Toxaphene: Position Document 1

Toxaphene Working Group
U.S. Environmental Protection Agency
April 19, 1977

50272-101

REPORT DOCUMENTATION PAGE	1. REPORT NO. EPA/SPRD-80/55	2.	3. Recipient's Accession No. PB 80 216732

4. Title and Subtitle

Toxaphene: Position Document 1

5. Report Date 4/19/77

6.

7. Author(s)

8. Performing Organization Rept. No.

9. Performing Organization Name and Address

Special Pesticide Review Division
Environmental Protection Agency
Crystal Mall #2
Arlington, VA

10. Project/Task/Work Unit No.

11. Contract(C) or Grant(G) No.

(C)

(G)

12. Sponsoring Organization Name and Address

Environmental Protection Agency
401 M Street S.W.
Washington, D.C. 20460

13. Type of Report & Period Covered

14.

15. Supplementary Notes

16. Abstract (Limit: 200 words)

Preliminary Risk Assessment: Examination of possible unreasonable risks associated with uses of pesticide and gathering of all available information to determine whether or not this or any other risk does exist. Initiates literature search and evaluates risk data. Limited information on exposure to forecast extent of risk.

17 Document Analysis a. Descriptors

0504,0606,0703

b. Identifiers/Open-Ended Terms

c. COSATI Field/Group

18. Availability Statement: Unlimited	19. Security Class (This Report) Unclassified	21. No. of Pages
	20. Security Class (This Page) Unclassified	22. Price

(See ANSI-Z39.18) See Instructions on Reverse

OPTIONAL FORM 272 (4-77)
(Formerly NTIS-35)
Department of Commerce

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I. BACKGROUND

A. Chemical/Physical Characteristics

Toxaphene (chemical name, chlorinated camphene) is a complex mixture of at least 177 polychlorinated C_{10} compounds with an empirical formula of $C_{10}\ H_{10}\ Cl_8$ (1). It occurs as an amber, waxy solid with a mild odor of chlorine and camphor and is prepared by the chlorination of camphene. It has a molecular weight of 414 and a density of 1.66 at 27°C. The melting point ranges from 65 to 90°C. It is highly soluble in organic solvents, especially in aromatic solvents. Its solubility in water is 0.5 parts per million (ppm). (Russian names include polychorpinene and polychlorocamphene.)

B. Formulation and Class

Toxaphene is classed and used as an insecticide and is available in emulsifiable concentrates, wettable powders, and dust formulations. A 20% dust is the standard commercial formulation, and a 10% dust is produced for use on certain insects. Emulsifiable concentrates range from 4 to 8 lb of toxaphene/gal, whereas oil solutions contain 90% toxaphene. Wettable powders contain 40% toxaphene. Toxaphene is also available as an emulsifiable concentrate in various mixed ratios with methyl parathion for use on cotton (2). It also occurs in registrations mixed with lindane, dichlorvos, malathion, sulfur, parathion, methyl parathion, dimethoate, dicofol, naled, zineb, cryolite, metallic copper, methoxychlor, EPN, dinocap, ethylene dichloride, metasystox R, BHC, trichlorofon, pyrethrin and piperonyl butoxide, monocrotophos, endosulfan, azinphosmethyl, chlordimeform, carbaryl, aramite, endrin, dioxathion, carbophenothion, Dacomil 2787, 24-D, MGK-264, and chlordane (3).

C. Registered Uses and Production

Toxaphene has been produced as a pesticide since 1947. Approximately 186 companies hold Federal registrations and manufacture 817 registered products. Sixty-one companies have state registrations and produce 176 products.

EPA records indicate that an aggregate total of 103,000,000 lb were produced in 1974 and 116,000,000 lb in 1975 (4). The "National Study of Agricultural, Governmental and Industrial Uses of Pesticides" (5) conducted by EPA's Human Effects Monitoring Branch related that an estimated 74,469,332 lb of toxaphene were used in agriculture in the United States during 1974. Cotton was by far the largest single use, consuming approximately 63,960,000 lb or 86% of the total domestic consumption figure. Soybeans accounted for an estimated 2,440,000 lb; wheat for 1,604,000 lb; cattle for 1,285,000 lb; corn for 1,219,000 lb; peanuts for 1,070,000 lb; swine for 530,000 lb; tobacco for 434,000 lb; alfalfa for 367,000 lb; tomatoes for 347,000 lb; sorghum for 254,000 lb; sunflowers for 233,000 lb; beans for 201,000 lb; lettuce for 105,000 lb; hay (pasture & forage) for 89,000 lb; oats for 71,000 lb; barley for 58,000 lb; radishes for 53,000 lb; potatoes for 33,000 lb; sheep for 24,000 lb; green peppers for 20,000 lb; ornamentals for 15,000 lb; carrots for 7,000 lb; other vegetables for 7,000 lb; onions for 3,000 lb; eggplants for 3,000 lb; spinach for 2,000 lb; nursey crops for 1,000 lb; and peaches for 96 lb. (A list of sites on which toxaphene has been registered for use since October 7, 1975, is given in Reference 6.)

The four primary sites listed for the use of toxaphene are cotton, livestock, soybeans, and peanuts (6).

D. Environmental Fate and Characteristics

As stated earlier, toxaphene is a complex mixture of compounds, and little is known of the metabolic pathways or of the metabolites themselves. Menzie (7) has stated that very little information is available about the metabolism of toxaphene. Dr. Phillip Kearney (8), Secretary to the IUPCA Commission on Terminal Pesticide Reviews, reported that knowledge of toxaphene metabolism in mammals, birds, and fish is "undoubtedly" limited. And Sanborn et al. (9) have stated that the environmental fate of toxaphene is very poorly understood. Scientific studies have been conducted, however, that give some insight into certain of toxaphene's characteristics (18).

