R E P O R T

of the

M I R E X

A D V I S O R Y

C O M M I T T E E

Revised March 1, 1972

REPORT OF THE MIREX ADVISORY COMMITTEE*

TO

WILLIAM D. RUCKELSHAUS, ADMINISTRATOR
ENVIRONMENTAL PROTECTION AGENCY

Revised March 1, 1972**

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*Established Under Provisions of Section 4.c. of the Federal Insecticide, Fungicide, and Rodenticide Act.

**Original report dated February 4, 1972.

CONTENTS

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PESTICIDE RESEARCH LABORATORY
~~ARCHER ROAD~~

March 1, 1972

Mr. William D. Ruckelshaus
Administrator
Environmental Protection Agency
Washington, D. C. 20460

Dear Mr. Ruckelshaus:

On behalf of the membership of the Mirex Advisory Committee, I am pleased to submit the attached revised report of March 1, 1972. In order to meet the statutory deadline, the February 4 report inadvertently contained several statements and interpretations that had not been approved by the entire committee. Consequently, a revision was considered necessary in order to reflect the more significant changes.

It is the opinion of the undersigned that the revision which begins with the last sentence on page 13 could be misinterpreted to mean that Lofgren *et al.* (1970) concluded these trials were a failure since total eradication was not achieved. In reality, Lofgren and co-workers clearly stated that all of the problems encountered in the eradication trials were surmountable and concluded from their data that elimination of the imported fire ant from very large isolated areas may be technically feasible.

It was on the evaluation of the eradication trials that the undersigned reached an empasse with several members of this committee, thereby allowing no possibility for both sides of the controversy to be equitably reflected in the revised report. This difference of opinion on the Advisory Committee is certainly understandable since it reflects the same divergent views that exists within the scientific community most closely associated with this general subject.

Please accept my apologies for the delay these revisions have caused in having a final printing of the Report of the Mirex Advisory Committee. If we can be of any further assistance in clarifying any statements in the report, please do not hesitate to contact any member of the committee.

Sincerely yours,

C. H. Van Middelem

C. H. Van Middelem
Chairman
Mirex Advisory Committee

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Attachment

COLLEGE OF AGRICULTURE   SCHOOL OF FOREST RESOURCES AND CONSERVATION   COOPERATIVE EXTENSION SERVICE
AGRICULTURAL EXPERIMENT STATIONS   CENTER FOR TROPICAL AGRICULTURE

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David L. Bowen
Secretariat to Committee
Environmental Protection Agency

INTRODUCTION

Mirex (Dodecachlorooctahydro-1,3,4-metheno-2H cyclobuta[cd]-pentalene) has been used extensively during the past decade in the southeastern states for the control of the imported fire ant, *Solenopsis saevissima richteri* Forel. A suit filed by the Environmental Defense Fund in August 1970 in the U.S. District Court for the District of Columbia sought an injunction and declaratory judgement to restrain the Department of Agriculture in its efforts to eradicate the imported fire ant.

In a separate case, involving DDT, this same court held on January 7, 1971, that the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) requires the Environmental Protection Agency (EPA) to initiate the administrative process for cancelling the registration of a pesticide whenever there is a substantial question about its safety.

On March 18, 1971, EPA sent a notice to the Allied Chemical Corporation to cancel the registration of products containing Mirex. This action was based on a substantial question about the safety of use of this chemical. Rather than accept the cancellation, the firm requested that the matter be referred to an advisory committee as is its right under the FIFRA. This committee consisting of six scientists was appointed on September 24, 1971, by the Administrator of EPA from a list of names furnished by the National Academy of Sciences. The following Charge was given to the Mirex Advisory Committee:

> The Environmental Protection Agency is presently evaluating the use of the pesticide Mirex. The Agency's decision concerning the continued registration of Mirex will involve balancing its benefits against its dangers. Thus, the Agency must determine and weigh (1) the nature of the benefit conferred by the use of Mirex or, put another away, the magnitude of the social cost of foregoing the use of Mirex, against; (2) the nature and magnitude of the foreseeable hazards associated with the use of Mirex.
>
> In order to assist the Agency's determination, the Committee is charged to consider and evaluate all relevant scientific evidence concerning the use of Mirex, particularly, for fire ant control and to prepare a report and recommendations concerning the scientific issues raised by such use. More specifically, the Committee is charged to consider the scientific evidence and, based thereon, express its opinion and recommendations concerning, _inter alia_, (1) the nature and extent of the problem posed _by the_ fire ant and the other insects at issue; (2) the effectiveness of the several types of control measures which utilize Mirex (e.g., localized use to control local infestations of fire ants; area-wide use to control the spread of fire ants; and a multi-state program to achieve the eradication of the fire ant); (3) the benefits expected to be achieved by each such control program, measured against the damage which will occur if no control were undertaken; and (4) the availability and effectiveness of, and the hazards connected with, alternative control measures.
>
> With respect to the hazards associated with the several uses of Mirex, the Committee is charged to consider the scientific evidence and, based thereon, express its opinion and recommendations concerning, _inter alia_, the nature, scope, and possibility of occurrence of any (1) direct hazard to the user and to the general public; (2) hazard to vegetation; (3) hazard to non-target vertebrate and invertebrate animals; and (4) hazard to the environment generally.

This report follows an outline which was designed to comply with all aspects of the Committee charge. It is divided into two primary sections, the first covers advantages and disadvantages associated with the use of Mirex for the control of the imported fire ant and other insects as well as possible present and future alternative means of control. The second section deals primarily with possible hazards associated with Mirex uses.

Initial evaluation included the nature and extent of the problem involving not only the imported fire ant but other insects controlled effectively with Mirex. The advantages and disadvantages of the various present control measures are covered. Currently available alternative insecticidal control measures as well as possible future non-insecticidal control techniques presently under investigation are discussed. The benefits expected to be achieved by the various control procedures are evaluated against the possible risks to man and his environment from the continued use of Mirex.

The second section of the report is devoted to an evaluation of the possible hazards to man and his environment as a result of past, present and future use of Mirex for the control of the imported fire ant and other insects. This section includes an evaluation of the significance of Mirex residues found in soils, water, natural food chains, human food and man himself as a result of past Mirex applications. Projections of expected environmental load are made as a result of past applications and future use of this toxicant on a more restricted basis. Various aspects of the very limited available toxicological information on Mirex are discussed including acute and subacute toxicology, reproductive effects, carcinogenicity, mutagenicity, absorption, metabolism and excretion. A brief section is devoted to the chemistry of Mirex, established tolerances, possible analytical interferences and suggested confirmation techniques.

I. NATURE AND EXTENT OF PROBLEMS POSED BY THE IMPORTED FIRE ANT AND OTHER PESTS THAT ARE CONTROLLED BY THE USE OF MIREX

A. Imported Fire Ant.

The identity of the imported fire ant, presently known as *Solenopsis saevissima richteri*, is in a state of flux. Some authorities consider that two species have been introduced into the United States: others think that only color forms are involved. All agree that a "dark form" first noticed near Mobile, Alabama about 1920 never dispersed widely and now is known to be the dominant form in only a restricted area of northeast Mississippi. It is similarly agreed that a different ant, smaller and more aggressive, the so-called "red form" appeared during the late 1930's or early 1940's. It spread quickly across the Gulf Coast states and now occurs throughout much of the 9-state area from Texas to North Carolina (Markin 1970).

The pest status of the imported fire ant is controversial. Claims have ranged from its being of no importance as a pest to its being the most dangerous and destructive of all pests in the infested area. Early statements emphasized injury to crops, particularly potatoes, seeds and young seedlings of a variety of crops (Wilson and Eads 1949, Wilson 1951, Culpepper 1953). It is now considered to be more important as a pest of humans than of agriculture. Previous claims about the destructive nature of the species as a pest of crops, livestock, and wildlife were greatly exaggerated. During the last decade, a considerable change has occurred in views on the pest status of the species.

Clearly, the imported fire ant is an important nuisance pests. It stings viciously when disturbed and its presence in areas used extensively, such as lawns, playgrounds, school grounds, parks, cemeteries and gardens, interferes with normal human activity (Mills 1967). Its presence in areas heavily used by small children is especially undesirable and dangerous.

The true significance of the imported fire ant to human health has probably not been evaluated properly in the past. A medical survey in Alabama, Georgia and Mississippi was recently completed involving almost 2500 medical doctors (Triplett 1971). This survey shows that for each year in the period 1969-71, over 10,000 patients were treated as a result of imported fire ant stings. Over 50% of the patients reported in this survey required medical treatment for secondary infections. A significant number of the patients were reported to have experienced some degree of allergic response, with a small percentage suffering such severe reactions that they progressed into a state of anaphylactic shock. These reactions are considered to be at least on a par with anaphylaxis caused by stings of other venomous Hymenoptera.

Information accumulated during the last 15 to 20 years shows that the imported fire ant is of virtually no importance as a direct pest of crops, livestock or wildlife. Occasionally, it may attack seedling plants such as potatoes, corn, and cabbage and the flowers and fruit of okra. Indirectly, the imported fire ant is more important as an agricultural pest. Because of its sting, it causes serious problems for hand laborers harvesting crops such as strawberry, pecan and tung nuts. Baled hay is especially attractive to the ants and large numbers may congregate under bales that are left in the field for several days. Workers handling the infested bales may be stung severely. Farm operations such as mowing improved pastures with sickle type mowers, mowing hay meadows and combine harvesting of crops are made more difficult and expensive by the presence of imported fire ant mounds. On heavy clay soils especially, the mounds may be so large and durable that wear and tear on equipment is excessive. In addition, time is lost in attempting to avoid the mounds and in cleaning and repairing equipment.

