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Biologicals aim for big role in pest control

Sex lures and a veritable army of microorganisms are out to catch more bugs—aided by the Federal Government, which is changing registration rules to ease new products into the marketplace, and by progress made in the formulation and application of biological agents.

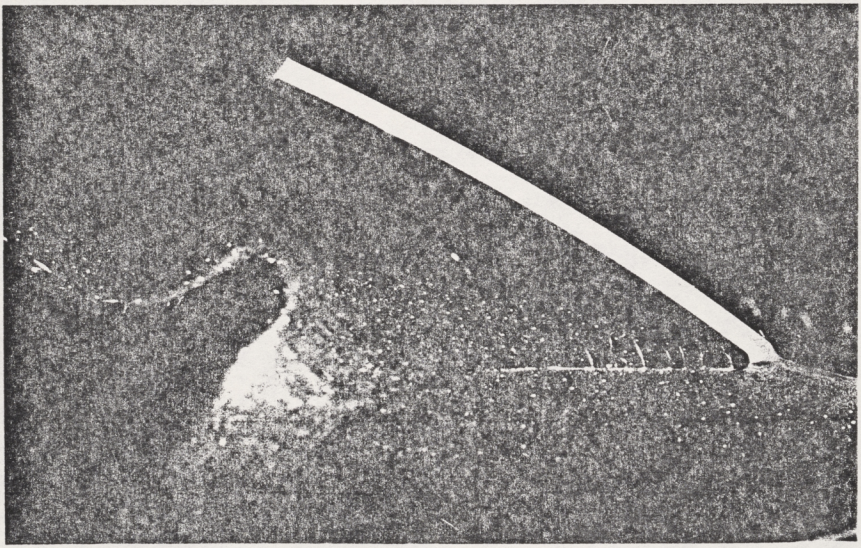
☐ There is little doubt that biological pesticides—a class that includes microbials (bacteria, viruses, fungi, protozoa) and biochemicals (pheromone sex attractants, hormonal growth-regulators)—have failed so far to live up to their early potential, at least in the U.S.* Indeed, although some have been around for almost 20 years, the difficulties and expense involved in producing, formulating and applying the agents (see box) have thwarted their bid for a major share of the U.S.'s billion-dollar pesticide market.

This lackluster past, however, is giving way to a bright future, brought about by the following developments:

■ The U.S. Environmental Protection Agency has proposed new guidelines for the registration of biologicals that will radically reduce the time and cost involved in testing for toxicity. Although final approval of the rules is not expected until year-end, EPA is said to be already operating unofficially under the new guidelines.

■ The recent Supreme Court ruling that upholds the patentability of new

*Other areas of the world—the U.S.S.R., Eastern European countries, China and Brazil—actually edge the U.S. in production and use of certain biologicals (mainly microbials). However, their technology—e.g., for formulating—is not as sophisticated, say experts.



Source: Albany International

Pheromone-filled fiber sticks to leaf after spraying from aircraft

forms of life has opened the eyes of researchers to the possibility of creating proprietary microbes through genetic engineering for pesticide use. Several chemical firms and universities, as well as the U.S. Dept. of Agriculture (USDA), already are engaged in such activities.

- Recently acquired knowledge on how to formulate and apply biologicals is helping to bring improved products into the marketplace. A host of new agents have been introduced in 1980-81, and more are expected to be ready for next year's agricultural season.
- Scientists at the Southwest Foundation for Research and Education (San Antonio, Tex.) are close to commercializing a method that will drastically reduce the cost of making viral insecticides.

NEW GAME PLAN—Current U.S. sales of biologicals have been estimated at an annual $15-$25 million by one source, and at considerably less than 5% of total pesticide sales by another. But, according to Sheldon Murphy, president of the agricultural consulting firm The Performance Management Group (Stamford, Conn.), the products have the potential to reach 25% of the sales volume of chemical pesticides (though not before the 1990s).

The new EPA rules are expected to provide a push in that direction. Operating on the premise that biologicals, being of natural origin (unlike chemicals), should be presumed safe unless the evidence proves otherwise, EPA's proposed toxicity tests are structured around a tier system, so that if a new biological agent satisfies the demands of first-tier tests (designed to prove, for example, that the organism doesn't live and propagate in test animals), there is no need to proceed to the second tier. "If you do a short-term test [as part of the tier system] and it shows no adverse effects, there's no point in going any further," says EPA official Frank Gee, who has been involved in developing the guidelines.

