: Make 1 to 2 applications of 3-3½ ounces of Dairy Spray Special at 14 day intervals. Apply as a fine mist spray to thoroughly cover all parts of the animal. If applied by fogging or misting equipment, the maximum spraying time per animal is 20 seconds.

CAUTION: Avoid inhalation of mist and contact with skin. In case of contact with skin or eyes, flush with plenty of water, for eyes get medical attention. Wash thoroughly with soap and water after using, and before eating or smoking. Harmful or fatal if swallowed. If swallowed, induce vomiting immediately and get medical attention. Atropine is antidotal. 2-PAM is also antidotal and may be administered in conjunction with atropine.

Keep out of reach of children. Do not mist or fog into air of closed buildings. Do not wet the skin of animals. Do not spray or store near an open flame. Do not contaminate feed, water or foodstuffs.

This product is toxic to fish and wildlife. Birds feeding on treated areas may be killed. Keep out of any body of water. Do not apply where runoff is likely to occur. Do not contaminate water by cleaning of equipment, or disposal of wastes. Apply this product only as specified on this label.

Do not re-use empty container. Destroy container by perforating and bury or discard in a safe place.

QUALITY CONTROLLED BY PURINA RESEARCH

717L EPA Est. 602—MO-1 Printed in U.S.A.

Source: Label for "Purina Dairy Spray Special"
EPA Reg. No. 602-186-AA (30 gal. container)
Ralston Purina Company, St. Louis, Missouri

Another combination formulation of note is a pressurized spray in which crotoxyphos is combined with eight other "active ingredients," plus pine oil and mineral oil. The formula, labeled by Chem Spray Aerosols, Inc., Houston, Texas 77088, includes 1.0% crotoxyphos; 0.25% dichlorvox and related compounds; 0.05% pyrethrins; 0.1% piperonyl butoxide; 0.168% n-octyl bicycloheptene dicarboximide; stabilizer; and petroleum distillate. This produce is used against biting flies (including stable flies, horn flies, horse flies, and deer flies), houseflies, mosquitoes and gnats on horses and ponies.

Another fly spray product, used only for dairy cows against stable flies, horn flies, mosquitoes, and gnats, is a ready-to-use oil formulation containing 1.0% crotoxyphos; 0.2% dichlorvos and related compounds; 0.03% pyrethrins; 0.11% technical piperonyl butoxide; plus petroleum solvents (Watkins Products, Inc., Winona, Minnesota 55987).

State Regulations - Regarding mammalian toxicity, crotoxyphos is in the "moderately toxic" category. Crotoxyphos is not subject to specific use restrictions under State pesticide laws or regulations.

Production and Domestic Supply

Volume of Production - According to the United States Tariff Commission's final reports on Synthetic Organic Chemicals for the years 1971, 1972, and 1973,1/ there has been only one basic producer of crotoxyphos in the United States, Shell Chemical Company, a Division of Shell Oil Company. Shell Chemical Company's Agricultural Division through which crotoxyphos is marketed is located in San Ramon, California.

In the Tariff Commission (TC) reports, the production and sales volumes of crotoxyphos are not reported individually. Crotoxyphos is included in the category of "pesticides and related products, cyclic" in a classification entitled "all other organophosphorus insecticides." This classification includes eight major, specified organophosphate insecticides (not including crotoxyphos), and "other phosphorothioates and phosphorodithioates, and others." The total production volume for this classification, according to the Tariff Commission reports, was 36,740,000 lb in 1971, 44,385,000 lb in 1972, and 53,265,000 lb in 1973.

1/ U.S. Tariff Commission, Synthetic Organic Chemicals, U.S. Production and Sales, TC Publication 681 (1971, 1972, 1973).

Compared to the major insecticides in this category, the production and sales volumes of crotoxyphos are so small that the Tariff Commission data is not significant in estimating crotoxyphos volumes.

Crotoxyphos was not included in two recent studies in which considerable detail on the production volumes and use patterns of selected pesticides was obtained (Lawless et al., 1972; von Rumker et al., 1974).[1-2]

The U.S. Department of Agriculture (USDA, 1974)[3] reports that 901,000 lb of crotoxyphos active ingredient were used on livestock in the United States in 1971 (141,000 lb in 1966). Exports of crotoxyphos appear to be small in volume, probably not exceeding 100,000 lb active ingredient.

Based on USDA's estimate for the domestic consumption of crotoxyphos in 1971, and assuming further that crotoxyphos exports in 1971 were 100,000 lb active ingredient or less, the total U.S. supply of the product in 1971, must have been on the order of 0.9 to 1.0 million pounds active ingredient. Data was not found on U.S. production or use of crotoxyphos. However, confidential discussions with representatives of the manufacturer, Shell Chemical Company, indicate these estimates are very high.

Imports - Imports of pesticides that are classified as "benzenoid chemicals" are reported by the U.S. Tariff Commission in its 1973 report on benzenoid chemicals.[4]

1/ Lawless, E. W., R. von Rumker, and T. L. Ferguson, The Pollution Potential in Pesticide Manufacturing, Pesticide Study Series - 5, Environmental Protection Agency, Technical Studies Report: TS-00-72-04 (1972).

2/ von Rumker, R., E. W. Lawless, and A. F. Meiners, "Production, Distribution, Use and Environmental Impact Potential of Selected Pesticides," Final Report, Contract No. EQC-311, for Council on Environmental Quality, Washington, D.C. (1974).

3/ U.S. Department of Agriculture, Farmers' Use of Pesticides in 1971 . . . Quantities, Agricultural Economic Report No. 252, Economic Research Service (1974).

4/ U.S. Tariff Commission, Imports of Benzenoid Chemicals and Products, 1972, TC Publication 601 (1973).

