EPA REGULATION OF BIOLOGICAL PESTICIDES

A great deal of interest has recently been expressed in biological pest control agents and the degree to which the Environmental Protection Agency's policies and practices act as a stimulus or obstacle to the development and use of these products.

The vast majority of the more than one thousand pesticide active ingredients regulated by the EPA are man-made organic chemicals. There is, however, a class of pesticides which is inherently different from those products which function as pesticides through their innate toxicity. The pesticides which function by modes of action other than innate toxicity include true biological agents, living or reproduced biological entities such as viruses, bacteria, fungi, and protozoans and naturally occurring biochemicals such as plant growth regulators, insect pheromones, and hormones. At this time "biological" pesticides account for less than 1 percent of all pesticide products registered by the EPA.

During the last decade there has been an upsurge in commercial and governmental activity in the development and use of biologicals. EPA and other agencies (e.g., USDA) have sought to stimulate this area of technological innovation by research efforts and by utilization of such materials in governmental pest control programs. The need to design registration requirements specific to this category of pesticides has been identified as a high priority by a number of scientific groups, including the National Academy of Sciences. Because of the recent interest in the development and regulation of biological pesticides, this paper has been prepared to provide a short history of the subject and the Agency's expectations for future policies and direction.

BACKGROUND

EPA is responsible for administering the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), which provides authority to regulate the marketing of pesticides and requires, among other things, that such products be registered with the Agency. Under the amended FIFRA, the registration of any pesticide is contingent upon the availability of data adequate to demonstrate that the product will not pose the risk of unreasonable adverse effects on man or the environment when used in accordance with its label directions or in accordance with commonly recognized practice. The recently enacted 1978 amendments to the Act do not change this fundamental mandate. Under FIFRA, "pesticides" are

defined as "any substance or mixture of substances intended for preventing, destroying, repelling, or mitigating any pest." Biological agents therefore, clearly fall under this definition. Generally, biologicals can be divided into three categories:

(1) classical biological controls, including parasite and predator species;

(2) naturally occurring biochemicals that may attract, retard, or destroy pests--for example, pheromones, hormones, and plant growth regulators;

(3) micro-organisms such as viruses, bacteria, protozoa, and fungi, which have replicative potential.

While all three of these categories could be regulated as pesticides under FIFRA, EPA had decided informally to exempt from regulation the kinds of parasites and predators in category (1) above. These pest control agents are recognized as posing no known human health hazards. Their ecological effects are currently monitored under the various pest control authorities of the U.S. Department of Agriculture and the U.S. Department of the Interior.

The other two categories, however, are subject to the registration provisions of the Act. These products must undergo Agency review before marketing to insure that they meet the statutory standard of not posing any "unreasonable adverse effects" on man or the environment.

REGISTRATION OF BIOLOGICAL PESTICIDES

EPA recognizes that registration requirements for testing and data under the existing Agency guidelines are oriented toward the more traditional pest control chemicals and are generally not applicable to biological agents. Because of the wide variety of biological pesticides, however, there is potentially great variance in the testing and data necessary for EPA to be able to decide that an agent can be used safely. Thus, registration of biological pesticide agents has been handled on a case-by-case basis. Informal guidance on registration requirements has been developed

and published in books and professional journals; however, most registrants have had to consult with EPA on which data requirements are most appropriate to their particular biological control agent.

Although the volume of applications for registration of biological control agents has remained low and all submitted have received registration, it may well be that the lack of guidelines for registration of biologicals has introduced such a large degree of uncertainty into the registration process that potential registrants are "scared off" and do not even attempt to register and market their products. Furthermore, the lack of guidelines may result in the imposition of unnecessary data requirements that are both costly and time consuming to the registrant. EPA recognizes that registration guidelines which are specific to biological pesticides are desirable and would alleviate uncertainty over data requirements. Consequently, in order to improve the registration process for these compounds, the Agency will:

(1) Develop guidelines specifying data requirements for registration. These are scheduled to be published for public comment on a staggered schedule beginning in July 1979. Final guidelines will be promulgated in 1980.

(2) Complete the development of efficacy guidelines under contract with the American Institute of Biological Sciences for pheromones, hormones, and viruses.

(3) Continue the panel of virology experts developing agreed protocols, areas of protocol research needs, and risk information for viral pest control.

(4) Establish a panel of university, USDA, environmentalists, and industry experts to provide recommendations on risk assessment data requirements for insect hormones and pheromones.

(5) Draft regulations clearly excluding non-microbial biological control agents from FIFRA regulation.

(6) Publish a general policy statement explaining the Agency position on regulation of biological pesticides in the Federal Register.

DATA REQUIREMENTS FOR BIOLOGICAL PESTICIDES

There is no reason to assume that a biological agent will not result in adverse effects simply because it is biological, just as more traditional pesticides cannot be judged harmful simply because they do not occur naturally. Clearly, EPA must determine whether biologicals cause any health or environmental hazards, and this consideration must be reflected in any new registration guidelines for them. The Agency will be careful, however, to require only data relevant to adequate scientific assessment of the compound's potential risk in accord with the nature of the pesticide.

Viruses, for example, may undergo some alternations which could potentially pose a hazard to humans or other organisms. The forthcoming biological pesticide registration guidelines will outline generally what kinds of hazard information will be needed in this regard, and will describe how EPA will use the data. Waivers for exempting a product from a particular data requirement will be set forth in the guidelines, and attention will also be paid to assessing a compound's potential for exposure to humans, wildlife, and the environment. EPA will require few data for registration in cases where a material is of a class determined by scientific evidence and judgment to be relatively innocuous, and where the potential for exposure is low.