The elimination of long-term testing will save time and money, adds Gee. How much, is anyone's guess. But Murphy estimates that toxicity tests for a new chemical pesticide could run 2.5-3 years, at a cost of $2.5-$3 million. For biologicals, this could be cut to about six months, at a cost of $75,000-$80,000.

In addition to supporting the abbreviated testing for biologicals, EPA, under pressure to promote environmentally acceptable pesticides, recently went on record with a promise to expedite all requests for registration of such products.

ENHANCING THE EFFECT—The use of genetic engineering techniques to pack more power into biologicals also is a recent phenomenon. Most of the firms doing this kind of work would

Biologicals and their role in integrated pest management

The term "biological" (or biorational) encompasses a wide spectrum of active agents that share some characteristics. Many are specific to a particular insect species, so—unlike chemicals—they do not kill off harmless or beneficial insects that might be natural predators of pests. And, in general, they do not pose environmental hazards as a result of accumulation in the air, soil and water.

On the other side of the coin, they are difficult to produce, formulate and apply, and they frequently break down rapidly after spraying. Says Terry Couch, section head of entomology at Abbott Laboratories: "What has held biologicals back is growing the organisms, formulating the products, and educating the growers in how to use them. In the case of microbials, we have had to put them in stable and sprayable form, render them amenable to mixing in the field and modify them so that they can be handled by existing equipment. In other words, we have had to adapt them to existing technology."

Also, the reputation of microbials has suffered because of their sometimes erratic effects. Explains Sheldon Murphy, president of The Performance Management Group (Stamford, Conn.): "A microbial product can work well only if the user understands the organism itself and its susceptibility to environmental factors, that is, humidity, temperature, etc. For example, if you use a chemical pesticide in the desert, at 110°F, its effectiveness probably won't be diminished, but such conditions may blunt the performance of a microorganism."

Pheromones, too, present problems. The complex substances—long-chain hydrocarbon alcohol esters or aldehydes—are difficult to synthesize, and costly (anywhere from hundreds to thousands of dollars for one pound). Used in small amounts (grams), they volatilize rapidly in the field.

"Insect control with pheromones is a dramatic departure from accepted practices," says Bill Brooks, technical director of Albany International's Environmental Chemicals Group (Columbus, Ohio). "It means treating in advance, to protect against heavy infestations. We call it a prophylactic, rather than a therapeutic, approach."

Pheromone treatment means investing in sophisticated monitoring techniques (traps) to get an early warning of the presence of insects, and then saturating the area with pheromones to disrupt mating. "Farmers find it difficult to adopt this approach because it involves spending part of their pest-control budget at a time when they would normally be doing nothing at all," says Brooks.

And if insect infestations become too heavy, pheromones don't work well because there are so many insects that inevitably some will mate, and their population won't be really decimated.

For these reasons, biological pesticides do not have the "knockout" reputation of chemicals, even though the end-result might be equivalent. Nevertheless, their role in integrated pest-management programs seems clearcut. Murphy, for example, sees them as a complement to chemicals. "Since they are most effective in the early stages of insect development, they can be used at this point. And if the insects' natural predators fail to control the remaining infestation, farmers can follow up with chemicals. This way, lesser amounts of toxic chemicals will be used. This might mean a new lease on life for chemicals to which insects are developing a resistance. And, of course, it's environmentally beneficial."

prefer to keep their involvement a secret. But an expert says that the roster includes—besides several universities and USDA labs—such companies as Eli Lilly, Du Pont, Sandoz, Abbott Laboratories and Stauffer Chemicals.

Most of the research focuses on variations of *Bacillus thuringiensis*—the best seller of the biologicals world. Since its introduction around 1970 (under the tradename Dipel Bt, by Abbott Laboratories, North Chicago, Ill.), the bacterial agent has been gaining ground with farmers, who use it to combat the larvae of lepidopterae (mostly the *Heliothis* species) that ravage cotton. It has also been used extensively to fight the current gypsy moth infestation in the Northeast.

Abbott won't comment on its current efforts to improve *Bt* by genetic means. But researchers at Ohio State University's Dept. of Microbiology (Columbus) are not so reticent about their work on a different Bt strain (*B. thuringiensis* var. *israelensis*—better known as *Bti*) that attacks instead the larvae of blackflies and mosquitoes.

Donald H. Dean, associate professor of microbiology at Ohio State, says that the university has already identified the genetic elements that encode the *Bti* toxin, and, via genetic manipulation, is trying to stabilize and enhance its toxicity. Also by genetic engineering methods, researchers are trying to broaden the host range (vulnerable insect species) of all types of *Bt*. This would be done, for example, by combining the genes that attack a broad range of larvae into one microorganism.