The Tariff Commission classifies crotoxyphos as a "benzenoid chemical." According to the TC reports, there were no imports of crotoxyphos into the United States in 1972. It is unlikely that significant, if any, quantities of crotoxyphos were imported in more recent or in previous years because it is covered by a patent of Shell Chemical Company, the sole U.S. producer.

Exports - Pesticide exports are reported annually by the Bureau of the Census.1/ Technical or formulated crotoxyphos is not specifically listed in any of the commodity descriptions applicable to pesticides in Section 5, Chemicals (Revision 1/1/72). This is probably due to the following reasons:

1. Crotoxyphos exports, if any, are small in volume. (Usually, only pesticides whose export volume is significant are listed individually in the appropriate classifications.)

2. As a livestock insecticide, formulated crotoxyphos may have been included in Section 599.2090 (Schedule B), "Agricultural chemical preparations not elsewhere classified, including plant growth regulators and similar type preparations." This category includes prepared animal dips, cattle dips, sheep dips, stock dips.

More specific information on the export volume of crotoxyphos could not be obtained within the limitations of time and resources available. Based on available information, Midwest Research Institute estimates that the export volume of crotoxyphos for the last few years did not exceed 100,000 lb active ingredient.

Domestic Supply - Information reviewed indicates that the domestic consumption of crotoxyphos in the United States in 1971, was about 900,000 lb active ingredient. No data or estimates are available on the domestic consumption of crotoxyphos in 1972 or 1973, or in years between 1966 and 1971.

Formulations - Crotoxyphos by itself is available for commercial use in the United States in a number of different formulations, including emulsifiable concentrates, oil solutions, dust concentrates, and dilute dusts. Emulsifiable spray concentrates range in active ingredient content from 1.0 to 4.0 lb/gal. Several oil concentrates contain 14.4% active ingredient. Many dilute, ready-to-use crotoxyphos-in-oil formulations contain 1 or 2% active ingredient. Ready-to-use dust formulations contain 3% active ingredient. The dry manufacturing concentrate for local preparation of dilute dusts contains 80% active ingredient.

1/ U.S. Bureau of the Census, U.S. Exports, Schedule B, Commodity by Country, Report FT410.

In addition, a number of multi-ingredient formulations are offered in which crotoxyphos is combined with DDVP and/or synergized pyrethrins. The most popular combination formulation, offered under a number of different brand names and labels, appears to be one containing 1% crotoxyphos and about 0.25% DDVP. Several suppliers offer other crotoxyphos-DDVP combination formulations containing the two active ingredients at the same ratio as the dilute formulations (four parts of crotoxyphos to one part of DDVP). One typical product in this category contains 13.03% crotoxyphos plus 3.22% DDVP.

Three-way combination formulations include a ready-to-use oil-based dairy spray containing 1.0% crotoxyphos, 0.2% DDVP and related compounds, 0.03% pyrethrins, and 0.11% piperonyl butoxide; and a pressurized spray containing 1.0% crotoxyphos, 0.25% DDVP and related compounds, 0.05% pyrethrins, 0.1% piperonyl butoxide, 0.168% n-octyl bicycloheptene dicarboximide, stabilizer, pine oil, mineral oil, and petroleum distillate.

The 1972 and 1974 éditions of the Pesticide Handbook--Entoma (Frear, 1972; and Billings, 1974)[1,2] list a total of about 30 different products containing crotoxyphos as an active ingredient, marketed by at least 12 different companies, including Shell. There are a number of additional mostly smaller suppliers of crotoxyphos containing products not listed in the Pesticide Handbook--Entoma.

Use Patterns of Crotoxyphos in the United States

General - Crotoxyphos is a specialty insecticide which is registered in the United States only for the control of external parasites on livestock. Pests controlled by crotoxyphos include stable flies, horn flies, house flies, face flies, ticks, lice, and certain mites. The product is not federally registered for any uses on agricultural or other crops, for use on poultry or pets, nor for commercial, institutional, or residential pest control purposes. Products in which crotoxyphos is

1/ Frear, D. E. H., ed., Pesticide Handbook--Entoma, 24th ed., College Science Publishers, State College, Pennsylvania (1972).

2/ Billings, S. C., ed., Pesticide Handbook--Entoma, 25th ed., Entomological Society of America, College Park, Md. (1974).

combined with other active ingredients carry additional insect control claims, including control of, and/or repellent action against horse flies, deer flies, mosquitoes, gnats, fleas and maggots.

Crotoxyphos has been in commercial use in the United States for about 10 years. A U.S. Department of Agriculture report on pesticide use by farmers in 1964[1/] does not include crotoxyphos among the insecticides used by farmers on livestock. According to the pesticide use report for 1966,[2/] farmers used 141,000 lb of crotoxyphos active ingredient that year. In 1971, 901,000 lb were used (USDA, 1974).

Data on the livestock uses of crotoxyphos in the U.S. by type of livestock from the 1966 and 1971 USDA surveys is presented in Table 18. This data indicates that in both years, close to 80% of the total quantity of crotoxyphos used was applied to dairy cattle. Uses on beef cattle accounted for an additional 13% in 1966; almost 20% in 1971. Much smaller quantities of crotoxyphos were used on hogs, poultry, sheep, and other livestock, according to these sources. Crotoxyphos is not registered for use on poultry.

Table 18. PROPORTIONS OF CROTOXYPHOS CONSUMPTION FOR DIFFERENT LIVESTOCK USES IN THE U.S. IN 1966 AND 1971

Type of livestock	Year 1966	Year 1971
	Percent	
Dairy cattle	84.4	76.9
Beef cattle	12.8	19.6
Hogs	2.1	2.9
Poultry	-	.3
Sheep	-	.1
Other	.7	.2
Total	100.0	100.0

1/ U.S. Department of Agriculture, Quantities of Pesticides Used by Farmers in 1964, Agricultural Economic Report No. 131, Economic Research Service (1968).