(1) Persistence: Soils

Toxaphene is generally accepted as a persistent compound in both soil and water. Nash and Woolson (10) reported that 45% of the applied toxaphene remained in Congaree sandy loam soil after 14 years. Foster et al. (11)

indicated that repeated applications of toxaphene accumulated in the soil and affected the growth rates of several vegetables and field crops. Based on analytical procedures in use at that time, Foster determined that 29% of the toxaphene applied over 60 months in cold frames remained in the soil. According to a green house test, 66% of the total applied remained after 34 months. In the same study, a significant reduction in the yield of turnips (a root crop) resulted when they were planted in soil that had been contaminated by toxaphene, even though the turnips were never sprayed from time of planting through harvest. LaFleur (12) concluded that some toxaphene persists beyond the growing season, and that hazardous accumulation in soil, water, and air is a possibility. Nash et al. (13) reported that soils which were treated with 112 kg/hectare of toxaphene in 1951 contained 55.8 ppm (average of all plots checked) in 1952, and after 20 years (1971) those same soils still contained 24.24 ppm by soxhlet extraction, 28.08 ppm by shake extraction, and 21.61 ppm by GLC column extraction.

(2) Persistence: Water

Although never registered as a piscicide, toxaphene was in common use for a period of time to control undesirable fish. As a result of this use, a number of studies were conducted that give some indication of the persistence of toxaphene in surface waters. Terriere et al. (14) reported that toxic levels remained in a lake treated with 40 ppb after 6 years. Johnson et al. (15) reported that several lakes treated with 0.1 ppm of toxaphene could not be safely restocked for approximately 4 years. And Cohen et al. (16) reported, "From the limited experience with the stability of toxaphene in water, it seems clear that toxicity of toxaphene will persist...perhaps for as long as 33 months."

(3) Bioacummulation

Most organochlorine compounds are persistent and bioacummulate; toxaphene is no exception. Metcalf and Sanborn (17) showed that toxaphene is highly persistent and accumulates several thousand times in their model ecosystem. In a later study (9) they stated, "Continued use of toxaphene...will undoubtedly lead to greater contamination of humans and foodstuff by [this] environmentally recalcitrant pesticide...." Reimold and Durant (19) demonstrated in a study on toxaphene residues that water levels

were undetectable on September 2, 1972, in Terry Creek, near Brunswick, Georgia (levels less than 0.25 ppm were considered insignificant); yet mummichogs collected the same day contained 10.45 ppm toxaphene. On October 12, 1972, water samples contained 0.0014 ppm; salt water marsh grass contained 3.93 ppm; oysters contained 1.19 ppm; shrimp contained 2.88 ppm; and mummichogs contained 131.14 ppm. Herring and Cotton (20) reported that a lake in Mississippi had water residue levels of toxaphene of 1.92 ppb; sediments had 0.946 ppm, and bluegill sunfish had 20.0 ppm in the body and 35.7 ppm in the head and viscera. Schimmel et al. (21) reported that longnose killifish were exposed to toxaphene for 28 days. Resulting concentration factors were 13,300 to 33,000 in embryo/fry; 19,300 to 32,200 in advanced fry; 23,700 to 60,000 in juveniles; and 4,200 to 5,300 in adults. (Adults were exposed for only 14 days.)

In a study on channel catfish, Merhle and Mayer (22) learned that catfish fry bioaccumulated or concentrated the levels of toxaphene 40,000 to 91,000 times that found in water. Adult channel catfish accumulated about 54,000 times the lowest test level and 20,000 times the highest concentration used.

(4) Transport

Although toxaphene has been shown to persist in soils, it can also be readily transported from the site of application. Bradley et al. (23) reported that sufficient toxaphene was washed from a treated cotton plot into an adjoining pond to raise the detectable level of <1.0 ppb to a high of 65.2 ppb. Of 11 different calendar dates (from July 8, 1969, through October 3, 1969) when water residues were checked, all but one date showed levels of toxaphene in the pond equal to or exceeding the 96-hour median tolerance limit for bluegills. Bidleman and Olney (24) ran a study to see whether or not long range transport of toxaphene by volatilization was possible. By collecting air samples from a location in Bermuda and from a cruising ship, they learned that levels of toxaphene in the marine atmosphere of the western North Atlantic were equal to, and in some instances twice, those of PCB's and more than 10 times higher than those of other pesticides reported to that date in the same general location. Levels ranged from 0.4 to 1.6 nanograms per cubic meter.

E. Tolerances

Although tolerances have been granted which allow the use of toxaphene on various food and feed stocks, no acceptable daily intake has been set. Dr. Vettorazzi (25) reported the following when the FAO/WHO study group addressed problems with the pesticide toxaphene:

> Further work deemed to be necessary before an A.D.I. (acceptable daily intake) for man can be established comprises adequate toxicological information on campheclor (toxaphene) as currently marketed, including carcinogenicity studies and comparative studies evaluating the toxicological hazards associated with polychlorinated camphene of different manufacturers used in worldwide agriculture.