The ecological status of the imported fire ant in the United States has not been sufficiently assessed. It is a general predator and scavenger, relying heavily for food upon insects and related arthropods that comprise more than 95 percent of its diet (Hays 1958, Hays and Hays 1959, Wilson and Oliver 1969, Markin 1970). It appears to have competitively displaced the ant species *Solenopsis xyloni*, *S. geminata* and *Pogonomyrmex badius*, (Wilson 1951). It has also displaced the Argentine ant, *Iridomyrmex humilis*, from some areas. Less is known about its effect on populations of other species of ants.

Its role in agricultural ecosystems is difficult to establish as is the case with most species of general predators. It is an effective predator of the sugarcane borer, *Diatraea saccharalis*, (Hensley *et al*. 1961) and the lone star tick, *Ambylomma americanum*, (Harris 1971). It preys heavily upon the eastern subterranean termite, *Reticulitermes flavipes*, and many species of leafhoppers

(Wilson and Oliver 1969). On the other hand, it preys on predaceous insects to the extent that some entomologists believe that it seriously upsets the ecology of an area (Markin 1970). It also tends some species of aphids and protects them from attack by predators and parasites. Thus, its presence may be desirable in some situations and undesirable in others.

Acreage infested by the imported fire ant has continued to expand each year as illustrated in the following table:

Rate of spread of the imported fire ant (Markin 1970, USDA 1971d).

Year	Infested Acres (est.)
1932	200,000
1947	2,000,000
1959	26,000,000
1963	31,000,000
1967	106,000,000
1971	126,500,000

These data show that there was a 13-fold increase in number of acres infested during the 12-year period 1947-59. During the period 1959-71 an additional 5-fold increase occurred despite the conduct of large-scale control and eradication programs and the imposition of Federal and State quarantine and regulatory action that restricted the movement of infested material, especially nursery stock. Efforts to prevent movement into new areas have been notably unsuccessful. There are indications that the pest may be approaching the northern limits of its range but the extent of the area that it may eventually infest in the United States cannot be predicted on the basis of present knowledge.

B. Other Pests in the United States that are Controlled Effectively by Use of Mirex.

In addition to the imported fire ant, the following species of locally important pests are controlled effectively by the use of Mirex applied as bait formulations.

1. Western harvester ant.

The western harvester ant, *Pogonomyrmex occidentalis*, infests millions of acres of rangeland of the western states. It annoys man and animals by its painful sting, denudes areas of vegetation an average of more than 80 square feet around its mounds, collects seeds, cuts off seedling grass as it emerges, and damages the shoulders of highways. The unsightly appearance of the mounds and ability of the species to inflict a painful sting on humans make undesirable its presence in parks, playgrounds, lawns, and other areas heavily used by people (Crowell 1963, Lavigne 1966, Race 1966).

2. Texas leaf-cutting ant.

The Texas leaf-cutting ant, *Atta texana*, is a serious pest of pine seedlings, hardwood trees and cereal and forage crops in some areas of east Texas and west-central Louisiana. In heavily infested areas, damage to buds, needles and bark of all species of pine makes it impossible to establish natural reproduction. Seedling pines are often destroyed in such areas within a few days of planting. Foliage from a wide variety of plants is used by the ants as the substrate upon which they culture a fungus that provides their only known food. Nest areas of this species are characterized by numerous crescent-shaped mounds about one foot in diameter and from 5 to 14 inches in height. The mounds are confined to areas ranging from about 100 square feet to more than an acre. Huge colonies develop and foraging ants may range for hundreds of feet to obtain suitable foliage. These ants are often particularly destructive to gardens and shrubbery in rural and suburban areas. In the American tropics leaf-cutting ants are the most destructive pest of subsistence, "slash and burn" agriculture (Bennett 1958, Echols 1966, Cherrett 1969).

3. Other ants.

Other ants of several species tend and protect aphids, scales and mealybugs and thus aggravate the injury-producing capacity of such pests. It has long been recognized that control of these pests is often best accomplished by controlling the ants. A classic example is control of the mealybug wilt of pineapple in Hawaii by the control of ants, especially *Pheidole megacephala*. It provides transportation and protection for the pineapple mealybug, *Dysmicoccus brevipes*, which is responsible for this serious disease of pineapple. Spread of mealybug wilt in the pineapple plantations of Hawaii during the late 1920's was so rapid that it appeared probable the industry could no longer exist there. The industry was saved by discovery of the relationship between the disease and ants and the development of effective control measures for the latter (Smith 1971).

4. Yellow jackets.

Yellow jackets, *Vespula* spp., are ground-nesting social wasps characterized by aggressive behavior and a painful sting. Allergic reactions to their stings, similar to those of many other Hymenoptera including the imported fire ant, are not uncommon. Populations of these wasps appear to have increased significantly during the last few decades around parks and picnic areas in many sections of the United States. The availability of an abundance of food left by picnickers and campers appears to be a major cause of the increase in population. Their occurrence in large numbers in heavily used recreational areas is especially undesirable because of their aggressive behavior and the fact that a small percentage of the human population is hypersensitive to their venom (Parrish 1963, Keh *et al*. 1968).

II. PRESENT CONTROL METHODS AND ALTERNATIVES

A. Present methods

Technical Mirex, dissolved in soybean oil and sprayed onto corncob grits produces a bait consisting of 0.3 percent Mirex, 14.7 percent soybean oil and 85 percent corncob grits. This bait, used for control of the imported fire ant since 1962, rapidly replaced other insecticides used in cooperative Federal/State programs. Currently Mirex is used exclusively in these programs except for nurseries and other highly specialized situations that demand use of long-residual, persistent insecticides such as heptachlor or dieldrin.

Mirex bait is applied at the rate of 1.25 pounds per acre containing only 1.7 grams of the toxicant. This represents the application of an almost unbelievably small amount of insecticide on a per acre basis in comparison with the rates of application of other insecticides. Few of these are effective for control of agricultural pests at rates less than 100 times the amount of Mirex applied for control of the imported fire ant. Only some insecticidal seed dressings for control of seedling pests approach its effectiveness (Hays and Arant 1960, Bartlett and Lofgren 1961, 1964).

The development of such a highly effective and comparatively selective method of pest control is considered an outstanding achievement in applied entomology. "Mirex approaches many of the requirements for an ideal control chemical for the ant. It is relatively specific as formulated, rather than a broad-spectrum toxicant. It is comparatively nontoxic to vertebrates and to many other animals. It is a highly toxic and advantageously slow-acting stomach poison for the ants, and can be formulated as an attractive bait with potential for low-dosage broadcast in granular form. The chemical itself is exceedingly stable and of low volatility, although present bait formulations do lose their attractiveness and effectiveness in a relatively short period of time" (Mills 1967).

Mirex bait is highly attractive to the foraging workers and readily accepted by the ant. Its delayed toxic effects allow the workers to return to the colony with it where it enters the complex trophallactic food chain and eventually destroys the colony.

Mirex bait can be used effectively for control of the imported fire ant on acreage ranging in size from individual mounds in home lawns to the total infested area of the United States. Its most effective use from the standpoint of control of the ant would be for treatment of the entire infested area and the least effective method would be individual mound treatment (Markin 1971a). Three properly timed applications of Mirex bait, applied at appropriate intervals during a period of 1 year to 18 months at the rate of 1.25 pounds per acre per application, a total of 5.1 grams of Mirex per acre, to the entire infested area would almost eliminate the imported fire ant from the United States.

Results of three large-scale eradication trials (Lofgren et al. 1970) showed Mirex bait to be highly effective for control of the imported fire ant but eradicaton was not acheived. They also demonstrate the occurrence of a number of important operational and technical problems. One of the most important of these is the inadequacy of available survey and detection methods to monitor their effectiveness.

An eradication program for the approximate 126 million infested acres has been considered and rejected by the USDA (USDA 1971c). The current position of the USDA is that, although it may be technically feasible, eradication is no longer an objective of the Federal-State Cooperative Control program because of financial and logistical limitations. Moreover, they were concerned about the possible adverse environmental effects resulting from such large-scale use of Mirex bait.

Next to treatment of the entire infested area in the country, large-scale programs would give the best results. The residual activity of Mirex bait is so short that reinvasion of treated areas occurs rapidly. It appears that the imported fire ant, unassisted by man, may spread at the rate of about 5 to 10 miles per year. Clearly, the smaller the area treated, the more rapidly reinvasion may occur. The individual homeowner, farmer, cattleman, or a municipality, for example, might have to apply one application of the bait per year to suppress populations of the imported fire ant to acceptable levels.

Two or three applications of the bait over large areas might accomplish the same objective for a period of several years. There would be substantially less of the bait per unit area in such a program than where applications were made by the individual. Individuals, having less efficient means of applying extremely small quantities of bait, tend to overtreat. However, individuals would treat only those areas where the presence of the fire ant constitutes a problem whereas areawide treatments would be made to substantial areas where the presence of the fire ant does not constitute a problem. Thus, the relative amount of Mirex used by the two methods of treatment might not differ widely when the total amount applied to an area is considered.

