BIOLOGICAL CONTROL
MAKING IT WORK

PART 2: TECHNOLOGICAL STATUS

R. JAMES COOK

USDA, ARS Root Disease
and Biological Control
Research Unit
267 Johnson Hall
Washington State University
Pullman, WA 99164-6430

ROBERT R. GRANADOS

Plant Protection Program
Boyce Thompson Institute
Tower Road
Ithaca, NY 148)3-1801

The use of pesticides for control of insects, weeds, nematodes and plant pathogens includes a worldwide market in excess of $20 billion. However, there are known and/or perceived concerns for such reliance on chemical pesticides for pest control. It is clear that, while chemical pesticide use remains essential to maintain agricultural productivity, new, efficient, and safer products will be necessary to supplement those chemicals that are no longer effective or present a problem to the environment or human health. Moreover, despite this large pesticide usage, it is estimated that nearly 35 percent of the world's food and fiber is still lost as a result of damage by pests and pathogens. Many crop pests and diseases cannot be controlled by pesticides, and many pests once controlled by pesticides have developed resistance to them. Modern technologies rely heavily on the use of chemicals to control these pests.

Biological control strategies offer safe, efficient, and ecologically-based methods for pest and disease control. This report will summarize the current technological status of these agents and identify research needs which will accelerate the use of biologicals as alternatives to chemical control methods, or provide economic controls where none now exist or are acceptable.

CLASSICAL BIOLOGICAL CONTROL

The successful introduction of the vedalia beetle *Rodolia cardinalis* from Australia into California in 1888 to control the cottony-cushion scale

Icerya purchasi, an insect pest of citrus, is considered to mark the beginning of the modern era of biological control of plant pests. The spectacular, low-cost, and permanent success of the vedalia beetle demonstrated the enormous potential of this approach to controlling pests. Indeed, during the last 100 years, there have been over 300 documented examples of complete or significant successes in classical biological insect control. Other outstanding examples of classical biological control in the United States include the control of the olive scale, ***Parlatoria oleae,*** by the parasites, ***Aphytis paramaculicornis*** and ***Coccophagoides utilis,*** during the 1950s, and the control of the walnut aphid, ***Chromaphis juglandicola,*** by the aphidid parasite, ***Trioxys pallidus,*** during the 1960s. A recent highly successful biocontrol program in Africa was the use of the encyrtid parasitoid, ***Epidinocarsis lopezi,*** to control the cassava mealy bug, ***Phenacoccus manihoti.*** Equally spectacular results have been obtained for biological control of weeds as exemplified by the control of Klamath weed by the Klamath beetle, ***Chrysolina quadrigemina,*** in California. Three other complete successes against weeds since 1944 have resulted in annual benefits of over $150 million per year.

The classical approach of introducing natural enemies to reduce the population of plant pathogens below some economic threshold and in a density-dependent relationship (following the examples from insect and weed control) has met with little or no success for biological control of plant pathogenic fungi, bacteria, viruses or nematodes. The examples of successful classical biological control of insect pests and weeds have nearly always involved the use of an insect and rarely a microbial biocontrol agent and, not surprisingly, classical biological control of one microorganism with another is even more rare. Many studies have been carried out with mycoparasites applied to rust pustules or powdery mildew colonies to limit the amount of innoculum produced at the end of the disease cycle, but there is no commercial application of these kinds of biocontrol agents.

One emerging success story is ***Sporidesmium sclerotivorum*** applied to soil to keep the inoculum density of ***Sclerotinia*** spp. at or below an economic threshold. This method of biological control keeps the population of ***S. minor*** in field plots of lettuce in New Jersey in a state of suppression for two or three years following a single initial soil-application of the biocontrol agent. As with so many other promising technologies, the economics of producing a product for control of a single disease or pest tend to discourage companies from investing the capital necessary to produce, formulate, register, and market such a product. However, if used, it might well be the first example of classical biological control using a microorganism applied to soil for control of a soilborne plant pest.