Recently enacted amendments to the FIFRA include two provisions which may lessen the amount of data required for registration and should allow biological pesticide products to be marketed more quickly. The Administrator of EPA is now authorized to waive efficacy data in support of registration, consequently, the amount of efficacy data that the manufacturer must develop to satisfy EPA regulatory requirements will be reduced. The Federal Pesticide Act of

1978 also authorizes EPA to change over from the present product-by-product registration system to a broad, generic standard or chemical--rather than product specific registration scheme. Because generic standard building will take a number of years to fully accomplish, EPA has been authorized during the transition period to issue conditional registrations. That is, the Agency may issue registrations based on less than the full complement of supporting data, on the condition that the missing data will be developed and submitted in a timely manner during reregistration of all products containing the same active ingredients. EPA plans to begin issuing conditional registrations as soon as possible for old and new uses of products identical or similar to previously registered pesticides. New active ingredients can be conditionally registered if the Administrator finds that registration is in the public interest and there is enough hazard data available to determine that the risks of use of the compound during the period of time required to complete the data base are not unreasonable.

COST OF REGISTRATION REQUIREMENTS

The costs of EPA testing requirements to an applicant for registration are a critical factor in the decision to pursue registration since the applicant must have a reasonable prospect of recouping this investment. EPA will consider the economic impact of the requirements imposed on the marketing of biologicals in development of guidelines for their registration. As a first step in this direction, on June 20, 1977, the Agency announced a policy of waiving fees for tolerances (the legal limits of pesticide residues that may remain in or on raw agricultural commodities, processed food, or feed) for innovative pesticides when the need can be demonstrated by the applicant.

While guidelines might remedy the uncertainty in EPA registration requirements, and could reduce the costs of registration through more suitable data requirements, it should be noted that the ambiguity which presently exist in EPA registration requirements is only one of the several factors that may operate against introducing biologicals to the market.

The very specificity of many biological pesticides that makes them so environmentally desirable usually results in a restricted market, and therefore, usually limits potential profits. The biological pesticides that have been registered to date include products which have more general application and thus may provide a better return for the developer's investment. Such agents include those for use against relatively major pests or for limited portions of major crops (such as Gossyplure for cotton pest control and Altosid, a growth regulator, for mosquito control) and those which have a broader activity spectrum like Bacillus thuringiensis which is effective against a number of moth and butterfly larvae.

The costs of research into the properties of such products are not limited to developing the data required for EPA registration. This is also true for more traditional chemical pesticide products. It is estimated that research and development costs over a 7- to 8-year period between discovery and registration of a pesticide amount to between two and ten million dollars. Of that total R&D expenditure, approximately one-tenth, or between $200,000 and $1,000,000 can be attributed to meeting EPA registration requirements. In the case of both biologicals and traditional pesticide chemicals, minor market uses suffer due to low anticipated return from this large pre-market investment. The traditional chemicals usually penetrate one or more major markets to carry the cost of the minor uses.

In the specific case of biologicals, there has also been question in the past about the applicability of patent protection for the agents. However, patent protection was recently granted by the courts to a developer of a new life form and the method of producing it. For some of the biological agents, this will be added incentive to producers to register and market them.

More importantly, one of the recent amendments to FIFRA provides for exclusive use of data and will protect the original data submitter from competition for a period of 10 years after initial registration of a new pesticide active ingredient. This provision could have a favorable effect on the market situation for biologicals.

PROCESSING TIME FOR REGISTRATION

Length of time required for EPA review of applications for registration has the potential for frustrating would-be applicants. Under the current system of negotiating data requirements with each registrant, EPA has shortened its processing time of registering biologicals. As both EPA and potential registrants have gained more experience in this area, the system has been streamlined. A recent registration action on Gossyplure, a pheremone registered to the Conrel Corporation for pink bollworm control, was accomplished quite expeditiously:

- an experimental use permit was issued in early 1977;
- formal application for registration was received by EPA in September 1977;
- following an expedited review of the application, Gossyplure was registered in February 1978.

The 5 months required to review this application is substantially less than the 19-month average for review of applications for more traditional pesticides. (The review period includes the time from formal submission of an application for registration to approval of the registration, including time when the applicant may be developing missing data.)

REGISTRATIONS

The following table displays the biological agents and compounds, including pheromones and juvenile hormones that have been registered by EPA and its predecessor agency.

NEW GENERATION PESTICIDE SUMMARY

PESTICIDE	USE PATTERN	REGISTRATION STATUS
I. BIOLOGICAL AGENTS		
Bacillus thuringiensis	Lepidopteran Larvae Many crops	Registered 1962
Virus of *H.zea* (NPV)	Heliothis Species, Cotton	Registered 1974
Virus of tussock Moth	Forest Use	Registered 1977
Bacillus popilleae	Japanese Beetle, Lawns	Registered 1975
Virus of Gypsy Moth	Forest Use (hard woods)	Registered 1978
Colleotrichum gloediosporiodes (Mold)	Weed Control (rice)	EUP (Expt'l Use Permit)
Nosema locusteae (Protozoan)	Locust, Rangeland	EUP
Hirsutella thompsonii (Mold)	Citrus Mites	EUP
Phytophthora citropthora (Mold)	Citrus, Milkweed Vine	EUP
Bacillus sphaericus	Mosquitoes (Larvae)	Field Research
Virus of *Autographa californica*	Broad Spectrum Lepidopteran Larvae	Field Research
Sawfly Virus	Forest Use	Field Research
II. CHEMICAL AGENTS		
Altosid (Juvenile Hormone Analog)	Diptera (Mosquitoes, Flies)	Registered 1972
Gossyplure (Pheromone)	Pink Bollworm, Cotton	Registered 1978
Disparlure (Pheromone)	Gypsy Moth, Forest	EUP
Multilure (Pheromone)	Pine Bark Beetle, Forest	EUP