The present program proposed by the U.S. Department of Agriculture (USDA 1971c) for future use in control of the imported fire ant has been described as follows:

"...After thorough consideration of all relevant factors, the Department's position on imported fire ant control is as follows:

1. Mirex bait will be applied aerially to those areas where the ant is causing trouble, where the property owners have expressed concern, and where the State and local governmental agencies have requested Federal cooperation in a control program. Under the plan, forested areas which are not prime fire ant habitat and sensitive areas such as estuarine areas, and State and Federal game refuges will not be treated. Application pilots will be briefed with respect to all sensitive areas, including water, and instructed to avoid application to those areas. Compliance will be closely monitored by ground personnel and aerial supervision.

2. The Federal Quarantine will be continued to minimize further spread of infestations. In support of regulatory activities, outlying isolated infestations and extensions of peripheral areas beyond the regulated areas will be treated... .

The above program is designed to provide relief to those people most seriously affected by the imported fire ant. The proposed cooperative program would be carried out in those States where there is an interest and funds are available for State and/or local participation."

The U.S. Department of Agriculture clarified this proposal by answering the following three questions posed by the Committee:

"1. How do we define prime wildlife habitat?

With respect to the imported fire ant control program, prime wildlife habitat is described as Federal and State game refuges, estuary and marsh areas, wooded areas bordering streams, rivers, and other bodies of water. Heavily wooded areas are not treated because they do not support imported fire ant populations.

2. What is the largest contiguous block that would be treated under this one treatment concept?

In open general farming areas without streams or heavily wooded areas, 50,000 or more contiguous acres may be treated. As a general guideline, if 75 percent or more of the area is open, an electronic guidance system is employed. Cutouts such as rivers, heavily forested areas, and game refuges are marked on the pilot's map, and the recording tape in the aircraft marks these areas that are cut out. When less than 75 percent of the total area is to be treated, small aircraft are used due to the many cutoffs required.

3. What do we plan to do along the peripheral areas?

Treatments are planned in peripheral areas when there is threat of spread to uninfested States or to a new area of an infested State. These treatments are to be made in support of the Federal quarantine."

Economic thresholds, more properly tolerable or comfort thresholds, have not been established. For instance, the current position of the USDA states in part: "Mirex bait will be applied aerially to those areas where the ant is causing trouble, where the property owners have expressed concern, and where the State and local governmental agencies have requested Federal cooperation in a control program" (USDA 1971c). Obviously, these are not objectively determined thresholds. In an eradication or suppression program the presence of any imported fire ant may be critical, but in a control program, treatment thresholds become critical.

Control of other species of ants is normally obtained by individual nest treatment or by broadcasting Mirex bait by hand or ground equipment with treated areas being from several square feet to a few acres. An exception would be treatment of crops where ants are part of an agricultural problem, such as the ant-mealybug complex on pineapples. Here the entire crop acreage might be treated as well as adjacent unpopulated dry areas.

Yellow jacket treatment with Mirex bait is an area treatment not an individual nest treatment. However, the bait is dispensed in containers visited by the insects and not released into the environment. The baited areas would not exceed a square mile or so.

B. Alternative Methods.

1. Current insecticidal

Chlordane, dieldrin, heptachlor and related compounds are quite effective for control of the imported fire ant, are convenient to apply as granules, and give incidental control of ticks, chiggers, and some other pests (Blake _et al_. 1959, Lofgren _et al_. 1961, Lofgren _et al_. 1964). These alternative materials are inexpensive and available. Risk of acute toxicity to people is nil with formulations and dosages used.

These same insecticides are also quite effective in controlling many other ant problems in outdoor situations. However, some leaf-cutting ants are not readily controlled by these insecticides and fumigation is required. Fumigation with either methyl bromide or carbon bisulphide or use of arsenic and sulphur dioxide introduces an acute toxicity hazard to humans.

Baits have a unique advantage for yellow jacket control because the insects seek it out. Chlordane is reported to be an effective alternative for Mirex in yellow jacket bait (Grant _et al_. 1968). Nest control with alternative insecticides is easy if the nest can be found, but this is often difficult.

The choice between Mirex bait and granular heptachlor and related materials for control of the imported fire ant and most other pest species of ants in outdoor situations should be made on the basis of environmental hazards associated with the two types of uses. The effective dosage rates of these alternative chemicals far exceed that used in Mirex bait. Mirex bait was developed for use in imported fire ant programs because of its relatively low environmental hazard. Adverse environmental impact of heptachlor, dieldrin and chlordane would be so much greater than that of Mirex bait that their use would be precluded except in very restricted situations. Moreover, these alternative insecticides are currently registered only for application to limited sites that are not devoted to the production of food and feed crops.

2. Possible future non-insecticidal

Research, until relatively recent time, has emphasized chemical control of the imported fire ant since this is the only practical and effective means of control. Possible alternative methods to insecticidal control are currently receiving increased attention primarily by the USDA and also through its cooperative research grants with various universities. Possible alternatives to chemical control include biological control with parasites, pathogens and predators, sterilization, insect hormones, pheromones and genetic manipulations. The imported fire ant is a remarkably successful species in the southeastern United States when compared to other members of the same genus. This phenomenon, not uncommon with introduced pests, strongly suggests that the imported fire ant has escaped from biological control agents which are effective in South America.

Control of the imported fire ant through the possible use of parasites, pathogens and predators probably offers the best potential for a successful biological control method. At present, there are no known biological agents that are effective in limiting the imported fire ant infestations in the U.S. Recent taxonomic studies (Buren 1972) have shown that the most abundant form of the imported fire ant in the U.S. (red form) is located only in the interior part of Brazil and possibly in sections of Paraguay and Bolivia. These areas are remote and not easily accessible. A parasitic ant associated with the black forms of the fire ant was located in Argentina and Uruguay but its usefulness in the control of the imported fire ant is doubtful. Natural parasites of the imported fire ant in the U.S. have been studied for a number of years in an attempt to find some whose effectiveness could be increased by either mass rearing or environmental modifications. This research is currently being expanded to include pathogens of the imported fire ant.

Considerable research has already been conducted on ant pheromones but more should be done. Some research has been initiated on insect hormones but much more remains to be done before this technique can be properly evaluated as a possible future control technique. A more thorough understanding of the chemical and physical communication system of the ant colony could possibly lead to new control approaches.

Because research on the genetics of ants in general is highly complex, insufficient information is available to assess the practicality of genetic manipulations as a means of controlling the imported fire ant. For example, attempts to develop basic techniques for inducing mating or artifically inseminating ants in the laboratory have not been successful. These techniques are a prerequisite to laboratory and field studies.

Sterilization is probably an impractical technique for imported fire ant control for several reasons. There are no current methods available for mating or rearing large numbers of males in the laboratory. Mating of the imported fire ant occurs during flights throughout the summer months. These flights usually are localized and not readily predictable. Consequently, proper timing of sterile male release to coincide with mating flights would be extremely difficult. The long lifetime of imported fire ant colonies would also complicate the procedure because releases of sterile males would have to be made over a long period of time. Applications of chemical sterilants directly in the field with a bait would also be impractical because they are not species specific, therefore, other invertebrates and vertebrates would be exposed to the sterilant.

It should be emphasized that at the present time there are no biological control measures that could be successfully employed in the near future for the control of the imported fire ant. Increased research on these non-chemical control measures is underway and even further expansion is encouraged. One must be tempered, however, by the reality that a future successful biological agent might also pose significant potential hazards to man and his environment.

III. BENEFIT-RISK EVALUATION

The nuisance effects, public health importance and indirect effects on agriculture of the imported fire ant are of such magnitude that effective control measures must be made available for treatment of areas where the need for control exists. The hazard to human life alone that is posed by hypersensitivity of a small percentage of the population due to the sting of this pest requires the availability of effective control measures. Control of the pest in home lawns, parks, playgrounds, schoolyards and other recreational areas is imperative if use of these areas is not to be denied to many individuals. It is generally agreed that the imported fire ant is a species that the United States would be much better off without.

Recent findings indicated that Mirex residues have been found in varying concentrations in a wide variety of organisms and natural food chains (Markin 1970, Duggan 1971, USDI 1971, Wilson, N.L. 1971). Evidence of delayed toxic effects on some species of crustaceans (Lowe et al. 1971, Ludke et al. 1971) and general paucity of information on ecological effects of large-scale application of Mirex call for reduction in use of this chemical until additional data are available on the significance of this information.

Consideration of the environmental impact of Mirex applications plus the technical and operational difficulties encountered in treating large areas have caused the USDA to reject an eradication program for the entire infested area of the Unites States. The 1971 USDA program using Mirex bait for the control of the imported fire ant avoided treating areas such as heavy woodland, water, estuaries and other poor ant habitats (USDA 1971c). However, the proposed Federal-State Cooperative Control program for 1972 would still involve the treatment of very large areas other than estuarine, heavily forested areas and State and Federal game refuges. Lack of information on such points as the metabolic fate of Mirex in plants and animals and the ecological effects of accumulation of substantial residues of the chemical by non-target species does not permit a final, unequivocal evaluation of the benefit-risk ratio involved in its continued use. It seems worthwhile, therefore, to evaluate the available options for future control of the imported fire ant in the United States on the basis of the information that is available.

Clearly, some level of control of the pest must be provided and use of Mirex bait can provide control at far less demonstrated adverse effect on the environment than any of the other available insecticides.