As of July 1, 1976, the Code of Federal Regulations (CFR 40, Section 180.138) reported the following tolerances in effect for toxaphene residues in or on raw agricultural commodities: 7 ppm in or on apples, apricots, beans, blackberries, boysenberries, broccoli, brussel sprouts, cabbage, carrots, cauliflower, celery, citrus fruits, collards, corn, cranberries, cucumbers, dewberries, egg-plants; fat of meat from cattle, goats, hogs, horses, and sheep; hazelnuts, hickory nuts, horseradish, kale, kohlrabi, lettuce, loganberries, nectarines, okra, onions, parsnips, peaches, peanuts, pears, peas, pecans, peppers, pimentos, quinces, radishes (with or without tops) or radish tops, raspberries, rutabagas, spinach, strawberries, tomatoes, walnuts, young berries; 5 ppm in or on barley, oats, rice, rye, sorghum grain, wheat; 5 ppm, calculated as a chlorinated terpene of molecular weight 396.6 containing 67% chlorine, in or on cottonseed; 3.5 ppm combined residues of DDT and toxaphene in or on soybeans (dry form), of which residues DDT shall not exceed 1.5 ppm and toxaphene shall not exceed 2 ppm; 3 ppm in or on bananas (of which residue not more than 0.3 ppm shall be in the pulp after the peel is removed and discarded) and pineapples; 2.0 ppm in or on soybeans (dry form); and 0.1 ppm in or on sunflower seeds.

F. Residues

(1) FDA Commodity Survey

The Food and Drug Administration (FDA) has been collecting food and feed samples for a number of years, analyzing each sample to determine pesticide residue levels and frequency of occurrence. A brief summary of toxaphene residues for the past 5 fiscal years is given in the chart below.

	# of Commodities Contaminated	# of Samples Checked	# of Positive Samples	% of Occurrence	Commodity Most Frequently Contaminated
1972	10	3516	118	3.3	Leaf & Stem Vegetables
1973	15	2906	150	4.8	Leaf & Stem Vegetables
1974	8	1919	109	4.6	Fish
1975	12	2317	118	5.0	Fish
1976	15	4228	257	6.0	Fish

The above figures disclose a slow but steady rise in the number of positives found on a percentage basis over the past five years. Although the commodity contaminated most in the past three years is fish, there are only two registered uses where toxaphene is directly applied to water, cranberries and rice. It is likely that the high incidence in fish is due to side-effects such as run-off and volatilization.

The following list indicates the commodities, the number of positives within the year, and the fiscal years (FY) when found contaminated:

Commodity	FY 1972	FY 1973	FY 1974	FY 1975	FY 1976
Beans	0	0	0	3	0
Large Fruits	1	0	0	0	0
Small Fruits	0	1	0	0	0
Leaf and Stem Veg.	50	66	38	19	34
Root Vegetables	24	2	8	15	18
Vine and Ear Veg.	4	10	6	6	23
Nuts	0	7	0	19	25
Hay Natural	0	12	0	0	0
Whole Grain-Human	0	4	13	0	0
Whole Grain-Animal	0	3	1	2	3
Whole Soybeans	0	6	0	0	3
Fish	27	10	40	22	65
Shell Fish	0	0	0	0	1
Grains, Ground	1	2	0	0	0
Processed Animal Feed Fish byproducts	13	0	0	12	15
Processed Animal Feed Oil seed byproducts	0	6	0	1	13
Processed Animal Feed Hay dehydrated	0	4	0	11	28
Processed Animal Feed Misc. Animal Feeds	6	0	0	2	2
Processed Animal Feed Processed Veg. byproducts	1	0	0	0	12
Processed Animal Feed Misc. Product Feed	1	6	0	0	0
Crude Veg. Oil	0	0	1	0	0
Processed Animal Feeds Cereal byproducts	0	0	2	6	16
Processed Animal Feeds Grains	0	0	0	0	1
Treated Seed	0	1	0	0	0
Whole Milk	0	0	0	0	2
Total # of occurrences	10	15	8	12	15

It is apparent from the above that toxaphene contaminates vegetables and fish, both basic food commodities.

(2) Air Residues

Six air samples were taken in the Stoneville, Mississippi area (26). The following are average toxaphene levels in nanograms per cubic meter (ng/m^3) for the six sampling dates.

1-2-76/2-5-76	-- 4.8	ng/m^3
2-5-76/3-2-76	-- 16.36	" "
3-2-76/3-31-76	-- 16.55	" "
3-31-76/4-30-76	-- 15.48	" "
4-30-76/6-1-76	-- 16.67	" "
6-1-76/7-2-76	-- 42.09	" "

A maximum weekly level of 1746.5 ng/m^3 occurred in the Mississipi Delta during a three-year study covering the years 1972-73 and 1974 (27). Levels were the highest during the months of August and September. Average levels during those months are listed below.

	1972	1973	1974
August	1540 ng/m^3	268.8 ng/m^3	903.6 ng/m^3
September	827 " "	322.6 " "	524.6 " "

Bidleman and Olney (24) reported that levels of 0.04 to 1.6 ng/m^3 of toxaphene were found in the atmosphere over the North Atlantic many miles from any direct source of contamination and suggested, "A possible source of airborne toxaphene is the southern U.S. cotton growing areas where the bulk of this pesticide has been used...."

(3) Water Residues

(a) Drinking Water

A series of commercial drinking water samples were collected and analyzed for EPA during 1975 and 1976 (28). Twenty-seven out of fifty-eight samples were positive for toxaphene. The levels ranged from <0.05 to 0.05 ppb. Of the samples reported prior to 1975, none gave a positive indication for toxaphene.

(b) Surface Waters

Herring and Cotton (20) reported on pesticide residues in 20 Mississippi Delta lakes, disclosing detectable toxaphene residues in 11 lakes with a maximum of 1.92 ppb. In the same study, sediments from the lakes were also checked. Levels of a trace to 2.46 ppm were found in 10 of the lakes. Levels of a trace to 35.7 ppm were found in the flesh of bluegills in 3 of the lakes. Seven lakes had no detectable toxaphene levels in the fish.

Reimold and Durant (19) reported that Terry Creek, near Brunswick, Georgia, and a toxaphene manufacturing plant, was dredged to both widen and deepen the creek bed. Water, sediment, and aquatic life were sampled before, during, and after dredging. The following chart shows that disturbing bottom sediments caused a rise in detectability of toxaphene residues in the water, flora, and fauna. Dredging began on September 7, 1972.