2/ U.S. Department of Agriculture, Quantities of Pesticides Used by Farmers in 1966, Agricultural Economic Report No. 179, Economic Research Service (1970).

Crotoxyphos Use Patterns by Regions - Table 19 presents a breakdown of the livestock uses of crotoxyphos in 1971, by geographic regions. The information on the use by type of livestock is taken from the USDA's survey of pesticide uses by farmers in the U.S. in 1971. The breakdown by regions was obtained by reference to the density of the different types of livestock in different parts in the U.S. (U.S. Department of Agriculture, 1973; U.S. Bureau of the Census, 1973),[1,2] and from RvR Consultants personal communications with trade sources.

According to Table 19, about 50% of the total domestic consumption of crotoxyphos in 1971 was used in the North Central states. About 75% of this subtotal (i.e., 330,000 lb) was used on dairy cattle, an additional 100,000 lb on beef cattle, and the small remaining balance on hogs and other livestock.

The Northeastern states accounted for the next largest volume of use of crotoxyphos in 1971, 144,000 lb, that is about 16% of the total U.S. use. More than 90% of the regional subtotal was used on dairy cattle; the balance on beef cattle, hogs, and other livestock.

The South Central states ranked third; approximately 12% of the national total, or 111,000 lb of crotoxyphos were used in this area in 1971. In this region, about 83,000 lb, or about 75% of the regional subtotal, were used on dairy cattle, an additional 25,000 lb (about 22%) on beef cattle, and the small remaining balance on hogs and other livestock.

Of the three remaining regions, the Southwest used approximately 76,000 lb (8%); the Southeast about 63,000 lb (7%); and the Northwest about 56,000 lb (6%) of crotoxyphos. As in the other areas, the largest share of each regional subtotal was used on dairy cattle, followed by beef cattle, hogs, and other livestock.

In summary, crotoxyphos is an insecticide used in the United States for the control of external parasites on livestock, primarily cattle. Small quantities of crotoxyphos are also used on hogs and other farm animals. Of the quantities used on cattle, about 80% are used on dairy

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1/ U.S. Department of Agriculture, Agricultural Statistics 1973, (1973).
2/ U.S. Bureau of the Census, Census of Agriculture, 1969, Vol. V., Special Reports, Part 15, Graphic Summary (1973).

Table 19. ESTIMATED PROPORTIONS OF CROTOXYPHOS CONSUMPTION FOR DIFFERENT LIVESTOCK USES IN THE U.S. BY REGIONS, 1971

	Type of livestock				
	Dairy cattle	Beef cattle	Hogs	Other livestock[a]	Totals, all livestock
	Percent				
Northeast[b]	19.5	2.9	7.7	16.7	16.0
North Central[c]	47.6	57.1	76.9	16.7	50.1
Southeast[d]	7.9	2.9	7.7	16.7	7.0
South Central[e]	12.0	14.3	7.7	16.7	12.3
Northwest[f]	5.1	11.4	negl.	16.7	6.2
Southwest[g]	7.9	11.4	negl.	16.7	8.4
Total	100.0	100.0	100.0	100.0	100.0

Sources: U.S. Department of Agriculture, op. cit. (1974).

a/ Including poultry, sheep.

b/ New England States, New York, New Jersey, Pennsylvania.

c/ Ohio, Indiana, Illinois, Michigan, Wisconsin, Minnesota, Iowa, Missouri, North Dakota, South Dakota, Nebraska, Kansas.

d/ Maryland, Deleware, Virginia, West Virginia, North Carolina, South Carolina, Georgia, Florida.

e/ Kentucky, Tennessee, Arkansas, Louisiana, Mississippi, Alabama, Oklahoma, Texas.

f/ Montana, Idaho, Wyoming, Colorado, Utah, Washington, Oregon, Alaska.

g/ New Mexico, Nevada, Arizona, California, Hawaii.

cattle. In line with this use pattern, the largest quantities of crotoxyphos geographically are used in the North Central region.

Crotoxyphos Uses in California - The State keeps detailed records of pesticide uses by crops and commodities which are published quarterly and summarized annually. Table 20 summarizes the recorded uses of crotoxyphos in California by individual uses for the 4-year period 1970 to 1973.

TABLE 20. CROTOXYPHOS USES IN CALIFORNIA BY CROPS AND OTHER USES, 1970 - 1973

Crop	Year 1973	1972	1971	1970[a]
	Pounds of active ingredient			
Cattle	3	-	-	
Other Miscellaneous Uses	1539	7	2891	
Total	1542	7	2891	

Source: California Department of Agriculture, Pesticide Use Reports for 1970, 1971, 1972 and 1973.

a/ No entry for crotoxyphos.

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

According to these state reports (Table 20), a total of 2,890 lb of crotoxyphos were used in California in 1971; 7 lb in 1972; and 1,542 lb in 1973. The 1970 California pesticide use report does not contain any entries for crotoxyphos.

It appears that crotoxyphos usage on livestock is not significant in California. However, it is possible that the system does not cover livestock insecticides equally as well as pesticides used on crops.

California officials concede that their pesticide reporting system is least reliable in regard to pesticides whose use is not restricted and which are applied by private individuals to their own crops or animals. Crotoxyphos falls into this category.

In the light of these facts, it appears that the California data summarized in Table 20 represents only a small fraction of the crotoxyphos quantities that were actually used in the state in 1971, 1972, and 1973. According to Table 19, an estimated 76,000 lb crotoxyphos active ingredient were used in the five Southwestern states in 1971. Taking into account the cattle population in California as compared to that in New Mexico, Nevada, Arizona, and Hawaii, MRI estimates that about half of this quantity was used in California in 1971.

