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Pesticides research

UNIVERSITY OF ILLINOIS, CORNELL UNIVERSITY, AND UNIVERSITY OF CALIFORNIA, BERKELEY AND RIVERSIDE - RESEARCH ON PESTICIDE CHEMICALS

It was, on motion,

RESOLVED RF 69073 that the sum of Six hundred thousand dollars ($600,000), or as much thereof as may be necessary, be, and it hereby is, appropriated for release at the discretion of the officers, in approximately equal amounts, to the UNIVERSITY OF ILLINOIS, CORNELL UNIVERSITY, the UNIVERSITY OF CALIFORNIA, BERKELEY, and the UNIVERSITY OF CALIFORNIA, RIVERSIDE, toward support of collaborative research and graduate training on the development of selective, non-persistent pesticide chemicals; this sum to be available for use during the three-year period beginning January 1, 1970.

The above action was taken after an oral presentation of the project by Dr. Myers and following discussion.

Among the considerations presented were:

Agricultural Sciences: Allied Interests - Quality of the Environment

Previous Interest: No assistance for, or related to, this purpose has been provided for Cornell University or the University of California, Berkeley.

Between 1950 and 1959, five grants totaling $165,000 were made to the University of Illinois for research programs on insect nutrition and biochemistry and the mode of action of insecticides.

The Foundation made two grants, in 1952 and 1954, totaling $30,000, to the University of California, Riverside, for research on insecticides at the Citrus Experiment Station.

General Description: There is increasing public concern about the adverse effects on the environment of pesticide chemicals used for agricultural, public health, and other purposes. Use of such chemicals is increasing at the rate of 10 percent per year in the

United States, and probably at about the same rate worldwide. It is not expected that an adequate alternative to chemical pesticides will be developed for the control of most pests in the foreseeable future. Therefore, their use may be expected to continue to grow, in the interests of producing increasing amounts of food, feed, and fiber; freeing man from a host of vector-borne diseases; and controlling insects that annoy man and domestic animals.

Some pesticide chemicals persist long after they are applied, and their toxic residues contaminate the biosphere. The more persistent ones may remain in the environment for months and even years. Some of them are accumulated and stored in organisms which ingest them, and when such organisms form part of the food chain the toxic chemicals are passed on to other organisms and often to regions far removed from the site of application. Most of the presently used pesticides, particularly the insecticides and herbicides, have toxicity to a broad spectrum of pests and, in the case of insecticides, also to beneficial insects and animals, as well as to man.

The concern about these adverse effects has already resulted in public action to limit use of certain pesticides. Sweden, for example, has banned the sale and use of DDT pending the development of additional information about it; legal efforts to ban it in Wisconsin appear likely to succeed; and other states, such as Michigan, Arizona, and California, have greatly restricted its use. Efforts toward similar action affecting a number of the most effective pesticides are almost certain to develop. Yet in view of the pressing need for pesticides in agricultural production, public health, and control of annoying insects - and the lack of any adequate alternative control methods - it is probably not feasible to prohibit their use. Although efforts to find nonchemical control methods should be continued and accelerated, the greatest hope is to develop chemicals which will control the target pests with no, or at least tolerable, effects on the environment.

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Pesticides are needed that have greater specificity of action and more rapid and controlled biological and chemical-physical degradability to nontoxic residues.

The four laboratory groups that have submitted the present proposal to the Foundation are the leaders in the United States in research on the basic physiological, biochemical, and organic- and physical-chemical aspects of specificity of insecticide action and degradability. In fact, little work in this important area is being done except in these laboratories. Research conducted in them to date indicates that promising avenues of attack on the problem of insecticide specificity may include the discovery of selective inhibitors of vital insect enzyme systems, the development of chemicals that will be selectively metabolized or detoxified by insect and other animal species, and the possibility of the use of synergists, which selectively inhibit the degradative mechanisms in target insect species.

More is known about the cholinesterases and about the detailed chemistry of their inactivation by organophosphorus and carbamate insecticides than about the operation of any other enzyme system in insects. There are substantial differences between the structural features of the cholinesterases in various insects, and also between those in insects and those in higher animals. It is possible that these differences can be utilized in the design of highly specific new insecticides.

Other enzyme systems - as yet less well known than the cholinesterases - for which it may be possible to develop selective inhibitors, include choline acetylase, NADH oxidase, and the enzymes involved in chitin synthesis. It is anticipated that effective and selective blocking agents may be designed for certain biochemical and neurological receptors such as neuromuscular junctions, GABA receptors, and oxidative phosphorylation systems. Intensive research on one or more of these systems, which will go beyond the present knowledge of them, is greatly needed.