Classical biological control using insects has proven to be an effective and efficient strategy for controlling exotic insect pests and some weeds that have been accidently introduced while escaping their natural insect enemies. It is expected that novel and traditional approaches of ecologically-based biocontrol methods will become even more important in pest management programs, along with genetically improved organisms. However, except for *Drosophila,* there are currently no procedures to engineer the genome of insect species and there is only a limited history of classical genetic modification of natural enemies for biological control of insects with other insects. Determining which characteristics to improve for field efficacy continues to be a major constraint on the genetic improvement of natural enemies. Insecticide resistance, bred into beneficial insects, is a desirable trait since it allows biological control of pests in IPM (Integrated Pest Management) programs that utilize chemical control strategies. Two successful cases of genetic improvement of beneficial insects involve the selection for insecticide resistance in predatory mites in apple (Michigan) and almond orchards (California). As transformation methods are developed in the future, we can expect other genetic alterations of beneficial insects to include host-finding ability, climatic tolerances, changes in host preference, etc.

MICROBIAL BIOCONTROL OF INSECTS

Entomopathogenic microorganisms — including bacteria, viruses, fungi, protozoa, and nematodes — may contribute significantly to regulation of pest insects of importance in agriculture, forestry, and medicine. However, the general lack of success with microorganisms in classical biological control relates in large part to their lack of persistence in the habitat of the target pest agent. This problem has been overcome by applying them repeatedly where needed — in some cases with the same technology used to apply chemical pesticides. It is currently perceived that these entomopathogens have high potential for a greater role in insect pest management by exploitation of naturally occurring entomopathogens as "microbial insecticides." Of the more than 1500 entomopathogenic microbes known, only eleven microbial products are registered by the EPA for use as insect pesticidal agents.

Bacillus thuringiensis (Bt) is the most widely used microbial product and is available worldwide under several brand names. Bt affects more than 150 lepidopterous species, and mixtures of Bt spores and toxin have been used to control caterpillar pests since the early 1960s. Recently, the use has been expanded because of development of improved strains and fermentation techniques that increased production of the bacterial toxin. Bt is currently used extensively for forest and vegetable insect pest control, and its use for stored grain and cotton pests is increasing. *B. thuringiensis* var. *israelensis,* registered in 1981, has been shown to be extremely effective on mosquitoes and black flies. It is used extensively for vector control in North Africa and is gaining greater acceptance for use by mosquito abatement control programs in the U.S. More recently, new Bt strains have been isolated having insecticidal activity against coleopteran (beetle) larvae including the Colorado potato beetle, black vine weevil, boll weevil, and elm leaf beetle. These observations indicate the occurrence in nature of novel Bt strains having activity against a broad array of insect species. This is borne out by the recently reported isolation of nematode-active Bt strains, registration, production, and commercialization of the *Heliothis zea* baculovirus during the 1970s was a major achievement and represented the first viral insecticide to be registered. Three other baculoviruses have since been registered by the EPA and two of these viruses (the gypsy moth and Douglas-fir tussock moth baculoviruses) are commercially available. Four baculoviruses are sold commercially on a small scale in Europe for forestry and agricultural applications. In Brazil, the baculovirus of the velvetbean caterpillar, *Anticarsiagemmatalis,* is used on over 2 million acres of soybean and represents an outstanding example of the use of a baculovirus as a microbial insecticide.

It is estimated that over 750 species of fungi have insect pathogenic effects. To date, only one species, *Hirsutella thompsonii,* is registered in the U.S.; however, this pathogen is no longer commercially available.

Several fungi are registered and have considerable usage overseas. ***Beauveria bassiana*** is currently in wide use in the Soviet Union against insect pests of orchards and forests. ***B. bassiana*** is used routinely on several million acres in the People's Republic of China, primarily against European corn borer in corn (maize), Dendrolimus in forest, and plant leafhoppers in rice. In Brazil, ***Metarhizium anisopliaeis*** produced commercially for spittle bug control on more than 400,000 acres of forage and sugarcane. In Europe, ***Verticillium lecanii*** is commercially available for the control of greenhouse aphids and white flies.