References

Billings, S. C., ed., Pesticide Handbook--Entoma, 25th ed., Entomological Society of America, College Park, Md. (1974).

California Department of Agriculture, Pesticide Use Reports for 1970, 1971, 1972 and 1973.

Frear, D. E. H., ed., Pesticide Handbook - Entoma, 24th ed., College Science Publishers, State College, Pa. (1972).

Lawless, E. W., R. von Rumker, and T. L. Ferguson, The Pollution Potential in Pesticide Manufacturing, Pesticide Study Series - 5, Environmental Protection Agency, Technical Studies Report: TS-00-72-04 (1972).

U.S. Bureau of the Census, Census of Agriculture, 1969, Vol. V., Special Reports, Park 15, Graphic Summary (1973).

U.S. Bureau of the Census, U.S. Exports, Schedule B, Commodity by Country, Report FT410.

U.S. Department of Agriculture, Agricultural Statistics, 1973, (1973).

U.S. Department of Agriculture, Farmers' Use of Pesticides in 1971 . . . Quantities, Agricultural Economic Report No. 252, Economic Research Service (1974).

U.S. Department of Agriculture, Quantities of Pesticides Used by Farmers in 1964, Agricultural Economic Report No. 131, Economic Research Service (1968).

U.S. Department of Agriculture, Quantities of Pesticides Used by Farmers in 1966, Agricultural Economic Report No. 179, Economic Research Service (1970).

U.S. Environmental Protection Agency, EPA Compendium of Registered Pesticides, Vol. III, p. D 46, 1-D 46.3.

U.S. Tariff Commission, Imports of Benzenoid Chemicals and Products, 1972, TC Publication 601 (1973).

U.S. Tariff Commission, Synthetic Organic Chemicals, U.S. Production and Sales, TC Publication 681 (1971, 1972, 1973).

von Rümker, R., E. W. Lawless, and A. F. Meiners, "Production, Distribution, Use and Environmental Impact Potential of Selected Pesticides," Contract No. EQC - 311, for Council on Environmental Quality, Washington, D.C. (1974).

PART III. MINIECONOMIC REVIEW

CONTENTS

This section contains a general assessment of the efficacy and cost effectiveness of crotoxyphos. Data on the production of crotoxyphos in the United States as well as an analysis of its use patterns was conducted as part of the Scientific Review (Part II) of this report. This section summarizes rather than interprets data reviewed.

Introduction

Crotoxyphos is an organophosphate insecticide that is used primarily for control of biting flies, ticks, and lice that attach to cattle. Its effectiveness, economic benefits and cost often depend upon the method of application, rate applied, and timing since contact with the animals may be difficult to achieve because of their mobility. Various devices have been developed to improve control of these insects. Back rubbers, dust bags, movable and rigid sprays are a few devices which are commonly used for application of crotoxyphos. The quanitity of insecticide used will vary with the method of application.

The method of application is also important for control of different insects. Some insects are controlled by only topside contact of the animal with the insecticide. Other insects are controlled by application about the legs, face, or in the ears or nostrils of the cattle. The way in which the insecticide protects the animal is also important to the control. If it acts only as a repellant, a portion of the animal may need to be contacted. If it acts on the larvae or adult insect, it may have to be applied at the site of infestation.

A final variable affecting the efficacy (and economic benefit) is the duration of control achieved. Control will vary with the type of insect. For some, seasonal control can be achieved with one or two applications. For other insects daily applications or periodic applications every 3 days or every week are necessary for good control.

Because of these variables, it is difficult to determine an overall economic benefit of controlling a pest on a specific animal. This evaluation is further complicated by the lack of data on the benefits of insect control on animals. Control of flies and ticks is often referred as good "herd management," and in many cases, it can prevent the spread of disease which could disable or destroy the animal. This type of insect control is a method of disease prevention; unfortunately, no data was found regarding the economic value of the method.

Limited data was available relating the use of crotoxyphos for the control of flies to weight gain or milk production in cattle. Where data was available, the economic benefits were determined by subtracting the cost of the crotoxyphos from the additional income generated by the increased weight gain or milk production. These benefits, based on 1972 cost data, are presented in dollars per animal per day or year.

Numerous articles were available on the efficacy of crotoxyphos on a wide variety of pests. The pests considered in this review include horn flies, stable flies and face flies on cattle; the southern cattle tick, cattle tick, lone star tick, winter tick, and horse tick on cattle and horses; the house fly in outdoor privies; and the rice weevil; confused flour beetle; and the lesser grain beetle in stored rough rice.

Efficacy Against Biting Flies Infestation - Horn flies, stable flies, and face flies are serious pests which attack cattle. Evidence is conflicting concerning the effect of these pests on cattle weight or milk production, but experimental tests have shown that under specific conditions gains in weight and milk production have been experienced when biting flies were controlled. Therefore, it has been considered as good herd management practice to control flies on cattle.

Horn flies - Control of the horn fly has been relatively easy because of its unique parasitic habits which make possible its control with only partial coverage of the animal.

The degree of control is dependent upon the method of application and the availability of the cattle for treatment. Various application devices and methods have been developed. These include conventional spray programs whereby animals are sprayed every 28 to 30 days throughout the summer; the application of concentrated insecticides to cattle in pastures or on rangeland through ultralow-volume aircraft or ground devices; use of forced or free choice self-application devices; or feeding of insecticide treated feed which kills the insects breeding in the manure.

Crotoxyphos has been found to control horn flies in concentrations as low as 0.125%. Hoffman et al. (1965)[1/] evaluated various concentrations of crotoxyphos applied to cattle passing through a low volume mist spray. They concluded that one application every 3 to 5 days would be adequate to control these flies.