	Sept. 2	Sept. 28	Oct. 12
Water	none detected	0.0013 ppm	0.0014 ppm
Salt Marsh Grass	0.82 ppm	2.04 ppm	3.93 ppm
Sediment	5.47 ppm	2.11 ppm	3.97 ppm
Mummichog (fish)	10.45 ppm	10.52 ppm	131.14 ppm

Samples of water from western streams were analyzed for pesticide residues from 1968 through 1971. No toxaphene residues were detected. Limits of detectability were listed as 0.5 to 1.0 micrograms per liter (ppb) (29).

(c) Fish

In spite of the low frequency of recorded occurrences of detectable toxaphene residues in water, fish have been found with significant levels in their tissues.

A massive fish kill in 1975 in Louisana disclosed toxaphene residues in fish and water of 2.017 and 0.0042 ppm, respectively, in the La Fourche Canal; of 5.058 and 0.004 ppm, respectively, in Joe Bayou; of 10.294 and 0.001 ppm, respectively, in the Beouf River; and of 4.399 and 0.0014 ppm, respectively, in Bayou Bartholomew. A drainage ditch that flowed into Bartholomew had water levels of 0.01 ppm (30).

Several lakes in Wisconsin were "cleaned out" for restocking using toxaphene (31). It was applied at a calculated dose of 0.1 to 0.15 mg/liter (ppm). Water levels after 4 months were 1 to 6 micrograms/liter (ppb). Fish were stocked 11 months after treatment; two months after stocking, samples of fish were removed and analyzed. Toxaphene residues were found to be 9.4 micrograms/gram (ppm) in bluegill sunfish and 10.6 micrograms/gram (ppm) in suckers.

According to Crockett et al. (32), 54 commerical catfish farms in Arkansas and Mississippi were sampled in 1970 to see if they were contaminated by pesticides. Of the samples taken, 96% showed toxaphene levels from 0.2 to 20.7 ppm in the fish. The average concentration was 2.1 ppm. The authors suggested that cotton production was the primary source of contamination and that, although actual routes of movement have not been clearly defined, aerial transport seemed most probable. Samples of sediments, fish feed, and water were analyzed but were not shown to be the sources of contamination.

Hawthorne et al. (33), using the same data base as Crockett et al. (32), reported that levels of toxaphene in commercially grown catfish sampled in 28 counties in Mississippi and in 22 counties in Arkansas disclosed positive occurrences in all but one sample in Mississippi and in Arkansas. Levels of detectability were 0.01 ppm. Whole body residues ranged from 0.2 ppm to 20.67 ppm.

(4) Livestock

Diephuis and Dunn (34) fed livestock (sheep and cattle) hay treated with varying levels of toxaphene. After 134 days of feeding cattle, and 133 days of feeding sheep, the following levels were determined.

Steers	Treatment Total lb/Acre	Hay Residues	Fat		Lean Meats		
			Subcut.	Abdominal	Shoulder	Rib	Rump
Control	0	0	0	0	0	0	0
#8	2	25-40 ppm	24 ppm	25 ppm	0.9 ppm	0	0
#10	4	81 ppm	338 ppm	243 ppm	6.8 ppm	6.8 ppm	6.6 ppm
#12	8	306 ppm	618 ppm	772 ppm	17.9 ppm	34.8 ppm	28.9 ppm
					Shoulder	Loin	Leg
Sheep							
Control	0	0	0	0	0	0	0
#7	2	25-40 ppm	42 ppm	60 ppm	1.6 ppm	5.5 ppm	3.1 ppm
#9	4	81 ppm	72 ppm	120 ppm	13.1 ppm	7.5 ppm	8.4 ppm
#12	8	306 ppm	162 ppm	317 ppm	51.2 ppm	30.0 ppm	22.4 ppm

G. Pesticide Episode Reports System (PERS)

EPA's Pesticide Episode Response (PER) Branch of the Office of Pesticide Programs (OPP) maintains a Pesticide Episode Reports System (PERS) which collects reports of pesticide exposure affecting humans, domestic animals, livestock, and wildlife (36). According to their records, there were 222 episodes from 1966 to 1975 involving the insecticide toxaphene. The large number of episodes may reflect the extensive use of toxaphene as a pesticide; in many instances, toxaphene was not the sole pesticide present. The following chart lists those reports.

Table 1. Toxaphene Episodes 1966-1975

Year	Human	Animal	Plant	Contamination	Not Specified	Total
1966		1				1
67	2	7				9
68		6				6
69	1	3				4
70	3	1		1		5
71	2	15		2	2	21
72	10	12		10	7	39
73	11	35		10	2	58
74	8	38		4		50
75	7	16	1	5		29
Total	44	134	1	32	11	222

Table 2 shows the result when the above data were reexamined to determine age groups of humans affected. Numbers in parentheses denote fatalities.

Table 2. Year of Age

Year	5	5-16	17-65	65 & Older	Unk.
1967	1 (1)		1		
68					
69			1 (1)		
70	2 (1)		1 (1)		
71		1	1 (1)		
72			6		4 (1)
73		2	8 (2)		1
74			8		
75		1	4		2
Total	3 (2)	4	30 (5)	0	7 (1)

Analysis of the above table shows the highest "at risk" age group to be 17 to 65 years of age. This age group represents those individuals most likely to be occupationally exposed. Of the eight fatalities reported, five involved exposure during some phase of application, i.e., spraying of crops or dipping of livestock. Two of the five involved the crash of aircraft during aerial application, and the remaining three involved exposure during ground application. The actual cause of death in these latter instances was vague due to exposure to mixtures of two or more pesticides. The remaining three fatalities of the eight reported involved two incidents of ingestion by children and one in which the circumstances of exposure were unknown.