Treatment of the total infested area with three properly timed applications of Mirex bait at the rate of 1.25 pounds of bait per acre per application (a total of 3.75 pounds of bait per acre containing only 5.1 grams of Mirex) would be by far the most effective method for suppressing imported fire ant populations. However, it would involve treatment of large acreages where the presence of the imported fire ant does not constitute a problem. The environmental impact of such treatment is too poorly understood and the expense too great to justify a program of such magnitude. The USDA is to be commended for changing its position and instituting programs involving control on more limited acreage.

Large-scale treatments for suppression and prevention of additional spread would be much more effective for control of the ant than treatment of limited areas. Treatment by this method would be by skilled, experienced personnel with sophisticated equipment so that the amount of insecticide applied per unit area would be minimal. The problem of re-infestation from adjacent untreated areas would be reduced depending upon the size of the area treated. Further spread of the pest would be slowed. The disadvantages of this method are the same, on a reduced scale, as for treatment of the total area infested in an attempt to achieve eradication.

Treatment according to the proposal described in the USDA position on imported fire ant control would result in adequate control of the pest and in a substantial reduction in further pollution of especially sensitive areas with Mirex. However, the method of control described would still result in the treatment of large areas of rangeland, unimproved pastures, land in soil bank and conservation reserve, and cropland where the imported fire ant may be abundant but does not pose a problem to people or interfere with agricultural operations. If the USDA were to amend its position and consider such areas the same as heavily forested areas, estuarine areas, and State and Federal game refuges, the program would then be one aimed at controlling the species in all areas where it is a pest rather than attempting to suppress populations over large areas.

Treatment of individual properties is the least effective method and would require up to one application per year because of the high rate of reinfestation from untreated areas. This method of treatment would allow the ant to infest the total area to which it is adapted in a relatively short time. It would result in a considerable amount of overtreatment per unit area because of the lack of proper equipment for applying the bait and the lack of training and skill in use of the bait by the property owner. The advantages of this method would be to confine treatment to those areas only where the imported fire ant is a problem and to place the cost of controlling the pest on the individual involved. Effectiveness and safety of individual property treatments could be enhanced by an increased educational program through the responsible state and local agricultural agencies. Because of emphasis on large-scale suppression programs in the past, proper instructions at the local level for small-scale treatment may not have received adequate attention.

Treatment by trained personnel in an organized program would avoid the problems of overtreatment and direct exposure of untrained persons to the Mirex bait. If such treatments were limited to specific locations where there was a demonstrated need, environmental disturbance would probably be less than from treatment by individuals and control would be much better.

It would appear that a method of control combining the best features of the USDA proposal with treatment confined to the minimum area of demonstrated need would have the most favorable benefit-risk ratio.

Benefits from use of Mirex bait to control the western harvester ant, the Texas leaf-cutting ant, the ant-mealybug complex on pineapple and yellow jackets far outweight the possible risks.

In summary, the Committee is unanimous in concluding that the benefits from the continued use of Mirex for the control of the imported fire ant and certain other pest species of ants and yellow jackets outweight considerably the possible risks, assuming that the recommendations in this report are implemented. The benefits to man and his environment are clear, but the risks are largely unknown at the present time.

IV. RESIDUE ESTIMATES

A. Soil (Including Sediments, etc.)

Following an application of Mirex bait (1.7 grams per acre) the theoretical amount of Mirex in a standard 3-inch soil sample would be approximately 4 ppb. Mirex residues in soils from open pastures following normal Mirex aerial treatments, have generally ranged from 0.1 to 10 ppb (Collins and Davis 1971, Markin *et al.* 1971a). Mud samples taken from pond bottoms and drainage ditches have yielded Mirex residues in about the same range as has been reported for soils (Collins and Davis 1971). Sediment samples from freshwater ponds pretreated with Mirex contained residues ranging from 0.01 to 21 ppb (Markin *et al.* 1971a). An exception to these rather low concentrations would be the analysis of mud from four ponds pretreated with 0.1 ppm Mirex which resulted in reported residues from 0.09 ppm, 7 days after treatment to as high as 32.7 ppm in one pond 112 days after application (Van Valin *et al.* 1968). From these studies, it was concluded that residues of Mirex are very stable in mud, water and aquatic vegetation.

B. Water

Mirex is essentially insoluble in water, therefore, its residues reported in fresh or sea water were probably adsorbed on particulate matter suspended in the water. Most analyses of both fresh and salt water samples indicated Mirex residues at below the limit of detection (0.01 ppb). Residues of 0.5 to 1.0 ppb were found in water samples taken from ponds pretreated with 0.1 and 1.0 ppm Mirex, respectively (Van Valin et al. 1968, Collins and Davis 1971, Duke 1971, Markin et al. 1971a, Markin 1971b, Maxwell et al. 1971).

C. Natural Food Chains

Following a single application, most of the Mirex bait on the ground is promptly picked up by the foraging fire ants and carried into their mound for transfer to other ants in the colony. The ants do not consume all of the Mirex, some remains inside the discarded grit and is returned to the soil surface. Among terrestrial communities, unused Mirex grits may be consumed directly by various insect scavengers (e.g., certain ants, crickets, wood roaches, ground beetles). These scavengers are in turn preyed on by certain spiders, reptiles, amphibians and insectivorous birds and mammals. The toxicant may be leached from the bait, washed or occasionally blown directly into aquatic habitats or carried there via food chains by immigrating organisms (Ludke et al. 1971, Markin 1971b, USDI 1971). Mirex bait is apparently resistant to leaching in seawater (Lowe et al. 1971) but is easily leached out by fresh water (Ludke et al. 1971). Preliminary information indicates that Mirex is not readily degraded by biological systems and organisms. Since Mirex is essentially insoluble in water, it probably becomes adsorbed to organic detritus and to sediments (Odum et al. 1969, Maxwell et al. 1971). Species of freshwater and estuarine communities (e.g., crayfish, river shrimps, penaeid shrimps, fiddler crabs and blue crabs) are general scavengers and accumulate Mirex by consuming detritus and sediments (Darnell 1958, Miller 1961, Tagatz 1968). Under laboratory conditions some of these species appear to assimilate Mirex as efficiently as would be expected of their natural food sources (calculated from data in Lowe et al. 1971). The levels of Mirex residues that are lethal to certain aquatic crustaceans are far below those for fish, amphibian, avian and mammalian species (Baker 1964, Dewitt et al. 1964, Naber and Ware 1965, Tucker and Crabtree 1970, Allied Chemical Exhibit No. 21, 1971, Lowe et al. 1971, Ludke et al. 1971, USDI 1971). These curstaceans are eaten by fishes and by birds and mammals that consume both crustaceans and fishes.

Certain aquatic algae have been found to contain relatively high values of Mirex compared to residues in surrounding bottom sediment and water (Markin et al. 1971a). Mirex residues can usually be detected in most fish taken from waters near treated areas, including edible species such as bass, bream, catfish and mullet. Bass and bream usually contain less than 0.5 ppm in their edible portions. Wild catfish and mullet have been found to contain residues as high as 1.0 to 5.0 ppm (Baetcke et al. 1971, Markin 1971b). Catfish residues, in general, have been found to decrease rapidly following a period of time since Mirex was applied, but wild freshwater catfish have been reported to contain up to 0.65 ppm Mirex six months after treatment (Collins and Davis 1971). Commercially raised catfish from artificial ponds in areas that had received a countywide coverage of Mirex bait contained no Mirex in 50 samples taken from 25 separate pond sites (Hawthorne et al. 1971).

Mirex residues have been detected in a significant percentage of marine-estuarine animals monitored in treated areas including oysters, whelks, brachyuran and anomuran crabs and shrimps. Residue levels in these marine species are usually less than 1.0 ppm. Organisms that are believed to feed directly on Mirex bait and the predators of these organisms appear to show a rapid loss of Mirex residues 12 months after the original treatment. Most of these invertebrates exhibited a 90% or greater decrease in Mirex residues during this period. However, a slower decrease was noted for some vertebrates (Allied Chemical Exhibit 21, 1971b, Markin 1971b).

Mirex residue levels are extremely low (<0.05 ppm) or nondetectable in terrestrial plants and in phytophagous animals selected from Mirex-treated areas. Most terrestrial invertebrates have been found to contain less than 0.1 ppm but general scavengers such as crickets and wood roaches may consume Mirex bait directly and have been reported to contain Mirex residues ranging from 10 to 30 ppm. However, within a year after treatment, formerly depleted species are still present but contain Mirex residues that have decreased considerably. Predaceous arthropods, such as spiders, have been found to contain higher residues than general invertebrate populations. Spiders may contain in excess of 1.0 ppm Mirex one year after treatment. Predaceous amphibians and reptiles that have been monitored usually contain relatively high levels of Mirex (1.0 to 5.0 ppm). Several toads have been found with residues of 10 ppm or higher.

Birds, as a group, appear to contain relatively high levels of Mirex. Most insect-eating birds collected in or near a treated area contained Mirex residues in excess of 1.0 ppm, with a few having as high as 10.0 ppm or even higher. The only wild bird egg samples that have been analyzed are from cattle egrets, five of which averaged approximately 13 ppm. It is not known what adverse effect, if any, residues of this level in eggs might have on reproduction. Much higher levels fed to chickens, mallard ducks and bobwhite quail resulted in no apparent adverse reproductive effects (Naber and Ware 1965, Heath 1971). Mirex is a very stable compound chemically and residues in certain species are remarkably persistent. For example, adult snowy egrets contained up to 0.64 ppm and nestlings were analyzed to have up to 3.5 ppm Mirex one year after treatment. Insectivorous land birds have been reported to contain from 0.22 to 9.1 ppm Mirex six to twelve months after treatment (Markin 1971a).