1/ Hoffman, R. A., J. L. Berry, and O. H. Graham, "Control of Flies on Cattle by Frequent, Low Volume Mist Spray Applications of Ciodrin," J. Econ. Entomol., 58:815-817 (1965).

Eschle and Miller (1968)[1] evaluated crotoxyphos applied to ULV sprayer at various Texas farms and achieved complete control of horn flies with 2% crotoxyphos spray and nearly complete control with 0.5% crotoxyphos spray. Costs ranged from 0.086¢/animal/day for 2 ml/day of 0.5% ULV crotoxyphos to 4.4¢/animal/day for 2 oz/day of 2% crotoxyphos applied as a mist spray. The savings for the ULV application was 98% over the mist spray.

Horn flies can also be controlled with dust bags. Poindexter and Adkins (1970)[2/] achieved 85% control when cattle had access to dust bags containing 3% crotoxyphos. They concluded that this method would be effective if the bags are frequently contacted by the cattle and they are maintained with dust. Similar results were found by Knapp (1972).[3/] Control varied from 81 to 99% for the season with 3% crotoxyphos. The difference in efficacy was attributed to the type of cattle, the location and use of the duster.

Back rubbers are commonly used for control of the horn fly. Dorsey et al. (1966)[4/] evaluated back rubbers for control of horn flies and found that a 0.75% crotoxyphos back oiler gave a 95% reduction of horn flies in tests in 1962.

1/ Eschle, J. L., and A. Miller, "Ultra-Low Volume Application of Insecticides to Cattle for Control of the Horn Fly," J. Econ. Entomol., 61:1617-1621 (1968).

2/ Poindexter, C. E., and T. R. Adkins, Jr., "Control of the Face Fly and the Horn Fly with Self-Applicatory Dust Bags," J. Econ. Entomol., 63:946-948 (1970).

3/ Knapp, F. W., "Evaluation of Dust Bags for Horn Fly Control on Cattle," J. Econ. Entomol., 65:470-472 (1972).

4/ Dorsey, C. K., J. O. Heishmann and C. J. Cunningham, "Face Fly and Horn Fly Control on Cattle--1962-1964," J. Econ. Entomol., 59:726-732 (1966).

Stable flies - The stable fly is a serious pest of cattle during the summer months because of its bloodsucking feeding habits. Experimental results have shown that stable flies can cause a reduction in milk production in dairy cows (Bruce and Decker, 1958)[1/].

Crotoxyphos has been used successfully to control the stable fly. Harris (1964)[2/] found that crotoxyphos was much more toxic to stable flies than chlorinated hydrocarbons. The LD_{50} value expressed as micrograms of insecticide per gram of fly weight was 1.04 for crotoxyphos, compared to 3.89 and 9.69 for two other pesticides tested.

Mount et al. (1953)[3/] found that crotoxyphos at 4 to 6 ppm resulted in 100% mortality of stable fly larvae. Against the adult flies, 98 to 100% mortality was achieved with concentration of 0.05 to 0.25%.

Hoffman et al. (1965) evaluated various concentrations of crotoxyphos applied to cattle passing through a low volume mist sprayer. Stable flies were killed when contacted by the spray, but no residual effectiveness was observed. Campbell and Hermanussen (1971)[4/] applied 2 qt of 0.5% crotoxyphos to the legs and lower body of cows and achieved an 85% reduction in flies after 1 day. However, this reduction dropped to 50% in 4 days and flies had increased to the same level as on untreated cows at the end of 7 days.

Face flies - The face fly, has become an increasing cattle pest problem in the past two decades. It has been reported as a cause of cattle annoyance and eye disorders (Dobson and Huber, 1961).[6/] Crotoxyphos is used for control of the face fly.

1/ Bruce, W. N., and G. C. Decker, "The Relationships of Stable Fly Abundance to Milk Production by Selected and Randomized Dairy Herds," J. Econ. Entomol., 51:269-274 (1958).

2/ Harris, R. L., "Laboratory Tests to Determine Susceptibility of Adult Horn Fly and Stable Fly to Insecticides," J. Econ. Entomol., 57:492-494 (1964).

3/ Mount, G. A., J. B. Gahan, and C. S. Lofgren, "Evaluation of Insecticides in the Laboratory Against Adult and Larvae Stable Flies," J. Econ. Entomol., 58:685-687 (1965).

4/ Campbell, J. B., and J. F. Hermanussen, "Efficacy of Insecticides and Methods of Insecticidal Application for Control of Stable Flies in Nebraska," J. Econ. Entomol., 64:1188-1190 (1971).

5/ Dobson, R. C., and D. A. Huber, "Control of Face Flies (*Musca autumnalis*) on Beef Cattle in Indiana," J. Econ. Entomol., 54:434-436 (1961).

Granett et al. (1962)[1] evaluated several insecticides for control of the face fly and found that crotoxyphos controlled 59 to 60% of the flies 24 hr after 1 pint of 0.5% active ingredient was applied to cattle. One pint of 1.0% active ingredient gave 75% control after 24 hr.

Hair and Adkins (1965)[2] found that a 1% crotoxyphos back rubber formulation gave 85% control of face flies during the season. However, Doresey et al. (1966) found seasonal face fly control with crotoxyphos varied from 11% to 64%. A 0.75% formulation on a back rubber provided 14% control while a 5% dust applied at 2 oz/head/week gave 64% control. In another test, dust bags containing 3% crotoxyphos gave 11% seasonal control. Poindexter and Adkins (1970) achieved a 43% control of the face fly on cattle exposed to 3% crotoxyphos dust bags.

Cost Effectiveness of Biting Flies Control - The economic benefits from controlling biting flies with crotoxyphos should be measurable in terms of weight gain for beef cattle or increased milk production from dairy cows. The results of several tests show that, under certain conditions, increased weight or milk production can be achieved.