Protozoa use and development has been somewhat more limited than the other microbials. However, one species, ***Nosema locustae,*** has been developed and registered for use against rangeland grasshoppers. This is the first protozoan receiving U.S. registration.

Entomopathogenic nematodes are being used for agricultural and horticultural insect pest control. Several species in the genera ***Steinernema*** and ***Heterorhabditishsve*** received the greatest study, and several products are available from commercial sources in North America, Europe, and Australia.

BIOTECHNOLOGICAL ADVANCES WITH INSECT PATHOGENS

In spite of decades of intensive research, relatively few microbial-based products are being used commercially for biological pest management. Clearly, there are major factors constraining the wider use of microbial pesticides and these include lack of environmental persistence, narrow host range, limited virulence, and high production costs. Unlike insect biocontrol agents, for which cloning vectors and other tools for genetic modifications are only now being developed, great advances have been made with the tools of recombinant DNA technology applied to microorganisms, especially bacteria and viruses. Recombinant DNA technology will provide the tools for developing safe, efficient, and cost competitive microbial biocontrol agents. This technology has already made a significant impact on the construction of novel Bt strains which exhibit enhanced insecticidal activity and greater persistence in the environment.

The M-cell delivery system, developed by Mycogen (San Diego, CA), is an example of a novel approach to increase foliar persistence of Bt by a biopackaging process involving microencapsulation of a toxin by the cell wall of a Bt-engineered *Pseudomonas fluorescens* bacterium. Expansion of the host spectrum activity was accomplished by Ecogen (Langhorne, PA) by conjugal transfer of Bt genes and the development of a bifunctional commercial transconjugant product, which has high activity against the Colorado potato beetle *Coleoptera* and the European corn borer *Lepidoptera*.

Both endophytic and epiphytic bacteria, as well as several plant species, have been engineered to express insecticidal Bt proteins. Crop Genetics International (Hanover, MD) is developing endophytic bacteria engineered with Bt toxin genes to protect corn from the European corn borer. Several companies have rapidly developed the technology for introduction and expression of heterologous genes, namely genes from microorganisms including viruses, in plants and have opened new opportunities for the development of insect and disease resistant crops. The utilization of genes encoding lepidopteran- or coleopteran-specific insecticidal proteins from Bt has been used to develop plants (tomato, potato, cotton, etc.) resistant to several insect species under laboratory and field conditions. Recently, Monsanto (St. Louis, MO) developed a novel strategy involving specific modifications of the structural Bt gene sequence that dramatically increased the levels of insecticidal proteins in transgenic cotton plants, and afforded high levels of protection against the cotton bollworm *H. zea* in greenhouse and field tests. In the case of plant diseases, remarkable results are being obtained in virus disease resistance using the coat protein gene of the virus expressed in the plant.

Biotechnological approaches are also being applied to the genetic improvement of baculoviruses. Knowledge of the molecular biology and genetics of baculoviruses has accelerated greatly in recent years, and this database is enabling the genetic manipulation of the viruses. The introduction of foreign genes (Bt toxin, diuretic hormone, and juvenile hormone esterase) into the baculovirus genome which could potentially deliver some deleterious gene product to the insect host has been accomplished, but only marginal insecticidal effects in treated insects have been obtained. It is expected that the engineering of baculovirus genomes with foreign pesticidal genes, possessing enhanced insecticidal activity, will be demonstrated in the very near future.

Studies of the genetics and molecular biology of entomopathogenic fungi, protozoa, and nematodes are still in very early development and it is not likely that recombinant DNA techniques will be utilized to engineer these types of organisms anytime soon.