Mirex residues can be detected in most small mammals following bait treatment, but are quite variable and apparently depend upon the feeding habits of the species. Most mammals contain less than 1.0 ppm Mirex. An apparent exception is the shrew, which is an insect feeder. Two specimens were found to have residues of 6.6 and 41.3 ppm. In one study involving a large number of monitored samples, most raccoons were found to contain residues well below 1.0 ppm, but a small percentage was observed to have values in the range of 2 to 5 ppm. Raccoons have been noted to contain as high as 1 ppm Mirex one year after final treatment (USDI 1971).

Mirex residue levels, as well as rates and direction of transfer in the natural food chain, are difficult to interpret or predict for several reasons: (1) Numerous organisms (e.g., omnivores, detritus feeders, filter feeders) cannot be classified into traditional trophic levels, their feeding habits change from larval stage(s) to adult and many are opportunistic feeders as adults (Bakus 1969). (2) Certain species may move considerable distances (e.g., marsh birds, raccoons, blue crabs) and carry residues with them. (3) Tidal flushing, storms and hurricanes can suspend sediments in fresh water lotic and lentic systems and in estuaries. Spring turnover in lakes (upmixing of nutrients from bottom sediments) may also cause resuspension of Mirex-bearing sediments. (4) Mirex residues measured in the past may be partially confused with the polychlorinated biphenyl, Aroclor 1260, and/or Dechlorane, which is chemically identical to Mirex.

From the data currently available, it is evident that Mirex is reaching some non-target organisms as a result of previous large-scale application for the control of the imported fire ant. It is also apparent that Mirex can be transferred through simple two-level food chains (Lowe _et al_. 1971) as well as further up certain food chains. Current and future restrictions on applications of Mirex to sensitive areas plus the possible reduction in dosage rates should result in a significant decrease in future Mirex residues at various levels of natural food chains.

D. Edible Food

1. Plant

In considering all types of biological samples for Mirex residues, the smallest amounts appear to be found in plants (Markin _et al_. 1971a). Earlier work by Allied Chemical Corporation indicated that no Mirex residues could be found in a large selection of field and vegetable crops (Allied Chemical Corporation 1971a). There is some indication that extremely low levels of Mirex may be translocated from the soil into growing plants such as bahiagrass roots and foliage. These were reported to contain from 0.3 to 17 ppb Mirex (Markin _et al_. 1971a).

2. Animal

Milk from cows fed 3 weeks on a daily ration with 0.01 ppm Mirex contained no detectable Mirex, whereas from 0.02 to 0.08 ppm was detected in the raw whole milk from cows fed 3 weeks on a diet containing 1.0 ppm Mirex (USDA 1971b). Milk from cows that had grazed in previously treated areas contained from 2 to 8 ppb. An average of 0.01 ppm Mirex was reported in the fat of raw milk selected from 12 cows grazed in previously treated areas (Baetcke et al. 1971). No detectable Mirex residues (sensitivity 0.3 ppb) were found in 60 milk samples selected from 5 different states involved in the use of Mirex for fire ant control.

Fat samples taken from 63 of 75 beef cattle raised in areas in Mississippi and Georgia, where Mirex has been used to control the imported fire ant, contained very low levels of Mirex (from 0.001 to 0.126 ppm). In general, the Mirex residues detected in these samples comprised a very small fraction of the total organochlorine residue detected (Ford et al. 1971). Mirex residues ranging from 0.05 to 1.6 ppm were found in adipose tissues of deer, quail, wild turkey and beef cattle (Baetcke et al. 1971).

3. Seafood

A recent sampling by the Food and Drug Administration of commercial fishes in Louisiana waters resulted in the detection of Mirex residues in 10 out of 21 total samples. These residues ranged from 0.01 to 0.18 ppm on an edible portion basis. The FDA has not encountered any Mirex residues in other foods tested, including its Total Diet Studies (Duggan 1971). Mirex residues can usually be detected in most fish from treated areas including edible species such as bass, bream and catfish. Usually less than 0.5 ppm Mirex is found in bass and bream. Catfish and mullet have been found to contain 1 to 2 ppm Mirex immediately following treatment, although subsequent monitoring indicated that within 24 to 48 hours the residues dropped to below the 0.5 ppm level (Markin et al. 1971a). This rapid decrease in Mirex residues, suggests that these bottom-feeding fish had ingested individual Mirex grits just prior to the time of analysis.

In marine estuaries, marshes and bays which have been treated, Mirex residues have been found in almost all marine animals including oysters, shrimps, crabs, bottom-feeding and swimming fishes. Three days after a third aerial application of 0.3% Mirex bait to an entire area, Mirex residues of from 0.32 to 2.59 ppm were detected in oysters, shrimps, crabs, catfish and mullet (Markin 1970).

The buildup of Mirex residues in uncaged channel catfish has been reported (Collins and Davis 1971), whereas caged catfish acquired almost no Mirex. One plausible explanation is that uncaged fish obtain their Mirex through the food chain, whereas the caged fish did not have access to the natural energy sources. Buildup of Mirex in uncaged channel catfish increased from no residues detected 10 days after an aerial application (0.3% bait) to the pond and surrounding drainage area, to 0.65 ppm Mirex six months after application. On the other hand, only 0.03 ppm was detected in the caged fish six months after application (Collins and Davis 1971).

No detectable Mirex residues were found in 50 samples of commercially raised catfish in Mississippi (limit of sensitivity 0.01 ppm) (Hawthorne _et al_. 1971). The lack of detectable Mirex residues in this study would indicate that the claim of wide-spread contamination by Mirex appears to be unfounded. It is also doubtful that Mirex residues could be responsible for the deformation or death of fishes (Hawthorne _et al_. 1971).

The edible portion of bluegill fish was found to contain from 0.12 to 0.39 ppm Mirex, whereas largemouth bass contained 0.44 to 0.76 ppm in their edible tissue (USDA 1971a). Catfish caught in the mouth of two rivers in Georgia contained 0.008 to 0.030 ppm Mirex (Curley 1971). Oysters from Savannah, Georgia, contained from 0.004 to 0.036 ppm Mirex, whereas oysters from the Gulf Breeze, Florida and Charleston, South Carolina areas contained no detectable Mirex.

Very low Mirex residues were found in a variety of marine life from the Savannah, Georgia area where Mirex bait had been applied several times (Markin _et al_. 1971c). The monitoring program, in general, failed to indicate that detectable Mirex residues were accumulating in marine life throughout the remainder of the southeastern United States, even though Mirex residues could have reached the sampled marine environment via streams and rivers draining previously treated areas.

In general, it would appear that Mirex residue concentrations currently found in soils, water, vegetables and field crops as well as in meat and milk selected from areas previously treated with Mirex, are so low as to be insignificant as far as any possible hazard to humans. If there is any possible hazard in certain seafoods, it would appear to be restricted to several bottom-feeding fishes in areas that had recently been treated several times with Mirex.

E. Man

Very little data are available on possible residues of Mirex in human beings as a result of treatments for the control of the imported fire ant. Only since April 15, 1971, have the contracting laboratories, Human Monitoring Survey of the States Services Branch of the Division of Pesticide Community Studies in the Environmental Protection Agency, been looking at possible residues of Mirex in the human samples which they collect and analyze. Prior to that time, analyses would not have revealed the presence of Mirex, if indeed any were present. Since that time, contract laboratories have reported the results of more than 700 adipose tissue analyses. These were collected by 55 pathologists in 23 states, including Macon and Atlanta, Georgia; and Pensacola, Florida; areas where Mirex has been used for the control of the imported fire ant. In only 12 of these samples have peaks been observed in the area where Mirex elutes on the gas chromatograph. Two of these were in Louisville, Kentucky; one in Little Rock, Arkansas; one in Atlanta, Georgia; two in Macon, Georgia; and three in Togus, Maine. The highest value observed was 1.03 ppm in the adipose tissue of one of the specimens from Macon, Georgia (Yobs 1971). It must be emphasized that identification of Mirex by gas chromatography in these samples is tentative at best. Considerable doubt is placed on this identification by the presence of significant concentrations of polychlorinated biphenyls (PCBs), several of which are known to elute in the same area on the gas chromatograph. Confirmatory identification of these samples is currently underway but the final results are not available. Further doubt, on the validity of these analytical identifications, is cast by the consideration that half of the 12 samples were reported from three cities which are a considerable distance from areas previously treated with Mirex for the control of the imported fire ant. It should also be noted that the same chemical substance has been widely used as a fire retardant under the trade name Dechlorane. There is the possibility that these human tissue levels, suspected to be Mirex, may be due to exposure to Dechlorane. Actually, it would be extremely surprising if Mirex were found in human tissue at this time, considering the relatively modest quantites of the insecticide used for the control of the imported fire ant and the fact that very little or no Mirex has been found in the human food chain.

F. Projections of Expected Environmental Load

Trends in the accretion, if any, of Mirex in the environment cannot be projected with any degree of confidence at the present time. Additional comprehensive studies need to be conducted in order to effectively evaluate the result of past and current applications of Mirex. As in the case of most other similar persistent pesticides found in the environment, the routes of movement of Mirex have not been well documented. Improved sampling methods are essential for valid censusing of key natural populations of terrestrial and aquatic organisms. Current data from monitoring and total diet studies by the Food and Drug Administration indicate that very little or no Mirex residues were found in man's food supplies (Duggan 1971).