Several tests have been conducted to determine the effect of flies on dairy cow milk production. Bruce and Ducker (1958) estimated from regression analysis that average rates of loss were 0.65% for butterfat and 0.7% for milk production per stable fly per cow and that these losses extended beyond the fly season. Cheng and Kessler (1961)[3] evaluated milk production and fly control over a 3-year period and concluded that herds that are well managed and liberally supplied with supplementary feeds will not have any significant loss of milk production when face, horn, and stable flies are present. Average daily milk production in these herds varied from a loss of 5.0 lb/day to gain 1.1 lb/day when herds were treated to control flies.

1/ Granett, P., E. J. Hansens, and A. J. Forgash, "Tests Against Face Flies on Cattle in New Jersey During 1961," J. Econ. Entomol., 55:655-659 (1962).

2/ Hair, J. A., and T. R. Adkins, Jr., "Dusting Stations and Cable Back Rubbers as Self-Applicatory Devices for Control of the Face Fly," J. Econ. Entomol., 58:39-41 (1965).

3/ Cheng, T. H., and E. M. Kessler, "A Three-Year Study on the Effect of Fly Control and Milk Production by Selected and Randomized Dairy Herds," J. Econ. Entomol., 54:751-757 (1961).

Miller et al. (1973)[1/] evaluated the effect of stable flies on milk production and concluded that they did not have a significant adverse effect on milk production. Milk production varied from a loss of 2.7 lb/day to a gain of 2.3 lb/day when the cows were exposed to the flies.

The results of these tests indicate that fly control of dairy cattle can produce changes in milk production ranging from a gain of 2.3 lb/day to a loss of 5.0 lb/day. At a milk price of $6.07/cwt in 1972, (Agricultural Statistics, 1973[2/] the additional income would range from a loss of $0.30 to a gain of $0.14/cow/day from the use of crotoxyphos to control flies.

The cost of the application will vary with the method used. Eschle and Miller (1968) estimated the cost of control per cow with crotoxyphos in tests conducted in 1967, ranged from 0.086¢/day to 4.4¢/day depending upon the method of application. Subtracting the high and low costs ot application from the additional income would result in economic benefits ranging from a loss per cow of 34.4¢/day to a gain of 13.9¢/day from the use of crotoxyphos on dairy cattle.

Roberts and Pund (1974)[3/] determined the effect of biting flies on the weight gain of steers in pasture. The treated steers gained 0.20 lb/day/animal more than the untreated steers in a 1969 test and 0.23 lb/day/animal more than a 1970 test. The total increased weight gain for a 112-day period in 1969 averaged 22.4 lb/animal. These results were also supported by Cheng (1958)[4/] who showed that cattle loose 1/4 to 3/4 lb of weight/day as the result of attacks by biting flies.

Using this range of 0.20 to 0.75 lb/day as the added weight for cattle from the control of biting flies, the additional income, based upon a 1972 cattle price of $33.50/cwt (Agricultural Statistics, 1973), would range from 6.7¢ to 25.1¢/head/day. Subtracting the costs of crotoxyphos and its application ranging from 0.086¢ to 4.4¢/day, the economic benefit would range from an average of 2.3¢ to 25.0¢/day/head.

Efficacy Against Cattle and Horse Tick Infestation - Crotoxyphos has been evaluated for control of ticks on cattle and other animals. These include cattle ticks, Southern cattle ticks, lone star ticks, winter ticks, and the horse ticks.

1/ Miller, R. W., L. G. Pickens, N. O. Morgan, R. W. Thimijan, and R. L. Wilson, "Effect on Stable Flies on Feed Intake and Milk Production of Dairy Cows," J. Econ. Entomol., 66:711-713 (1973).

2/ Agricultural Statistics, 1973, U.S. Department of Agriculture (1973).

3/ Roberts, R. H., and W. A. Pund, "Control of Biting Flies on Beef Steers: Effect on Performance in Pasture and Feedlot," J. Econ. Entomol., 67:232-234 (1974).

4/ Cheng, T. H., "The Effect of Biting Fly Control on Weight Gain in Beef Cattle," J. Econ. Entomol., 51:275-278 (1958).

Cattle tick - The cattle tick and the Southern cattle tick, once serious pests to agriculture in the U.S., have been eliminated as problems to domestic industry (Drummond et al., 1973).1/ However, imported cattle, particularly from Mexico, still remain a problem and must be treated. Treatment is most often performed at border stations.

Drummond et al. (1968)2/ found that crotoxyphos sprayed on cattle in concentrations of 0.15 and 0.30% gave 99.5 to 100% control of both ticks. Drummond et al. (1972)3/ conducted similar tests and obtained 99.8% control of the cattle tick with 0.075% crotoxyphos and 93.2% control of the Southern cattle tick. He concluded that 99% control of the cattle tick could be achieved with 0.075% crotoxyphos and 99% control of the Southern cattle tick could be achieved with 0.15% crotoxyphos.

Lone Star tick - The lone star tick infests horses and cattle in the spring and early summer. Drummond and Medley (1965)4/ compared various insecticides for control of this pest in Texas. Crotoxyphos at concentrations varying from 0.1 to 0.75% gave 80 to 99% control 1 day after application. At the end of 1 week, control at concentrations of 0.25 to 0.75% was 84 to 88%; by the end of 3 weeks, little or no control was experienced. Similar results were obtained by Drummond et al. (1967)5/ when 0.3% crotoxyphos gave 95% control after 1 day and 5% after 3 weeks.