Illinois, who will serve informally as leader of the coordinated program. Dr. Metcalf has been a pioneering research worker in this field.

The principal investigators in the four laboratory groups concerned propose to develop closely coordinated research programs through frequent communication, regular annual meetings, and exchanges of scientists and graduate students. Six eminent scientists are involved in this effort. Because of their association over many years they constitute a compatible, coherent group.

Although the four laboratory groups conduct similar research, their particular areas of emphasis make them complementary. For example, the group at the University of Illinois concentrates on enzyme systems and in developing and evaluating biochemical lesions in these systems. The Cornell University group concentrates on detoxification enzymes, the microsomal enzymes which are concerned with insecticide metabolism, the mechanism of synergistic action, and the molecular basis of action of axonic agents and neuromuscular blocking agents. The group at the University of California, Berkeley, emphasizes the biological and physical-chemical degradation pathways, including photodegradation and metabolism. The group at the University of California, Riverside, emphasizes organic and physical chemistry studies, including the synthesis of new chemicals and the relationship of chemical structure to insecticidal activity and target specificity.

Despite the obvious importance of research to the development of insecticides with great specificity and controlled degradability, support for it remains difficult to obtain. The four universities concerned with this project will provide the salaries of the investigators, research space and facilities, essential equipment, and limited operating funds. The U.S. Department of Agriculture, yielding to public opinion, has turned to nonchemical methods in most of its insect control research. And when it was engaged in pesticide

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Certain microsomal enzyme systems are apparently responsible for the metabolism of pesticide chemicals. Preliminary evidence indicates that there are important differences among insect species and between insects and other animals in the functional characteristics and chemical structures of these microsomal enzymes.

Hydrolytic degradation is an important avenue of detoxification. Information is being accumulated on the influence of steric configurations about the phosphorus atom on the selective detoxification of organophosphorus compounds in insects and mammals. Such information could open another path to the design of more selective insecticides.

Too little is now known about the chemistry of the degradation of insecticide chemicals to permit statements about the effects of various components of the environment. Were such information available, however, it would permit the design of chemical molecules with more rapid degradability under intended conditions of use. Also, there is evidence that certain chemicals either retard or accelerate the rate of degradation of such pesticides as DDT. More knowledge on those subjects could lead to effective control of the rate of degradation in a given environment.

In addition to the need for substantive research on the problems described above, there is a severe shortage of highly trained people to work in the area of insecticide development. Since the four laboratories for which the present aid is proposed are probably the foremost in the world in the basic study of insecticides, they can have a profound influence on the training of graduate and post-doctoral students in this critical area. The importance of this training effort to the fostering of future emphasis on the same kind of research is indicated by the fact that the principal investigators in each of three of the laboratories were graduate students of Dr. Robert Metcalf of the Department of Zoology of the University of

research its objectives were contrary to those proposed herein - it sought to develop pesticides with a broad spectrum of action and with persistence, which are distinct advantages to the user from the limited point of view of insect control but are responsible for the pervasive effects of pesticides on the environment.

It is anticipated that the success of the research proposed in this item would in time bring about increased support from public sources.

Finances: An initial grant of $600,000 for use over a three-year period beginning January 1, 1970, is recommended. The funds would be released by the officers, on the basis of approved budgets, in amounts of appproximately $50,000 annually for the laboratory at each university. The funds to be provided for the four laboratories would be used by each primarily for support of two to three post-doctoral fellows and three to four predoctoral scholars annually. Limited funds would also be provided for supplies and special equipment for each laboratory.

Comment: Pesticides, especially persistent insecticides, are important pollutants of the environment. They constitute a hazard to beneficial insects, to wild and domestic animals, and to man himself. But there is a continuing need for effective insect control methods, and in the absence of alternative effective methods for control of most insect pests, chemical pesticides will continue to be necessary. What must be hoped for, and what this proposal looks toward, is the development of new chemical pesticides which, because of their specificity of action and controllable degradability, will provide effective pest control while having no, or at least tolerable, adverse effects on the environment.

Future Implications: The investigators who have submitted this proposal believe that support for a five- to seven-year period may be required to make certain of the effectiveness of their approach and to stimulate more adequate support for it from federal and state

sources. If the proposed research progresses as anticipated and there is a continuing need for Foundation assistance at the end of the initial three years, the officers may wish to recommend further support at that time.

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