BIOLOGICAL CONTROL OF WEEDS

Until recently, biological control of weeds was limited to the use mainly of insect herbivores and some foliar pathogens (e.g. rust fungi) released to control specific weeds in perennial ecosystems such as rangeland and pastures. Typical of classical biological control, the success of these agents depends on their ability to multiply and maintain effective populations in response to increases in density of their weed host, and thereby keep the population of the targeted weed in a state of suppression. Such agents tend not to respond fast enough to eliminate a targeted weed within a given window of opportunity typical of most annual cropping systems.

At least four fungal plant pathogens, selected because of their pathogenicity to specific weeds, are now available as "mycoherbicides," and five or six more such products are under development or awaiting registration. The problem of slow response when the epidemic is allowed to develop from entirely natural sources of inoculum is overcome with mycoherbicides by mass production of suitable inoculum in fermentation culture and then applying this inoculum at a time when the weed is particularly vulnerable and temperature and moisture are suitable for infection. The particular pathogens are, in fact, selected because of their limited ability to disseminate naturally, which makes them more ideal as mycoherbicides.

Mycoherbicide products currently available are: DeVine®, a formulation of Phythophthora parasitica for control of milkweed vine in citrus groves in Florida; Collego® a formulation of *Colletotrichum gloeosporioides*var. *aseschynomene* for control of northern jointvetch in rice and soybean fields in Arkansas, an unnamed product consisting of *Acremonium diospyri* for control of persimmon in pasture land in Oklahoma; and Lubao No. 1, a formulation of *Colletotrichum gloeosporioides* for control of dodder in soybean fields in China. Several others are under development or waiting for registration. Like other microbial biocontrol products, mycoherbicides can be highly efficacious, but the very feature that makes them so attractive ecologically— highly specific for the targeted pest — is the feature that makes them economically unattractive to companies. It is difficult to justify the costs of developing, registering, and marketing a production that controls only one weed, often only one weed in one crop.

BIOLOGICAL CONTROL OF PLANT PARASITIC NEMATODES

Biological control of plant parasitic nematodes in soil by nematode trapping fungi, egg parasites, nematode pathogens, and other natural enemies has been studied for most of this century. Thus far, however, only one biocontrol product has come into the market, a strain of *Paecilomyces* applied to soil for control of nematodes in the Philippines and sold under the trade name Bioact®.

The experience with biological control of nematodes in soil is typical of experiences with biological control of soil-inhabiting insect pests and plant pathogenic fungi in soil: given enough time, e.g., the time provided by a 3-year or longer crop rotation, the naturally occurring biocontrol agents will lower populations of these pest agents below an economic threshold, but elevation or acceleration of these processes above the natural background intensity by deliberate introduction of specific microbial biocontrol agents is generally unsuccessful because of the great difficulty of establishing a microorganism in soil at a population higher than occurs there normally. The successful culture of nematode-susceptible crops without resorting to the traditional long crop rotations, and of replanting some nematode-susceptible orchard crops in the same sites time and again, has been made possible by the use of nematicides, many of which are no longer available or may soon be withdrawn as registration is cancelled or not renewed.

Interestingly, the value or need for crop rotations is now part of a national debate in the United States and elsewhere between advocates of so-called conventional agriculture, and those who practice “alternatives agriculture.” Crop rotation, one of the original and still best uses of biological control, has become so underutilized as to be considered an “alternative” practice in agriculture.

At present, the bacterial pathogen *Pasteuria penetrans* is attracting the greatest interest as a candidate microbial biocontrol agent for use against nematodes in soil. There are many strains of this pathogen, some highly specific for their nematode host. Moreover, several cases have now been documented in fields where the natural population of *P. penetrans* accounts, at least in part, for why a certain potentially very important nematode is not important in those fields or region. The limiting factor to use of this agent is the lack of technology for its mass production. When this problem is solved, products of *P. penetrans* can be expected to come onto the market for biological control of nematodes in soil.