Winter tick - The winter tick is found in the Northern United States, in the Western states and Texas. It can be a serious pest to cattle and horses. Drummond and Medley (1965) found that 0.25% crotoxyphos sprayed on cattle gave complete control of winter ticks 1 month after treatment. Complete control of the winter tick was also achieved on horses 1 month after a spray treatment of 0.3% crotoxyphos.

1/ Drummond, R. O., S. E. Ernst, J. L. Trevino, W. J. Gladney, and O. H. Graham, "*Boophilus annulatus* and *B. microplus*: Laboratory Tests of Insecticides for Control on Cattle," *J. Econ. Entomol.*, 66:130-133 (1973).

2/ Drummond, R. O., S. E. Ernst, J. L. Trevino, and O. H. Graham, "Insecticides for Control of the Cattle Tick and the Southern Cattle Tick on Cattle," *J. Econ. Entomol.*, 61:467-470 (1968).

3/ Drummond, R. O., S. E. Ernst, J. L. Trevino, W. J. Gladney, and O. H. Graham, "*Boophilus annulatus* and *B. microplus*: Sprays and Dips of Insecticides for Control on Cattle," *J. Econ. Entomol.*, 65:1354-1357 (1972).

4/ Drummond, R. O., and J. G. Medley, "Field Tests with Insecticides for Control of Ticks on Livestock," *J. Econ. Entomol.*, 58:1131-1136 (1965).

5/ Drummond, R. O., T. M. Whetstone, and S. E. Ernst, "Control of the Lone Star Tick on Cattle," *J. Econ. Entomol.*, 60:1735-1738 (1967).

Horse tick - The tropical horse tick is limited to Texas, Georgia, and Florida. It is of veterinary importance in Florida because it transmits equine piroplasmosis (Drummond et al., 1971b).[1] Drummond and Ossorio (1966)[2] found that 0.3% crotoxyphos in cottonseed oil or water or a 5% crotoxyphos dust were highly effective in killing the horse tick at all stages of development. The applications were made in the ears and false nostrils of the horses. Drummond et al. (1971b) evaluated several insecticides for toxicity to the horse tick.

Cattle Grub Control

The cattle grub causes economic loss to cattle through additional trim losses on beef carcases (Rich 1970).[3] Grubs are also thought to have an effect on milk production. Knapp (1972b)[4] found that lactating dairy cows sprayed twice daily with 2% crotoxyphos oil during the active period of the adult heel fly reduced the cattle grub from 74 to 96% in a series of tests. Since crotoxyphos is not a systemic insecticide it was postulated that the control was due to the crotoxyphos acting either as an ovicide or a repellent to the adult heel fly, or that the crotoxyphos residue killed the larvae.

Lice and Chorioptic Mange Mite Control

Dairy cattle are affected by various types of lice. Some of these are the cattle biting lice, long-nosed cattle louse, short-nosed cattle louse, and the little blue louse. Matthysse et al. (1967)[5] evaluated crotoxyphos for control of lice and mange mites. Crotoxyphos was sprayed on dairy cows with either a low or high volume spray. They found that two applications of 0.25% crotoxyphos resulted in elimination of lice 6 weeks after the second spraying. It was completely effective against all species of lice. In a later test, two applications of 2% crotoxyphos at 8 oz/cow eradicated lice and chorioptic mange mites.

House Fly Control

The common house fly is also prevalent around poultry, cattle, and outdoor privies. Crotoxyphos has been evaluated for toxicity and control of the house fly.

1/ Drummond, R. O., W. J. Gladney, T. M. Whetstone, and S. E. Ernst, "Testing of Insecticides Against the Tropical Horse Tick in the Laboratory," J. Econ. Entomol., 64:1164-1166 (1971b).

2/ Drummond, R. O., and J. M. Ossorio, "Additional Tests with Insecticides for Control of the Tropical Horse Tick on Horses in Florida," J. Econ. Entomol., 59:107-110 (1966).

3/ Rich, G. B., "The Economic Systemic Insecticides Treatment for Reduction of Slaughter Trim Loss Caused by Cattle Grubs, *Hypoderma* Spp.," Canadian Journal of Animal Science, 50:301-310 (1970).

4/ Knapp, F. W., "Prevention of Cattle Grub Infestation in Lactating Dairy Cows by Use of Daily Applications of Crotoxyphos," J. Econ. Entomol., 65:466-467 (1972b).

5/ Matthysse, J. G., R. F. Pendleton, A. Padula, and G. R. Nielson, "Controlling Lice and Chorioptic Mange Mites on Dairy Cattle," J. Econ. Entomol., 60:1615-1622 (1967).

Georghiou (1967)[1/] evaluated the susceptibility and resistance of house flies to insecticides and reported that resistance to organophosphates was increasing in the house fly. Labrecque et al. (1966)[2/] evaluated crotoxyphos for control of flies in outdoor privies on Grand Turk Island in the British West Indies. A 1.0% crotoxyphos in diesel oil sprayed at 100 to 200 mg/ft^2 in the pits of the privies gave up to 3 days of 100% control. The authors indicated that the diminishing number of outdoor privies in the United States has relegated the problem of house fly control in this environment to a minor role. However, they note that this problem is still urgent in many countries.

1/ Georghiou, G. P., "Differential Susceptibility and Resistance to Insecticides of Coexisting Populations of *Musca domestica*, *Fannia canicularis*, *F. femoralis*, and *Ophryra leucostoma*," *J. Econ. Entomol.*, 60:1338-1344 (1967).

2/ Labrecque, G. C., M. C. Evers, and D. W. Meifert, "Control of House Flies in Outdoor Privies with Larvicides," *J. Econ. Entomol.*, 59:245 (1966).

References

Agricultural Statistics, 1973, U.S. Department of Agriculture (1973).

Bruce, W. N., and G. C. Decker, "The Relationships of Stable Fly Abundance to Milk Production by Selected and Randomized Dairy Herds," J. Econ. Entomol., 51:269-274 (1958).