Many of the key environmental species in the areas treated by Mirex for the imported fire ant have been monitored in the past. These monitoring studies are continuously being improved for the future projections of the environmental impact by the continued use of Mirex. Currently available monitoring information clearly indicates that residues of Mirex are appearing in most invertebrate and vertebrate animals that are in close proximity to treated areas. Some invertebrate species that may feed directly on Mirex bait in treated areas suffer significant population declines for a period of time following treatment. However, after a year of no further Mirex treatment, these invertebrate populations appear to recover in the previously treated areas. There is no available information to indicate that any vertebrate populations have been adversely affected despite rather high Mirex residues in certain terrestrial animals such as toads, lizards and insect-eating birds. Vertebrates exposed to Mirex in the field generally contain considerably less of the chemical than that required to affect laboratory animals in controlled studies.

Most monitoring studies in the past few years have been conducted in areas that had been subjected to eradication tests, where three closely spaced applications of Mirex were applied more or less indiscriminately to all parts of the environment including estuaries, marshes and other sensitive areas.

Current and future control programs will attempt to avoid all sensitive areas in the environment and will involve only one application per year versus the previous three-application treatment. Continuous improvement in the Mirex-latex bait should assure that less Mirex will be available to non-target organisms. There is also a very good possibility that a lower dosage level of active toxicant will be utilized to control the imported fire ant. It is projected, therefore, that future Mirex residues encountered in the treated areas of the environment should show a continuous decline.

Since Mirex is a very persistent pesticide and apparently is not readily metabolized in nature, its residues, however minute, are expected to remain in the environment for the foreseeable future. However, because of the extremely small quantity used and the restrictions that have been and will be enforced, the environmental load of Mirex is not considered to be alarming in comparision with other persistent pesticides currently in the environment.

V. TOXICOLOGY

A. Acute and Subacute Toxicity

Very little data are available on the acute and subacute toxicity of Mirex to experimental animals and none on its chronic toxicity. One single study reports that Mirex has an acute LD_{50} of 365 mg/kg in female Sherman rats (Gaines and Kimbrough 1970). This figure is somewhat lower than that reported previously in Sherman strain rats which was 740 mg/kg in males and 600 mg/kg in females (Gaines 1969). In addition, the chronicity factor of Mirex was determined by the technique described by Hayes (1969). The chronicity factor is defined as the single dose LD_{50} in mg/kg divided by the 90-dose LD_{50} in mg/kg per day. The 90-dose oral LD_{50} of Mirex was found to be 6 mg/kg per day giving a chronicity factor of 60.8 (Gaines and Kimbrough 1970). This chronicity factor is by far the highest observed of any pesticide to date. It may be compared to a chronicity factor of less than 5.6 for DDT and of 12.8 for Dieldrin, both of which are considered to be highly persistent compounds. Male and female rats were also fed Mirex at 0, 1, 5 and 25 ppm in the diet (10 animals per group) for 166 days. The livers of these animals were examined by light microscopy in both males and females. At the 5 ppm feeding level, approximately one-half of the rats developed significant, but minimal, pathologic changes. They exhibited slightly enlarged liver cells, vacuolated cytoplasm and occasional inclusions. At the 25 ppm feeding level, most of the rats had definitely enlarged liver cells which were multinucleated with smooth or vacuolated cytoplasm, which showed cytoplasmic inclusions and biliary stasis. Examination of these livers by electron microscopy showed an increase in smooth endoplasmic reticulum, free ribosomes, lipid vacuoles, myelin figures and osmophilic-dense bodies.

In other subacute toxicity experiments, Mirex was fed to rats in the diet for 13 weeks at concentrations of 0, 5, 20, 80, 320 and 1280 ppm (Larson 1968). Deaths were observed at the highest dose level and growth suppression at 320 ppm. Enlarged livers and pathologic changes including swelling and vacuolation of liver cells were found at 80 ppm. The same investigator also fed Mirex to dogs daily at concentrations of 0, 4, 20 and 100 ppm. Deaths were observed at the 100 ppm feeding level, but at 20 ppm no effects were observed. Further studies demonstrated that Mirex was absorbed through skin of rabbits producing toxic effects. Two of 10 rabbits died when a 5% Mirex in corn oil solution was applied at a rate of 10 milliliters per kilo.

B. Reproductive Effects in Mammals

Very few experiments have been conducted on the reproductive effects of Mirex on experimental mammals. Female Sherman rats were fed 25 ppm of Mirex in the diet for 45 and 102 days (Gaines and Kimbrough 1970). The males to which these females were bred were exposed to Mirex in their diet only during the seven-day breeding period. In these animals, significantly fewer offspring were born alive and fewer survived to weaning than the control rats. Furthermore, 33 to 46% of the offspring of these breedings developed cataracts, whereas none were observed in the control animals. At the

5 ppm feeding level, however, no reproductive effects were observed. Further experiments indicated that the pathologic effects of Mirex on the eyes of newborn rats is primarily due to the ingestion of Mirex during the suckling period.

Another study involved large scale feeding of two strains of mice to measure the effect of 5 ppm Mirex fed in the daily diet (Ware and Good 1967). With one strain, Mirex produced a significant increase in parent mortality, whereas parent mortality was not affected in the other strain of mice. In both strains of mice, the Mirex diet resulted in reduced litter size and number of offspring produced per day.

C. Carcinogenicity and Mutagenicity

Only one experimental evaluation has been reported on the possible carcinogenicity of Mirex (Innes *et al*. 1969) but none on its mutagenicity. Mirex was selected as one of the pesticides to be tested at the Bionetics Research Laboratory in a unique massive screening program for tumorigenicity. In this study, a total of 130 compounds was evaluated of which 104 were pesticides. Seven known carcinogens were included as positive controls as well as 19 industrial chemicals. The compounds to be studied were selected on the basis of widespread usage, suggestive chemical structure and evidence of toxicity described in the literature suggesting a potential hazard to man.

Each compound was tested by two routes of administration, oral and subcutaneous, in two hybrid strains of mice. Eighteen male and 18 female mice of each strain were utilized for each test procedure.

In the subcutaneous test, Mirex was administered in a maximally tolerated single dose of 1000 mg/kg. In the oral experiments, a dose of 10 mg/kg per day was given from the 7th to the 28th day. The mice were then fed for the duration of the experiments at the level of 26 ppm in the diet. All mice in both experiments were sacrificed approximately 18 months after the beginning of the experiment.

In the subcutaneous experiment, almost all of the 72 mice survived the 18-month test period to sacrifice. The primary tumors observed in these animals were reticulum cell sarcomas Type I (10/72), pulmonary adenomas (3/72) and hepatomas (7/72). Of the 72 mice to which Mirex had been administered, a total of 20 were found to bear tumors. The incidence of mice developing reticulum cell sarcomas and hepatomas as well as the total tumor-bearing mice fed Mirex was significantly different from the controls at the 99% level.

In the oral administration tests, all mice died prior to the completion of the experiment at 18 months. Twenty-nine of 72 mice developed hepatomas, compared to 14 of 338 control mice (99% significance).

The significance of this bioassay is enhanced by the demonstration that the seven known carcinogens were found clearly to be tumorigenic by this testing procedure. Mirex by oral administration in this bioassay procedure was judged to have a relative risk of 0.945 by comparison with an average of the seven known carcinogens. This would mean that by this bioassay procedure Mirex is very close to being equal in carcinogenic potency to the seven known carcinogenic compounds.

From the results of this testing procedure in which Mirex, fed at relatively high dosages, was found to be tumorigenic in two strains of mice of both sexes, it was concluded that this substance is tumorigenic for this species. These results, however, could certainly not be translated to man. No satisfactory testing procedure for orally ingested carcinogens to which man may be exposed in his diet has been developed. In lieu of this, reliance must be placed on the concept that man is but one species of animal and that testing must be carried out in as many species as possible. If a consistent result is obtained in a number of species, this result probably has significance for man. Therefore, it is urgently desired that Mirex be tested for carcinogenicity in other species so that conclusions about its possible carcinogenic potential for humans can be reached.

D. Toxicity to Aquatic Life

Exposure to Mirex under laboratory conditions affects certain estuarine crustaceans by causing irritability, loss of equilibrium, paralysis and even death. The most susceptible species were found to be juvenile brown and pink shrimp and juvenile blue crabs, whereas pinfish apparently were not affected by the Mirex treatments (Lowe *et al*. 1971). The toxicity of Mirex bait is directly related to temperature, that is, there is a greater manifestation of lethal effects at higher temperatures (McKenzie 1970). Studies on juvenile brown shrimp verify the phenomenon of delayed toxicity exhibited by Mirex which has been previously reported in several other aquatic and terrestrial species (Mahood *et al*. 1970, Markin 1970, Ludke *et al.* 1971, Markin *et al.* 1971a, and W. E. Martin, written communication 1971).

Under controlled laboratory conditions, decreases in population density were observed to occur in ciliate protozoa when placed in a suspension of 1 ppb Mirex (Duke 1971). Two species of freshwater crayfish (*Procambarus blandingi* and *P. hayi*) were found to be extremely sensitive to Mirex under laboratory conditions (Ludke *et al.* 1971). An earlier study of adults of another species of crayfish (*P. clarki*) indicated that they were not sensitive to Mirex (Muncy and Oliver 1963). This was confirmed by a recent study of *P. clarki* in south-central Louisiana which indicates that Mirex is not an important threat to the crayfish industry (Markin *et al.* 1971b). Such discrepancies in results between laboratory experiments and field studies emphasize the species specific effects of Mirex on animal populations.