BIOLOGICAL CONTROL WITH PLANT-ASSOCIATED MICROORGANISMS

An important breakthrough for biological control of plant diseases is the discovery that on every plant, or within every plant population, there reside microorganisms at a low frequency with the ability to act as antagonists if their numbers were higher to protect that plant or plant population against disease. The evidence suggests further that the frequency of these beneficial microorganisms increases in response to disease outbreaks, but typical of many biological controls, 1- any given population of antagonistic microorganism rarely controls more than one pathogen, and often works only in specific environments, e.g., specific soils, and 2- the antagonistic population of microorganisms tends to build up in response to, rather than in advance of, disease and thus is too late or too slow to control the disease. In spite of these limitations, the prospect exists that the benefits of these microorganisms might be increased significantly by an "inoculative release" with the seed at the time of planting.

The natural occurrence of bacteria represented *by Agrobacterium radiobacter* strain K-84, having the ability to protect plants against crown gall caused by *A. tumefaciens,* and the antibiotic-producing strains of fluorescent *Pseudomonas* species with the ability to protect wheat against take-all caused by *Gaeumannomycesgraminis var. tritici*both fit the model of 1- naturally occurring strains of microorganisms on the plant or soil around the plant that 2- increase in numbers in response to the diseases caused by the pathogens they inhibit and 3- provide biological control when introduced in advance of infections by artificial inoculation of the planting material. By inoculating the planting material with these microorganisms, the natural processes involving them are initiated in advance of infection rather than at the end of the disease cycle. Strain K-84 is currently marketed worldwide for biological control of crown gall, and the research on fluorescent ***Pseudomonas*** strains active against wheat take-all is part of a major research effort worldwide aimed at eventual commercialization of root-associated bacteria for biological control of root pathogens on many crops.

Six microbial biocontrol agents have been or were once registered in the U.S. with the EPA for use against plant diseases. All are plant-associated microorganisms. These are: ***Phlediagigantea (-Peniophoragigantea)*** to control annosus root rot of pines and other conifers; ***Trichoderma*** applied as BINAB T® to pruning wounds to protect against wood-rotting fungi; ***Agrobacterium radiobacter*** strain K-84 for use as a bare-root dip to protect fruit tree and rose bush transplants against crown gall; Dagger G®, a peat-based product containing a strain of ***Pseudomonas fluorescens*** for in-furrow application with cotton seeds to control seedling blights caused by ***Rhizoctonia*** and ***Pythium*** spp; ***Gliocladium virens*** for control of ***Pythium*** and ***Rhizoctonia*** on ornamental plants, F-stop® a ***Trichoderma-based*** product for use as a biological seed treatment on peas, beans, corn, and other crops to control damping-off In addition, a strain of ***Bacillus subtilis,*** sold as Quantum 4000® is registered for use as a seed treatment of crops, e.g., peanuts in Alabama, because of its plant growth-promoting properties. Plant "growth promotion" is commonly attributable to control of undiagnosed damage caused by subclinical root pathogens.

Plant-associated microorganisms established in the infection court in advance of the pathogen may be used to prevent infection, or as colonists of the infected tissues to arrest disease development. They also maybe used to turn on (induce) plant defense genes in the plant. They may even include the pathogen in some avirulent, hypovirulent, or disarmed form (e.g., ice-minus ***Pseudomonas syringae)*** introduced onto or within the plant to carry out any one of these functions. Plant-associated microorganisms are part of a vast and largely untapped natural biological resource interacting with crop plants. Some, e.g., certain endophytes, have also been shown to control insect pests of plants. Select strains are ready-made biocontrol agents because they are both adapted to the plant or plant part where they must function, and they can be chosen because of their unique ability to protect the plant. Where genetic resistance has not been found, e.g., to the many root- and stem-attacking pathogens, and where soil fumigation is too expensive or not acceptable, epiphytic and endophytic microorganisms are being found with the ability to inhibit these pathogens. Plant-associated microorganisms are another option in plant improvement.