Table 3. Animal Episodes 1966-1975

Year	Wildlife	Bees	Livestock	Fish	Total
1966			1		1
67			5	2	7
68		1	4	1	6
69			1	2	3
70				1	1
71			6	9	15
72			2	10	12
73			4	31	35
74	1		8	29	38
75		1	6	9	16
Total	1	2	37	94	134

Sixteen of the 37 episodes involving livestock were direct applications to cattle (10), swine (3), horses (2) and sheep (1). Fish kills were involved a total of 94 times. Forty of these episodes were reported to be the result of toxaphene applications to or near water. The specific circumstances of thirty-nine of the episodes were unreported.

The Pesticide Episode Response Branch concluded, after examining the records closely, "The most common circumstance leading to fish mortality involved runoff from treated fields following applications to rice, cotton and corn".

II. REGULATORY ACTIONS

Toxaphene has been subjected to several Federal regulatory actions since its original registration. Twelve of the following 15 actions were initiated during the period

when USDA was responsible for the regulatory control of pesticides. The remaining three were EPA actions. In most instances, actions concerned the absence of finite tolerances or exemptions from tolerances, or the extension of time to develop information for tolerance. All were published in the Federal Register. (Some Federal Register notices on toxaphene, in addition to the PR notices, are listed in Reference 37).

Pesticide Registration (PR) Notice 68-3 issued on January 10, 1968, classified certain chemical use patterns as nonfood uses. Toxaphene use on seeds of velvet beans and the uses listed as uses on agricultural premises, i.e., barns, shed, animal shelters, fences, and farm buildings except dairy barns, poultry houses, and milk rooms were included. (This and all following PR Notices are cited in Reference 38.)

PR Notice 68-5 issued January 30, 1968, extended certain "no residue" and "zero tolerance" registrations beyond December 31, 1967. Toxaphene use on alfalfa (seed crop only) and clover (seed crop only) were extended until January 1, 1969.

PR Notice 68-6 issued on February 1, 1968, proposed the cancellation of several uses of toxaphene on the basis of an "absence of finite tolerance or exemptions." Those uses included all uses on alfalfa (except when grown for seed only), asparagus, avacados, beets, blueberries, currants, gooseberries, grapes, huckleberries, cherries, clover (except when grown for seed crop only), almonds, cashews, chestnuts, dates, figs, filberts, olives, persimmons, plums, pomegranates, prunes, endive, birdsfoot trefoil, buckwheat, flax, grasses, hops, lespedeza, millet, pasture grass, safflower, sugarcane, sugar beets, vetch, garlic, guavas, hay, mangoes, mint (peppermint and spearmint), mustard, passion fruit, potatoes, salsify, sweet potatoes, swiss chard, papayas, turnips, cantaloupes, endine, melons, mustard greens, pumpkins, squash (summer and winter), watermelons, watercress, dairy cattle, milk rooms, and mushroom houses. (Several of the following PR Notices are in response to an appeal, made by the manufacturers of toxaphene, of PR Notice 68-6.)

PR Notice 68-8 published on April 24, 1968, classified certain chemical use patterns as nonfood uses, allowing these uses to be continued in the absence of finite tolerances. For toxaphene, these uses were in grainbins and grain elevators.

PR Notice 68-9 published on April 24, 1968, granted an extension of certain "no residue" and "zero tolerance" registrations beyond the original deadline (December 31, 1967) until January 1, 1969. Those toxaphene uses were on alfalfa, clover, birdsfoot trefoil, lespedeza, potatoes, sugar beets, and vetch.

PR Notice 68-19 published on November 29, 1968, classified certain compounds which required a label statement with regard to their hazard to honey bees. Toxaphene was classified as toxic to bees, needing the following label statement: "This product is toxic to bees and should not be applied when bees are actively visiting the area."

PR Notice 68-20 published on December 2, 1968, extended certain uses of specific economic poisons beyond a December 31, 1968, cutoff date. Toxaphene use on alfalfa, birdsfoot trefoil, clover, lespedeza, potatoes, sugar beets, and vetch was extended until January 1, 1970.

In February 1969 the USDA issued PR Notice 69-5 cancelling the registration of toxaphene products bearing directions for use on lettuce and cabbage. Certain information showed existing registered uses on lettuce and cabbage resulted in illegal residues. It was ordered that labels showing those uses should be corrected immediately to state "do not use after heads start to form", and in the instance of leaf lettuce, to prohibit use after the seedling stage. The label change was complied with, and the compound continued to be used on those crops.

PR Notice 70-1 published on January 19, 1970, extended certain uses of specific economic poisons beyond the December 31, 1969, deadline date. Toxaphene use on alfalfa, range grass, alfalfa (seed crop), and potatoes was extended until January 1, 1971.

PR Notice 70-4 issued on February 26, 1970, proposed the cancellation of several uses of toxaphene on the basis of an "absence of finite tolerances or exemptions." Those uses were birdsfoot trefoil, clover, clover (seed crop), lespedeza, sugar beets, and vetch.

PR Notice 70-23 published on October 9, 1970, followed a recommendation made by an interdepartmental review panel relative to the continued registration of "Certain Chlorinated Hydrocarbon Insecticide Products Bearing Directions for Repeated Applications." It stated, "It is the recommendation of this Review Panel (USDI, HEW, and USDA) that USDA expeditiously notify registrants that, on August 31, 1971, use patterns calling for repeat

applications of DDT, DDD, dieldrin, aldrin, endrin, heptachlor, toxaphene, BHC and chlordane will not be accepted. The Secretary of Agriculture must authorize deviation for repeat applications deemed essential." As a result, the notice stated that, after the August date, labels bearing directions for repeat applications of the above mentioned compounds would not be acceptable except for uses deemed essential and supported by efficacy data.