Mortality of adult crabs and shrimps was observed in a small pond on Cat Island after exposure to higher than normal dosages of Mirex (Markin 1971b). Similar mortalities were not noted in other ponds or a bay on the same island.

In 1969 a cooperative USDA and USDI experiment was initiated at Charleston, South Carolina to study the effects of Mirex on crab and shrimp populations (Duke 1971). Mirex was applied to a 2-square mile area of marshland and estuaries. Samples of crabs and shrimps within the treated areas were collected at biweekly intervals during the three-bait application and for 10 weeks afterwards and analyzed for Mirex residues. Mirex residues in crabs averaged 0.02 ppm during the experiment. There was no observed mortality and crabs and shrimps could be caught at all times following the Mirex bait applications.

Paralysis or death of fiddler crabs may occur within one to several weeks following the ingestion of a single Mirex bait granule under controlled laboratory conditions (Lowe *et al*. 1971). However, in the Cat Island experiment (Markin 1971b), fiddler crab populations were observed to be high at the time of the third Mirex application. No population decline was observed at varying lengths of time following the last of the three applications.

It has been reported that wild catfish in Mirex-treated areas may feed directly upon the bait or obtain Mirex through the food chain. Commercial catfish in 25 ponds in Mississippi from areas where Mirex was used contained no detectable Mirex at 0.01 ppm limit of sensitivity of the method (Hawthorne *et al*. 1971). Another study (Maxwell 1971) reported no adverse effects or mortality to catfish fed 10 and 15 ppm Mirex in their diet for 6 weeks.

There is little evidence to corroborate the lethal effects of Mirex found under controlled laboratory conditions with those in natural aquatic communities. Based on all available monitoring data, there is also little evidence at this time of any serious hazards to populations of fish and crustaceans as a result of standard Mirex bait applications for the control of the imported fire ant. However, previous sampling methods usually have not been adequate for valid censusing of these natural populations. Additional and much more comprehensive studies should be conducted on population densities of Mirex-sensitive aquatic organisms in their natural habitats.

E. Toxicity to Wildlife

Although a decline in populations attributed to Mirex has been reported for crickets, oil-loving ants, and ground beetles (Wilson, N.L. 1971), there is no evidence available to indicate that these populations are permanently affected. A number of LD_{50} values has been established for Mirex and these values indicated that this pesticide is rather low in its toxicity to rats and a few species of adult birds (Larson 1968, Gaines 1969, Gaines and Kimbrough 1970, Baetcke *et al*. 1971).

Despite the fact that significant Mirex residues are being found in numerous key environmental species being monitored in areas previously treated with multiple aerial applications, there is no evidence to date of any significant adverse effects on natural populations of fishes, amphibians, reptiles, birds and mammals. Investigations are still required to evaluate any possible latent effects of Mirex residues on key vertebrate species in the field to determine possible adverse effects on their behavior, brood size and survivorship. There is always the possibility of subtle adverse effects on certain wildlife species subjected to long-term, sublethal residues of Mirex in treated areas.

F. Absorption, Metabolism and Excretion

Even less data are available on the absorption rate and excretion of Mirex in experimental animals than on the biological effects. A single unpublished and incomplete report is available on the administration of carbon-14 labeled Mirex (Matthews 1971). Following a single dose to rats, the radioactivity of various tissues and excreta were determined. As might be expected, Mirex was found to be stored in adipose tissue. Data from this report indicate that Mirex has a half-life of at least 25 days, which is considerably longer than the half-life values cited for other persistent pesticides. This half-life value for Mirex probably constitutes an underestimation of the extrapolated data (Matthews 1971). Thin-layer chromatography of extracts of the tissues and excreta revealed the presence of no metabolites. Mirex was incubated with homogenized liver fractions of rats, mice and rabbits for a period of up to 36 hours. These studies indicate that there is no evidence of any metabolites of Mirex. Very preliminary information from the U.S. Forest Laboratory at the Research Triangle indicated that Mirex at the concentrations used exhibited no effect on populations of soil microorganisms, and that Mirex was not found to be degraded by the microorganisms under the conditions of the experiment (Matthews 1971).

G. Biochemical

Fragmentary evidence is available which indicates that Mirex is a stimulator of the liver microsomal oxidative metabolism pathway (Baetcke *et al.* 1971). Proliferation of the endoplasmic reticulum and an increase in oxidative metabolism has been observed.

VI. MISCELLANEOUS

A. Chemistry

The chemical name for Mirex is dodecachlorooctahydro-1,3,4-metheno-2H cyclobuta[cd]pentalene and the empirical formula is $C_{10}Cl_{12}$. Mirex has a closed 10-carbon structure, with all valence points chlorinated. It is nonflammable and insoluble in water. Since Mirex is totally chlorinated and has no free reactive groups readily available for chemical attack, it is a very stable compound chemically (Markin 1970).

B. Tolerances

Established tolerances for residues of Mirex in or on raw agricultural commodities were published in the Federal Register (36 FR 3965 March 3, 1971) as follows: 0.1 ppm (negligible residue) in the fat of meat of cattle, goats, hogs, horses, poultry, and sheep; 0.1 ppm (negligible residue) in milk fat and eggs; and 0.01 ppm (negligible residue) in or on all other raw agricultural commodities.

C. Possible Analytical Interferences and Misinterpretations

It is quite possible that some earlier Mirex residues, particularly in aquatic samples, may have been partially misidentified. As with many other chlorinated pesticides, Mirex can be confused with PCBs eluting from a gas chromatograph. For example, Aroclor 1260 has an almost identical retention time with Mirex on many commonly used gas chromatographic columns. Adequate techniques for separating PCBs from organochlorine pesticides were not available until 1970 and were not developed and tested for Mirex until more recently. In one particular study (Markin et al. 1971c), the first analyses of samples by a standard cleanup method indicated that 40% contained Mirex residues. However, utilizing a new technique to separate Aroclor 1260 from Mirex, it was determined that the first analyses had been in error since part or all of the original gas chromatographic peak could be attributed to Aroclor 1260.

Another possible source of analytical misinterpretation might result if a commercial fire retardant called Dechlorane was present in environmental samples being analyzed for Mirex residues. Since this contaminant is chemically identical to Mirex, it would be impossible to differentiate between the two compounds by gas chromatographic or any other usual means of analyses. Sales of Dechlorane in the past decade have been over four times those for Mirex during the same period (Communication to Mirex Advisory Committee by Allied Chemical Company December 21, 1971). The distribution of Dechlorane in the environment is unknown.

D. Analytical Confirmation

It is very important to employ adequate analytical confirmation techniques before publishing pesticide or PCB residue data obtained from environmental samples. Even the use of two gas chromatographic columns of varying polarity may not be adequate. Further confirmation should be made by thin layer

CONCLUSIONS

In compliance with its charge to consider and evaluate all relevant scientific evidence concerning the use of Mirex, particularly for fire ant control, the Mirex Advisory Committee has reached the following conclusions based on careful evaluation of all available data.

A. Problems Posed by the Imported Fire Ant

1. The imported fire ant currently infests more than 126,000,000 acres in nine southern states and continues to expand its range.

2. The imported fire ant is a major nuisance pest because of its sting. Its presence restricts the use of recreational and other public areas as well as private property.

3. The imported fire ant is a health hazard because of the development of secondary infection and allergic reactions to its venom. A small percentage of its victims are hypersensitive to the venom and may suffer anaphylactic shock.

4. The imported fire ant is of relatively minor importance as an agricultural pest. The threat of being stung interferes with hand labor involved in the cultivation and harvest of some crops and the mounds may damage mowing machines and combine harvesters.

5. The imported fire ant is an aggressive predator of other arthropods including both pests and beneficial species. Present information is not adequate for an evaluation of its impact on the populations of these organisms. It is also a scavenger of undetermined significance.

B. Control of the Imported Fire Ant

1. Mirex bait is effective for control of the imported fire

ant when applied in minute amounts of active ingredient per acre. One application usually eliminates more than 90 percent of the mounds in a treated area. Three applications at about six-month intervals virtually eliminates all mounds exposed to treatment.

2. Mirex bait may be used on a scale ranging from a single application to one mound to multiple applications to the entire infested area of the southern states. The degree of control of the imported fire ant would be correlated with the size of the area treated and the number of applications.

a. Individual mound treatment is the least effective of all control programs. Broadcast treatment of individual properties would give adequate short-term control in the areas treated. Retreatment on an annual basis would be required in such a program because of reinvasion from adjacent untreated areas. Environmental contamination would be minimal. Handling of bait by untrained people would result in the possibility of excessive application rates and more direct human exposure than in other methods of control.

b. A publicly sponsored control program involving application of Mirex bait as needed, based on pest population assessment, offers the greatest relief with minimal environmental impact. Such a program would give satisfactory control of the pest for a year or more with one application. Subsequent single applications would be made as needed.

c. Multiple treatment of large contiguous areas for suppression of imported fire ant populations results in effective control of the pest for several years and reduces reinvasion from untreated areas, but would do little more to alleviate the problem than a control program such as that considered in the preceding paragraph. Large areas where the ant is not a pest would be treated with Mirex resulting in the possibility of unnecessary environmental contamination and greater initial costs.

d. A successful eradication program would yield the greatest long-term benefits. The possibility of adverse environmental impact is such that it could only be considered if success were assured. The possibility that eradication of the imported fire ant could be achieved with current technology is still a controversial issue. However, eradication of the pest is no longer an objective because of financial and logistical limitations and possible adverse environmental effects.