Noting that the university "has made great progress recently," Dean predicts that within one year there will be marketable varieties of *Bt* that will be a great improvement over those now on the market. Right now, he says, *Bt* is quickly decimated in nature, which is one reason why users typically need more than one application to control pests. "Other available contact [chemical] agents can do a better job," adds Dean.

Terry Couch, section head of entomology at Abbott's Chemical and Agricultural Chemicals Div., explains that more than one application is needed to control gypsy moths "because of their staggered hatching cycle. Two applications usually are needed to lower the population sufficiently."

Abbott makes *Bt* by deep-tank fermentation, via the submerged-culture technique, "much as you would produce an antibiotic," says Couch.

THE ELUSIVE VIRUSES—For the past three years, work on a tissue-culture process for viral insecticides has been carried out at the Southwest Foundation—initially under Agriculture Dept. sponsorship, but most recently under a grant from the National Science Foundation.

James Vaughn, head of the insect pathology lab at USDA's research center in Beltsville, Md., which assists in the project, says that the goal is to grow viruses in insect-cell cultures, using techniques and equipment similar to those employed in commercial fermentation processes—e.g., aerated, agitated vats.

This would be a vast improvement over the present method, which involves mass-breeding of insects and feeding them an artificial diet that contains the infecting virus. For harvesting, the insects must be killed (by freeze-drying) and ground up. After the mixture is subjected to some primary purification to separate the insect parts, the resulting virus is freeze-dried.

All this entails high capital investment—e.g., for mass-breeding facilities. And there is always the possibility of the insects getting contaminated by other microorganisms, which would give rise to severe quality-control problems.

Vaughn says that, at this point, the new method has been developed to the stage where it can produce seed virus needed to inoculate insects. But there are scaleup problems to be solved—notably with the oxygen supply. Oxygen bubbled into the fermenters creates shearing forces that disrupt the insect cells.

One possible answer is to attach the cells to rotating disks that periodically rise to the surface for aeration and then submerge again into the liquid medium. Another alternative under consideration is the use of a perfusion technique, in which the liquid medium is taken out of the vat, aerated, and brought back in. To prevent the cells from exiting with the medium, these are attached to a fixed surface.

Noting that the process is at least 2-3 years from commercialization, Vaughn says, "The yields are now about 90% of what they need to be in order to compete with insect growing. But the saving in capital investment would be considerable."

NEW BIOLOGICALS—Only 15 or so biological agents have been registered with EPA so far, but more are on the way. In the U.S., the leaders in the microbials business are two pharmaceutical firms—Abbott and Sandoz, Inc. (East Hanover, N.J.).

Sandoz has been making microbials since 1972, when it acquired the biological products line of IMC Corp.; this included the bacterial insecticide Thuricide (based on a *Bt* strain). In 1975, the company introduced Elcar—a viral agent active against the larvae of the *Heliothis* species, which include the tobacco budworm and the cotton bollworm.

Two years ago, Sandoz' viral-agent manufacturing facility became fully operational in San Diego, Calif. And this year, it will start selling *Bti* to state mosquito-abatement districts under the tradename Teknar. Also in 1981, Sandoz will start marketing another *Bt* strain, under the label Certan, for controlling the wax moth in beehives.

As for Abbott, it has just introduced the first two U.S. commercial fungal agents* for use in agriculture, says Herbert Bromberg, the firm's director of sales and marketing. Both products are made by fermentation. DeVine is a mycoherbicide, aimed at controlling milkweed vine in citrus trees. Mycar is a biological miticide that infects and kills the citrus rust mite. In 1982, the firm will introduce a *Bti* serotype, said to be effective against blackflies and mosquitoes.

SCENT OF DEATH—For years, pheromones have been used to survey insect populations (monitoring). But in recent times, they also have been functioning as control weapons. The most promising approach is to saturate a field with the synthetic scent, overpowering the natural odor emitted by the females. This prevents the confused males from locating and mating with the females, which then lay sterile eggs and die.

The first to obtain EPA approval to sell a pheromone as a control agent—against the pink bollworm, a cotton pest—was Albany International, in 1978. The firm's Environmental Chemicals Group (Columbus, Ohio)

*Other countries have used fungi for insect control. Brazil, for example, has registered one for controlling spittle bugs, which infest the sugar cane. Others are being employed in China and Eastern Europe.

now synthesizes about 55 different pheromone compounds, the bulk of which go to the Controlled Release Div. in Needham Heights, Mass., for formulation into commercial products.