PR Notice 70-27 issued on November 12, 1970, rescinded the PR Notice 70-23 mandatory date of August 31, 1971, because after further consideration it was deemed impossible to review all the compounds and their respective uses that required repeat applications.

PR Notice 71-3 issued March 12, 1971, proposed cancellation of the registrations of several specific chemical compounds and uses in the absence of finite tolerances or exemptions for use on food or feed crops. Toxaphene registrations for use on potatoes were proposed for cancellation.

PR Notice 71-7 issued on May 7, 1971, rescinded PR Notices 70-23 and 70-27. It stated that an in-depth review of each compound was being initiated "to identify which, if any, of the presently registered products present substantial questions of safety that should trigger the administrative process of cancellation."

PR Notice 72-4 issued on March 10, 1972, proposed the cancellation of the use of toxaphene on range grass along with the cancellation of several other uses of other compounds "for use on foods in the absence of finite tolerances or exemptions." Additional time was later granted to develop information for tolerance determinations.

Although not registered for such use, toxaphene was used extensively as a piscicide. Even when applied at very low levels (0.05 to 0.2 ppm), it would result in a complete kill in most waters. It is extremely toxic to most fish species, and in some instances can remain active for long periods of time (6 years and longer). However, it was also extremely toxic to other aquatic organisms. Because of its extreme toxicity and its persistence, the Federal Fish and Wildlife Service discontinued its use as a piscicide in 1963 and recommended that Federal funds no longer be granted to states for the use of toxaphene in fish control or rough fish eradication programs (39).

III. SUMMARY OF SCIENTIFIC EVIDENCE OF REBUTTABLE PRESUMPTION CRITERIA

The following adverse effects of toxaphene use have been found to exceed the criteria for issuance of a rebuttable presumption as stated in Section 162.11 of the Code of Federal Regulations (CFR 40). (Risk criteria not used for issuance of a toxaphene RPAR at this time are listed in Reference 73.)

A. Acute Toxicity, Hazard to Wildlife: Aquatic Species

40 CFR Section 162.11(a)(3)(i)(B)(3) specifies that a rebuttable presumption shall arise against a pesticide use if such use "results in a maximum calculated concentration following direct application to a 6-inch layer of water more than 1/2 the acute LC_{50} for aquatic organisms representative of the organisms likely to be exposed...."

Toxaphene is registered for the control of armyworms and cutworms on cranberries and for the control of armyworms, grasshoppers, chinch bugs, and cutworms on rice. (Representative label contents are listed in Reference 40.)

To determine whether toxaphene use in aquatic environments meets rebuttable presumption criteria, the Working Group utilized the LC_{50} values for representative aquatic species, as listed in Table 4.

Calculations based on these values (45) and on label amounts and directions for use (40)[1/] indicate that any application of toxaphene to water, under current representative label directions, would be expected to exceed 1/2 the acute LC_{50} in a 6-inch layer of water for all species listed in Table 4.

1/ Sample use directions for cranberries include application of 10 to 25 lb/acre of a product containing 2 to 5 lb active ingredient (AI); 3 to 5 pts/acre of a product containing 8 lb AI/gal; for rice, 6 to 10 lb/acre of a product containing 2 lb AI; 2 to 2 2/3 pts/acre of a product containg 6 lb AI/gal; and 2 to 3 1/2 pts/acre for a product containing 8 lb AI/gal.

Table 4. Acute Toxicity of Toxaphene to Fresh Water and Marine/Estuarine Species

Organism	24-hr	48-hr	96-hr	References
Gammarus lacustris (scud)	180 ppb	70 ppb	26 ppb	Sanders (72)
Pteronarcys californica (stonefly niad)		7 ppb		" "
Salmo gairdneri (rainbow trout)		4 ppb		" "
Daphnia pulex (water flea)		15 ppb		Sanders & Cope (41)
Simocephalus serrulatus (daphnid)		10 ppb		" " "
Ictalurus punctatus (channel catfish)			13 ppb	Macek & McAllister (42)
Ictalurus melas (black bullhead)			5 ppb	" " "
Lepomis macrochirus (bluegill)			18 ppb	" " "
Micropterus salmoides (largemouth bass)			2 ppb	" " "
Salmo trutta (brown trout)			3 ppb	" " "
Oncorhynchus kisutch (coho salmon)	13 ppb	10.5 ppb	8 ppb	" " "
Perca flavescens (yellow perch)			12 ppb	" " "
Oncorhynchus tshawytscha (chinook salmon)	7.9 ppb	3.3 ppb	2.2 ppb	Katz (43)
Gambusia affinis (mosquito fish)	0.45 ppm	0.024 ppm	0.008 ppm	Chaiyarach et al. (44)
Palaemonetes kadiakensis (grass shrimp)	0.091 ppm	0.068 ppm	36 ppm	" " "
Procambarus simulans (crawfish)	0.045 ppm	0.045 ppm	0.029 ppm	" " "
Penaeus duorarum (pink shrimp)			1.4 ug/l (ppb)	Schimmel et al. (21)
Palaemonetes pugio (grass shrimp)			4.4 ug/l (ppb)	" " "
Cyprinodon variegatus (sheepshead minnow)			1.1 ug/l (ppb)	" " "
Lagodon rhomboides (pinfish)			0.5 ug/l (ppb)	" " "
Fundulus similis (longnose killifish)			10.0 ug/l (ppb)	" " "

With a recommended toxaphene treatment on cranberries of 3 to 4 pts/acre of an 8 lb AI/gal solution, the following concentrations would result (45).