BIOLOGICAL CONTROL OF PLANT DISEASES EFFECTED THROUGH THE PLANT

The greatest progress in biological control of plant diseases during the past 70-80 years has been the approach of improving ability of crop plants to defend themselves, achieved through plant breeding for more resistant cultivars. Some of this effort goes on at a fairly high level of sophistication involving the deployment of specific resistance genes or gene combinations in the plant in response to anticipated or documented (through monitoring) increases in frequency of new virulent biotypes of the pathogen. As expected of biological control, the genetically controlled mechanisms of self-defense in the plant are regulated to turn on when needed, i.e., in response to the pathogen, and where needed, i.e., in the specific cells, tissues, or organs challenged by the pathogen.

The tools to move genes from microorganisms into and express them in plants raises the prospect that many biocontrol mechanisms might be moved into plants, thereby precluding the need to introduce the agent(s). The example of fluorescent pseudomonads active against wheat take-all illustrates both the opportunity and the problems. The genes for phenazine production in the fluorescent *Pseudomonas* species active against take-all have now been cloned and might, therefore, be candidates for transfer to and expression in plants. However, this would require that a root-specific and, preferably, a wound-induced promoter could be used to help insure that the genes would be expressed where the antibiotics are needed, not throughout the plant, and only in response to infection or other root injury, not constitutively. It is also unlikely that one or a few genes from a single strain of bacteria could duplicate the multiple mechanisms of disease suppression usually operative with that strain and operative with mixtures of naturally occurring strains responsible for suppression of take-all. Moreover, the use of microorganisms, rather than the plant, to deliver the products of biocontrol genes or biosynthetic pathways can overcome the problem of needing the genes in so many different varieties. There are possibly 30 wheat varieties grown each year across the U.S. in the many areas where take-all and other root diseases are important, and many, if not most, of these are replaced with new varieties every five to ten years. Not all genes need to be in the seed. Some genes may be best deployed in microorganisms delivered with the seed.

BARRIERS TO THE DEVELOPMENT AND USE OF MICROBIAL BIOCONTROL OF INSECTS AND PLANT DISEASES

The success of biological control, including biotechnology-based pest control during the 1990s and beyond will depend on several issues that must be resolved. We must improve the long term, interdisciplinary research on both basic and applied biocontrol problems. Research is needed in areas such as ecology, physiology, and molecular biology to provide the basis of knowledge needed to effectively use biocontrol agents or to genetically improve their pesticidal properties. The transfer of biological control technology from the laboratory to the field is clearly inadequate and must involve a greater enhanced educational program and stronger support of the university extension system. It is imperative that federal and state agencies increase the funds necessary to carry out the research and transfer of technology. In addition, industrial support for some of these programs should be encouraged.

The use of transgenic plants that have been engineered to contain genes which confer pest resistance will have a major commercial impact. However, concerns about the potential development of pest resistance must be addressed by the elaboration and implementation of resistance management strategies. In contrast to this problem, which is real, reference to transgenic plants with ability to express the Bt protein or virus coat protein as "pesticidal plants," or plants with the ability to manufacture their own "chemical pesticides" is not scientifically based and is counter-productive to the advance of this very exciting new approach to biological control of plant pests and diseases.

Repeated examples of natural biological control microorganisms, have revealed a wealth of genetically and taxonomically diverse candidate biocontrol strains. However, the tendency among biological control researchers has been to evaluate the first 10,25, or possible 50 strains, pick one or two, and then use these as models for studies of mechanisms. We are witnessing an information explosion, mainly because of research on mechanism. It is important to expand the scientific base for biological control, but imagine by analogy a plant breeding program that evaluated only 10, 25 or 50 genetic lines and then ceased to screen lines and concentrated only on mechanisms of disease resistance.