Campbell, J. B., and J. F. Hermanussen, "Efficacy of Insecticides and Methods of Insecticidal Application for Control of Stable Flies in Nebraska," J. Econ. Entomol., 64:1188-1190 (1971).

Cheng, T. H., "The Effect of Biting Fly Control on Weight Gain in Beef Cattle," J. Econ. Entomol., 51:275-278 (1958).

Cheng, T. H., and E. M. Kessler, "A Three-Year Study on the Effect of Fly Control and Milk Production by Selected and Randomized Dairy Herds," J. Econ. Entomol., 54:751-757 (1961).

Dobson, R. C., and D. A. Huber, "Control of Face Flies (Musca autumnalis) on Beef Cattle in Indiana," J. Econ. Entomol., 54:434-436 (1961).

Dorsey, C. K., J. O. Heishmann and C. J. Cunningham, "Face Fly and Horn Fly Control on Cattle--1962-1964," J. Econ. Entomol., 59:726-732 (1966).

Drummond, R. O., S. E. Ernst, J. L. Trevino, W. J. Gladney, and O. H. Graham, "Boophilus annulatus and B. microplus: Laboratory Tests of Insecticides for Control on Cattle," J. Econ. Entomol., 66:130-133 (1973).

Drummond, R. O., S. E. Ernst, J. L. Trevino, W. J. Gladney, and O. H. Graham, "Boophilus annulatus and B. microplus: Sprays and Dips of Insecticides for Control on Cattle," J. Econ. Entomol., 65:1354-1357 (1972).

Drummond, R. O., S. E. Ernst, J. L. Trevino, and O. H. Graham, "Insecticides for Control of the Cattle Tick and the Southern Cattle Tick on Cattle," J. Econ. Entomol., 61:467-470 (1968).

Drummond, R. O., W. J. Gladney, T. M. Whetstone, and S. E. Ernst, "Testing of Insecticides Against the Tropical Horse Tick in the Laboratory," J. Econ. Entomol., 64:1164-1166 (1971b).

Drummond, R. O., and J. G. Medley, "Field Tests with Insecticides for Control of Ticks on Livestock," J. Econ. Entomol., 58:1131-1136 (1965).

Drummond, R. O., and J. M. Ossorio, "Additional Tests with Insecticides for Control of the Tropical Horse Tick on Horses in Florida," J. Econ. Entomol., 59:107-110 (1966).

Drummond, R. O., T. M. Whetstone, and S. E. Ernst, "Control of the Lone Star Tick on Cattle," J. Econ. Entomol., 60:1735-1738 (1967).

Eschle, J. L., and A. Miller, "Ultra-Low Volume Application of Insecticides to Cattle for Control of the Horn Fly," J. Econ. Entomol., 61:1617-1621 (1968).

Georghiou, G. P., "Differential Susceptibility and Resistance to Insecticides of Coexisting Populations of Musca domestica, Fannia canicularis, F. femoralis, and Ophryra leucostoma," J. Econ. Entomol., 60:1338-1344 (1967).

Granett, P., E. J. Hansens, and A. J. Forgash, "Tests Against Face Flies on Cattle in New Jersey During 1961," J. Econ. Entomol., 55:655-659 (1962).

Hair, J. A., and T. R. Adkins, Jr., "Dusting Stations and Cable Back Rubbers as Self-Applicatory Devices for Control of the Face Fly," J. Econ. Entomol., 58:39-41 (1965).

Harris, R. L., "Laboratory Tests to Determine Susceptibility of Adult Horn Fly and Stable Fly to Insecticides," J. Econ. Entomol., 57:492-494 (1964).

Hoffman, R. A., J. L. Berry, and O. H. Graham, "Control of Flies on Cattle by Frequent, Low Volume Mist Spray Applications of Ciodrin," J. Econ. Entomol., 58:815-817 (1965).

Knapp, F. W., "Evaluation of Dust Bags for Horn Fly Control on Cattle," J. Econ. Entomol., 65:470-472 (1972).

Knapp, F. W., "Prevention of Cattle Grub Infestation in Lactating Dairy Cows by Use of Daily Applications of Crotoxyphos," J. Econ. Entomol., 65:466-467 (1972b).

Labrecque, G. C., M. C. Evers, and D. W. Meifert, "Control of House Flies in Outdoor Privies with Larvicides," J. Econ. Entomol., 59:245 (1966).

Matthysse, J. G., R. F. Pendleton, A. Padula, and G. R. Nielson, "Controlling Lice and Chorioptic Mange Mites on Dairy Cattle," J. Econ. Entomol., 60:1615-1622 (1967).

Miller, R. W., L. G. Pickens, N. O. Morgan, R. W. Thimijan, and R. L. Wilson, "Effect on Stable Flies on Feed Intake and Milk Production of Dairy Cows," J. Econ. Entomol., 66:711-713 (1973).

Mount, G. A., J. B. Gahan, and C. S. Lofgren, "Evaluation of Insecticides in the Laboratory Against Adult and Larvae Stable Flies," J. Econ. Entomol., 58:685-687 (1965).

Poindexter, C. E., and T. R. Adkins, Jr., "Control of the Face Fly and the Horn Fly with Self-Applicatory Dust Bags," J. Econ. Entomol., 63:946-948 (1970).

Rich, G. B., "The Economic Systemic Insecticides Treatment for Reduction of Slaughter Trim Loss Caused by Cattle Grubs, Hypoderma Spp.," Canadian Journal of Animal Science, 50:301-310 (1970).

Roberts, R. H., and W. A. Pund, "Control of Biting Flies on Beef Steers: Effect on Performance in Pasture and Feedlot," J. Econ. Entomol., 67: 232-234 (1974).

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