Application rate	Concentration ppb	Concentration ppm
4 pts/acre (4 lb/acre)	2945	2.945
3.5 pts/acre (3.5 lb/acre)	2577	2.577
3.0 pts/acre (3.0 lb/acre)	2209	2.209
2.5 pts/acre (2.5 lb/acre)	1841	1.841
2.0 pts/acre (2.0 lb/acre)	1472	1.472

With a recommended toxaphene treatment on rice of 1 1/3 qts/acre, or 2 to 2 2/3 pts/acre, of a 6 lb AI/gal solution, the following concentration would result (45).

Application rate	Concentration ppb	Concentration ppm
2 2/3 pts/acre	1472	1.472
2 1/3 pts/acre	1288	1.288
2 pts/acre	1104	1.104

Additional studies are cited in the Toxaphene Criteria Document submitted in the Public Hearing on Proposed Toxic Pollutant Effluent Standards. Those studies and the data therein have been accepted as valid studies by the Administrator (46).

The foregoing data and calculations establish that the recommended applications for toxaphene products registered for aquatic use exceed the acute toxicity criteria of Section 162.11(a)(3)(i)(B)(3) for representative fresh water and marine/estuarine species. Accordingly, the Working Group recommends a rebuttable presumption be issued against the registration of toxaphene products labeled for these registrations and any other that call for direct application to water at rates resulting in concentrations in water which exceed the 1/2 LC_{50} rate.

B. Chronic Toxicity

(1) Oncogenic Effects in Test Animals

40 CFR Section 162.11(a)(3)(ii)(A) provides that a rebuttable presumption shall arise "if a pesticide's ingredient(s)...(i)nduces oncogenic effects in experimental mammalian species or in man as a result of oral, inhalation or dermal exposure...." Section 162.3(bb) defines the term oncogenic as "the property of a substance or a mixture of substances to produce or induce benign or malignant tumor formation in living animals."

The National Cancer Institute on November 8, 1976, issued an Experimental Design Status Report (Carcinogenesis Bioassy) with accompanying documents (47). Each copy was marked "Preliminary - Incomplete - Not Verified"; the compound tested was toxaphene.1/

Verified NCI data have since been received by EPA's Carcinogen Assessment Group (CAG) (75). It was statistically analyzed for that group by an EPA statistician.

On the basis of the verified data and the statistical analysis reported above, CAG (74) concluded that an increase in the frequency of malignancies was found in toxaphene-treated male rats. High dose-treated female rats showed a significant increase in the frequency of tumors of the reproductive system, but not for the individual reproductive organs.

In the instance of toxaphene-treated male and female mice, a highly significant dose-related increase in hepatic carcinomas was found. The Working Group therefore recommends issuance of a rebuttable presumption against toxaphene registrations pursuant to Section 162.11(a)(3)(ii)(A).

1/ Dr. Melvin Reuber (48), a specialist in pathology and oncology, examined the preliminary data and determined that toxaphene was in fact carcinogenic in male and female mice. He also found it to be tumorigenic in female rats and possibly tumorigenic in male rats.

(2) Other Chronic and/or Delayed Toxic Effects

40 CFR Section 162.11(a)(3)(ii)(B) provides that a rebuttable presumption shall arise "if a pesticide's ingredient(s)...(p)roduces any other chronic or delayed toxic effect in test animals at any dosage up to a level, as determined by the Administrator, which is substantially higher than that to which humans can reasonably be anticipated to be exposed, taking into account ample margins or safety...." The following studies demonstrate that exposure to toxaphene produces changes in growth and bone composition in fathead minnows, brook trout, and channel catfish, as well as in black ducks and rats. In the absence of an established level at which there is no demonstrated effect and with a consequent lack of basis for choice of an "ample margin of safety," it may be presumed that current exposure is sufficient to produce these, or similar, chronic or delayed effects in humans.

(a) Aquatic Species

(i) Fathead Minnows

Fathead minnows have long been an accepted test animal for acute testing of pesticides and have been generally thought of as an important representative of fish forage species. The LC_{50} for fatheads as reported by Macek and McAllester (42) in 1970 was 0.014 ppm.

In 1975 Merhle and Mayer (49) investigated toxaphene effects on the growth and bone composition of fathead minnows, Pimephales promelas, and found that at all concentrations tested (55-123 ppt) toxaphene "altered the development and quality of the backbone [reduced collagen and increased calcium], and induced biochemical manifestations of the brokenback syndrome." Radiographic analyses of the fish supported their findings that toxaphene induced a weakened, fragile backbone.

(ii) Brook Trout

The same authors (50) also checked brook trout, Salvelinus fontinalis, an important commercial and sporting species, and found the same effect of the brokenback syndrome (with altered collagen and calcium levels of the bone). They also found that, although hatchability was not affected, all fry exposed to 288 and 502 nanograms/liter (ppt) died at 60 and 30 days, respectively, and that growth decreased at all test concentrations (39, 68, 139, 288, and 502 nanograms/liter) after 90 days.

(iii) Channel Catfish

The effects on channel catfish, another important commercial and sporting species, was also investigated by Merhle and Mayer (22). In this study it was found that toxaphene concentrations of 224 and 535 ng/liter (ppt) caused significant decreases in growth after 30 days. At levels as low as 44 ng/liter (ppt) of toxaphene, catfish, like the fathead minnow and brook trout, had decreased collagen content and increased calcium content of the bone, the biochemical manifestation of the brokenback syndrome.

(b) Avian Species

Finley and Ludke (51) reported that "clutch size [in black ducks], number of eggs incubated, hatchability and duckling survival was lowest in the group fed 50 ppm toxaphene when compared to controls and the 10 ppm group." The authors also indicated a significant decrease in the collagen content and an increase in the calcium content of bone following treatment, similar to that seen in the studies using fish as test animals (49), (50), (22).