Bill Brooks, technical director of the Environmental Chemicals Group, says that Albany has several EPA registrations for pheromone applications. It is about to register a new one—for disrupting the mating of the tomato pinworm—and will soon have another, to combat the *Heliothis* species that infests cotton.

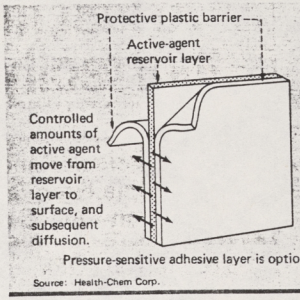
Albany's main competitor—Health-Chem Corp.'s Hercon Div. (New York City)—doesn't make pheromones. Its marketing clout hinges on a patented dispenser for pheromones that releases the costly and volatile compounds at a controlled rate—a key tool for wide-scale pheromone application. Hercon's sandwich configuration* (see figure) is in marked contrast to Albany's patented controlled-release system, which employs tiny, hollow plastic fibers (open at one end) as vessels for holding liquid pheromones. When distributed from an airplane, the fibers (coated with an adhesive) attach to plants; the pheromone then evaporates from the open end.

This year, Hercon has gone into large-scale selling of its gypsy-moth traps, aimed at the homeowner. Baited with pheromone, the traps come armed with insecticide strips to kill the pests. Next year, the firm may introduce a complete pheromone package for cotton growers, encompassing the pink bollworm and the tobacco budworm (which also affects lettuce crops).

Keyed exclusively to the consumer is J. T. Baker Chemical Co. (Phillipsburg, N.J.), which has been in the pheromone business for about 5 years. The firm, which claims to have been the first to develop a Japanese-beetle trap baited with pheromone and a floral lure (an added attractant for the insect), has introduced two new products this year to aid homeowners in controlling gypsy-moth caterpillars: one is *Bt* in sprayable form; the other is a pheromone trap containing an insecticide.

Raúl Remírez

* The firm claims to have received more than 100 U.S. and foreign patents covering the controlled release of a wide range of biologically or physically active agents through a variety of plastic membranes.



Hercon© controlled-release dispenser

Superfund—its critics find few superlatives

Criticism is being heaped upon the hazardous-waste cleanup program and how it is being run by the U.S. Environmental Protection Agency. Industry's main complaint: EPA wants to spread liability for damages from abandoned dumpsites.

☐ The U.S. Environmental Protection Agency is gradually easing into place the Comprehensive Environmental Response, Compensation and Liability Act (Superfund), designed to launch a nationwide cleanup of abandoned hazardous-waste sites. However, EPA is facing heavy fire from environmentalists, industry, and Congress for the pace and manner in which the program is proceeding.

EPA's management of Superfund has raised criticism ranging from anger at the delays to concern that so many critical issues remain unresolved. The fact that the agency has committed only $9.7 million of the $68 million appropriated for Superfund this fiscal year (*Chem. Eng.*, July 13, p. 50) has also drawn fire.

EPA administrator Anne M. Gorsuch appeared at July 29 House hearings to report on the program's progress and reassure critics that the agency has made the Superfund program its "highest priority." But subcommittee chairman James J. Florio (D.-N.J.) nevertheless accused the agency of "dragging its feet," and EPA officials admit there are many problems that still need to be worked out before the program is completely underway.

FOCUS OF CRITICS—Months of discussion within the agency have failed to resolve the fundamental question of how clean is clean—i.e., to what degree must an abandoned landfill be cleaned up before it can be considered safe. EPA officials explain the delay by pointing out that the agency has had little prior experience in the area of hazardous waste. "There are lots of issues that need discussion because they haven't been dealt with before," says Elaine G. Stanley, an executive officer of EPA's Office of Hazardous Emergency Response, "and when the new administration moved in, they raised even more questions."

A sore point for most critics is the delayed release of the revised National Contingency Plan (first written in 1968) on which the Superfund program hangs. One group, the Environmental Defense Fund (Washington, D.C.), is threatening the agency with a suit if it fails to show evidence that it has set a deadline for promulgation of the plan, which was due for a June 9 inspection by the Office of Management and Budget.

Even after EPA sends OMB the plan, which is to coordinate federal and state action and set uniform guidelines for cleanup, the long regulatory process may delay its finalization for another