3. A program involving multiple applications of Mirex bait to the periphery of the infested areas has probably delayed, but not prevented, continuing spread of the pest. Lack of adequate survey methods results in treatment of some uninfested areas and failure to treat some infested areas. Because of the size of the infested area in the United States, effective treatment of the peripheral areas would require repetitive application of Mirex bait to a contiguous area that would involve millions of acres.

C. Control of Miscellaneous Pests

The Western harvester ant, the Texas leaf-cutting ant, and other species of ant pests are controlled with Mirex bait applied to individual nests or small areas. The most effective way of controlling some serious agricultural pests, particularly aphids, scale insects and mealybugs, is to control the ants that protect and transport these pests. Yellow jackets are nuisances in recreational areas, and a small percentage of people stung are hypersensitive to the venom. Mirex baits provide highly effective and comparatively selective control for all of these pests. Compared to effective alternative methods of control, such baits are safe and have little, if any, adverse environmental effects.

D. Alternative Control Measures

1. For the past several years, the USDA has conducted a continuing screening program for new, less persistent insecticides to replace Mirex. Although several compounds have shown promise in laboratory tests, none has proved to be an effective alternative in field experiments.

2. Aldrin, chlordane, dieldrin and heptachlor used to control the imported fire ant prior to the development of Mirex remain as available alternatives. However, these compounds are currently registered for use only for limited sites that are not devoted to production of food and feed crops and could not be used for broadcast applications over extensive areas. The effective dosage rates of these alternative chemicals far exceed that use in Mirex bait and, therefore, their substitution is considered inadvisable.

3. A search is underway for an effective biological control agent to replace chemical control of the imported fire ant. No method of biological control presently under investgation shows promise in the immediate future of effectively supplementing or replacing chemical control.

E. Potential Hazards Associated With the Use of Mirex

1. No instances of any acute intoxication to users have been reported due to the handling or application of Mirex bait in over a decade of use.

2. There is no evidence of damage to vegetation from the use of Mirex bait. No significant absorption of Mirex by, or translocation of residues from soil into, plants consumed by man or his domestic animals has been reported. Residues of Mirex in edible food or feed are nonexistent or extremely low. The significance, if any, of these minute residues to the health of man or his domestic animals is unknown.

3. Most investigations of the effects of Mirex on invertebrates and vertebrates in the natural habitat have failed to demonstrate any significant changes in their populations. Field studies have shown significant population declines of several terrestrial invertebrate species, most but not all of which apparently feed directly on the Mirex bait. Sampling methods have not been adequate for censusing some natural populations of terrestrial and aquatic organisms. Laboratory experiments have shown toxic effects on juvenile crustaceans exposed to low concentrations of Mirex. Monitoring studies have indicated considerable Mirex residues in some invertebrates and vertebrates, especially those that are predaceous on ants and other insects.

4. Mirex residues in water appear to be non-detectable or minimal as a result of normal Mirex treatments to control the imported fire ant. Residues in soil occur where Mirex has been

used and are minimal in magnitude. Mirex residues, although occurring at low concentrations in aquatic sediments, may be of some biological importance because of the probable ingestion of organic detritus and other components by bottom-feeding crustaceans. Very preliminary studies indicate that Mirex residues are not degraded by biological systems and organisms.

5. Monitoring of Mirex in certain edible food products selected from treated areas indicates insignificant residues, if indeed they occur at all, presently in the human food chain despite the widespread application of Mirex during the past decade for the control of the imported fire ant in the infested areas. In preliminary studies, only a small percentage of human adipose tissue samples analyzed showed the presence of suspected and unconfirmed Mirex residues.

6. Insufficient data are available on most mammals for an accurate evaluation of the acute toxicity of Mirex. In rats, it exhibits a low degree of acute toxicity, but subacute studies indicate pathologic changes in the liver at low feeding levels. Subacute feeding experiments in dogs produced no pathological effects at low chronic feeding levels.

7. No data are available on the chronic toxicity of Mirex for experimental animals. Such data are urgently needed before valid conclusions on the possible hazards of Mirex to man can be drawn.

8. Mirex caused significant reproductive effects in rats when fed at relatively high levels in the diet but no effects when

fed at rates likely to occur on food or feed as a result of applications made for control of the imported fire ant. Mirex produced no measurable reproductive effects in bobwhite quail or mallard ducks when fed at relatively high levels in the diet in long-term studies.

9. Based on meager and preliminary data from a rat feeding experiment, no metabolites of Mirex have been detected. It is stored in the fat depots of animals and appears to have a biological half-life of at least 25 days.

10. Mirex has been demonstrated to be tumorigenic to two strains of mice when fed relatively high dosages. However, no conclusions can be reached concerning the carcinogenicity of Mirex for man until it has been studied in other mammalian species.

F. Miscellaneous

During the past decade, Dechlorane, which is chemically identical to Mirex, has been used for numerous industrial applications in amounts far greater than amounts of Mirex used for imported fire ant control. The degree of environmental pollution from this source is unknown.

RECOMMENDATIONS

1. The registration of products containing Mirex should be continued with labeling restrictions to minimize environmental contamination.
2. Publicly supported control programs should be limited to Mirex application, according to need based on pest population assessment, to infested areas where the imported fire ant is a problem because of use by people or interference with agricultural operations. Estuaries and other aquatic habitats, wildlife refuges, and heavily forested areas should not be treated.
3. Where publicly sponsored programs are unavailable, broadcast treatment of lawns, pastures, schoolgrounds, parks, and similar areas by individuals is recommended instead of mound treatment. Educational programs should instruct infested property owners as to how Mirex can be applied for the most effective control of the imported fire ant with minimal environmental contamination.
4. To implement control programs, much more information is needed to establish economic or nuisance threshold levels requiring Mirex treatment as well as on rates of reinfestation and population recovery in areas receiving a single bait treatment.
5. Considerably more research on the possible hazards of Mirex to man and his environment must be conducted before the role of Mirex, as a pesticide, can be accurately assessed. Chronic toxicity, carcinogenicity, mutagenicity, teratogenicity and the metabolic fate of this compound in multiple species should be

further studied. Additional work on the biological stability, persistence and routes of movement of Mirex under field conditions is needed. Continued and expanded monitoring of key environmental carriers and selected commercially important species for Mirex residues should be carried out with emphasis on the detection of any significant contamination of the human food chain. More thorough studies on the effects of Mirex on aquatic crustaceans are needed, especially the monitoring of population densities in the field. Greater effort should be made to correlate laboratory and field research. Increased research is to be encouraged for the non-insecticidal control of the imported fire ant.

Respectfully submitted,

C. H. Van Middelem

C. H. Van Middelem, Ph.D., Chairman

March 1, 1972

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PERSONS APPEARING BEFORE THE COMMITTEE

First Meeting

October 27 & 28, 1971

Mr. Harold G. Alford, Pesticides Regulation Division, Environmental Protection Agency

Dr. W. G. Eden, University of Florida

Mr. Leo G. K. Iverson, Animal and Plant Health Service, U. S. Department of Agriculture

Dr. William A. Knapp, Allied Chemical Corporation

Mr. Donald J. Mulvihill, Attorney for Allied Chemical Corporation

Mr. George A. Robertson, Office of General Counsel, Environmental Protection Agency

Dr. R. Faser Triplett, Mississippi Allergy Clinic, Jackson, Mississippi

Dr. Robert J. Weir, Bionetics Research Labs., Inc.

Second Meeting

November 17 & 18, 1971

Dr. Karl Baetcke, Mississippi State University

Dr. R. R. Bates, National Cancer Institute, National Institutes of Health

Mr. J. Phil Campbell, Under Secretary, U. S. Department of Agriculture

Dr. Thomas W. Duke, Gulf Breeze Marine Laboratory, Environmental Protection Agency

Dr. O. Garth Fitzhugh, Office of Pesticides Programs, Environmental Protection Agency

Mr. James O. Lee, Jr., Animal and Plant Health Service, U. S. Department of Agriculture

Dr. Robert J. Livingston, Florida State University

Dr. George P. Markin, Animal and Plant Health Service, U. S. Department of Agriculture, Gulfport, Mississippi

Mr. William E. Martin, Fish and Wildlife Service, U. S. Department of the Interior

Dr. H. B. Matthews, National Institutes of Environmental Health Services

Dr. F. J. Mulhern, Animal and Plant Health Service, U. S. Department of Agriculture

Mr. M. T. Pender, Animal and Plant Health Service, U. S. Department of Agriculture

Mr. D. R. Shepherd, Animal and Plant Health Service, U. S. Department of Agriculture

Dr. James Smith, Pineapple Growers Association of Hawaii

Dr. D. Weidhaas, Entomology Research Division, U. S. Department of Agriculture, Gainesville, Florida

Dr. Anne Yobs, Division of Community Studies, Environmental Protection Agency

Third Meeting

December 21 & 22, 1971

Mr. Roy Bailey, Allied Chemical Corporation

Dr. Frederick Coulston, Albany Medical College of Union University

Dr. William A. Knapp, Allied Chemical Corporation

Mr. Donald J. Mulvihill, Attorney for Allied Chemical Corporation