(c) Mammalian Species: Rats

Chernoff and Carver (52) administered toxaphene to female rats through gastric intubation in doses of 35, 25, and 15 mg/kg/day during days 7 through 16 of gestation. The toxaphene was in a corn oil solution with an intubation volume of 0.1 ml. With regard to fetal effects, the authors reported, "Dose-related reductions also occurred both in the average number of [fetal] sternal ($p<0.05$) and caudal ($p<0.001$) ossification centers with increasing toxaphene dosage."

The above studies demonstrate that exposure to toxaphene produced changes in growth and bone composition in aquatic, avian, and mammalian species. Since the dose levels at which these effects are induced are not substantially higher than current human exposure, the Working Group recommends that a rebuttable presumption be initiated pursuant to Section 162.11(a)(3)(ii)(B).

(3) Population Reduction in Nontarget Organisms

40 CFR Section 162.11(a)(3)(ii)(C) provides that a rebuttable presumption shall arise when a pesticide's use "(c)an reasonably be anticipated to result in significant local, regional, or national population reductions in nontarget organisms...."

Studies showing that toxaphene use has deleterious effects on nontarget organisms and can lead to population reduction in such nontarget species have already been discussed in previous sections of this document.

In Section I.D.(3), a study by Reimold and Durant (19) reported that toxaphene bioaccumulates in mummichogs, oysters, and shrimp. Herring and Cotton (20) reported bioaccumulation in bluegill sunfish, and Schimmel et al. (21) reported bioaccumulation in all growth stages of longnose killifish.

Section I.F.(3)(b) and (c) contained reports showing toxaphene residues in mummichogs (19) and in commercially grown catfish (32), (33). A fish kill in Louisiana was also attributed to toxaphene (30).

Section I.G. contained a discussion of PERS reports which showed that accidents involving toxaphene occurred in wildlife, bees, and fish (36).

Section III.B.(2)(a) and (b) contained reports showing that toxaphene use has produced deleterious effects (decrease in bone collagen and increase in calcium) in fathead minnows (49), brook trout (50), channel catfish (22), and black ducks (51).

Physiological change, metabolic interruptions or disturbances of hormonal or enzymatic systems, behavioral changes, as well as other changes in body processes or functions resulting from pesticide exposure usually result in reduced survivability of young, and at times significant adult mortalities, in fish, birds, or wild mammalian populations. The studies discussed in the foregoing sections indicate that such effects do occur in bees, fish, and birds. Since these adverse effects can reasonably be anticipated to result in significant local, regional, or national reductions in nontarget organisms, the Working Group recommends that a rebuttable presumption be issued against toxaphene pursuant to Section 162.11(a)(3)(ii)(C).

IV. OTHER RELEVANT ADVERSE EFFECTS

A review of the scientific literature suggests several other areas of adverse effects of toxaphene (summarized below) not included in the Position Document at this time. The Working Group will continue to investigate these effects and may issue a supplementary Position Document discussing these effects in greater detail. The Working Group also recommends that the Agency solicit comments on the evidence listed below, and request submission of any additional studies or relevant information on toxaphene-related mutagenesis, endocrine effects, reproductive effects, enzymatic effects, population reductions in nontarget organisms, and fatalities to members of endangered species. (Complete bibliographic citations for the following studies are given in the List of References to this Position Document. These studies are also available for public inspection with this Position Document in the Office of Special Pesticide Reviews (WH-566), Office of Pesticide Programs, Environmental Protection Agency, East Tower, Room 447, 401 M Street, S.W., Washington, D.C. 20460.)

With regard to mutagenesis, Samosh (53) has reported chromosomal changes in peripheral leukocytes of women exposed to polychlorocamphene.

With regard to endocrine effects, Hurst et al. (54) reported that toxaphene stimulated thyroid growth and I^{131} uptake in bobwhite quail. Makovskaya et al. (55) reported that endocrine glands in rats, mice, and rabbits are sensitive to the effect of polychloropinene.

With regard to reproductive effects, Mayer et al. (56) reported that toxaphene reduced viability of brook trout eggs. Welch et al. (57) reported that pretreatment of rats and mice with toxaphene increased the activity of liver microsomal enzymes that metabolized estrone. Blekherman and Il'ina (58) reported that women exposed to toxaphene showed a deviation from the norm in the menstrual cycle and in estrogen levels.

With regard to enzymatic effects, Desaiah and Koch (59) reported that exposure of channel catfish to toxaphene inhibited Mg^{2+}, NA^{+}, and K^{+} ATPase in brain, kidney, and gill tissues. Kuz'minskaya and Alekhina (60) reported that exposure of rats to toxaphene produced conditions of hypoxia and disturbed the normal course of metabolism in

liver tissues. Welch et al. (57) reported that pretreatment of rats and mice with toxaphene increased the activity of certain microsomal enzymes. Gertig and Nowaczyk (61) reported that rats treated with toxaphene showed decreases in certain enzymatic activities and increases in others.

With regard to population reduction in nontarget organisms, Hunt and Keith (62) reported that toxaphene was responsible for a bird kill in California. Johnson (64) reported a bird kill in South Dakota in which three of the animals had high toxaphene residues. Flickinger (66) reported on a bird kill in Texas in which all of the animals had toxaphene residues. McEwen et al. (69) reported that toxaphene use to control insects on short-grass ranges resulted in bird kills and caused significant population decreases. Toxaphene incidents involving a raccoon (63), the death of a large number of white pelicans in California (65), and a waterfowl kill in Arizona (67), (68) have also been reported.

With regard to fatalities to members of endangered species, toxaphene residues have been reported as being involved with the death of brown pelicans (Pelecanus occidentalis), a rare and endangered species, in the Gulf Coast area of Louisiana in 1975 (70), (71).

Toxaphene: Position Document 1
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