Research programs must be able to both expand our understanding of biological control and continue to examine the virtually unlimited microbial germplasm for new strains or new genes for strain improvement. The ultimate application may take place in the form of microbial biocontrol products, as a new cultural practice favorable to the activity of resident microbial biocontrol agent(s), or both. Such advances, from basic discovery to practical implementation, require long-term commitment by both the researchers and the funding agencies, and they require teamwork and cooperation, including across national boundaries.

Protocols must, and probably can be, developed to both overcome and take advantage of the high degree of specificity of microbial biocontrol agents. We may have no choice but to use different strains or mixtures of strains customized for the disease complexes in specific environments. It should be possible to mass-produce and formulate the individual strains of any given group of microorganisms using a common or standardized technology developed for that taxonomic group, thereby providing some simplification in the use of strain mixtures. Desired mixtures could be produced for the different environments or mixtures of diseases at the local level, possibly even by the user. U.S. farmers already concoct their own mixtures of crop varieties (e.g., wheat) and chemicals according to test results from the experiment stations and advice from the Cooperative Extension Service or local agribusinesses. In a similar but more sophisticated approach to biological control of plant diseases, mixtures of genes are deployed in the same variety or multiline variety and changed periodically according to the ever-changing disease complex and environment.

It is now possible to combine the best traits of several strains into a single strain and possibly preclude the need for complex mixtures of microorganisms. However, scientists taking this approach must be allowed to release their new strains genetically improved by the use of the best tools available. And the system must be in place for the free exchange of microbial germplasm, including across international boundaries, for use in improvement of local strains of microbial biocontrol agents. Imagine where crop production would be if farmers could only grow naturally occurring land races of crops. The current "climate" of unfounded public fears of so-called "genetically engineered microorganisms" and the tendency to over-regulate this technology has discouraged commercial development and use of these engineered products.

Somehow our concept of microbial biocontrol as a component of plant health management must shift away from the chemical paradigm and back to a biological paradigm. Microbial biocontrol agents should be reviewed by the plant quarantine authorities for status as a pest or potential pest, and by the appropriate authorities for safety to people in the workplace or to people or livestock if eaten as a seed treatment, but otherwise every effort should be made to avoid policies based solely on the fact that the biocontrol agent is a microorganism. Microbial biocontrol agents such as mycoparasites, plant-associated microorganisms, and many, if not most, categories of antagonists of plant pathogens or nematodes that have no ability as plant or animal pathogens should be given broad approvals as biological control agents and not be regulated under statutes developed for chemicals. The EPA guidelines for the testing and registration of naturally occurring microbial agents are designed to expedite and facilitate the review of applications. An approach that uses different strains or strain mixtures in different geographic areas, zones, or soils cannot succeed in the context of the existing paradigm, where the regulatory agencies require a separate registration package for each strain or strain combination.

Strain improvement and release programs could be modeled after cultivar improvement and release programs. It would seem likely that companies would eventually take over the work, just as seed companies have eventually taken over the breeding and distribution of some crop cultivars when the economics have been attractive. This model describes almost exactly the sequence of events in the highly successful introduction, and now worldwide use, of strain K-84 of *Agrobacterium radiobacter* for biological control of crown gall.

SELECTED REFERENCES

Adams, P.B. 1990. The potential of mycoparasites for biological control of plant diseases. ***Annu. Rev. Phytopathol.*** 28:59-72.

Biotechnology, Biological Pesticides and Novel Plant-Pest Resistance for Insect Pest Management. Proceedings of Conference, Ithaca, NY, July 18-20,1988. D.W. Roberts & R.R. Granados, eds. 175 pp.

Cook, R.J., and K.R Baker. 1983. ***The Nature and Practice of Biological Control of Plant Pathogens.*** APS Press. St. Paul, MN. 539 pp.

Grossman, J. 1989. Update: Biological control of weeds: What's happening, what's needed. ***IPMPractitioner*** II: 1-11.

National Academy of Sciences. 1987. ***Report of the Research Briefing Panel on Biological Control in Managed Ecosystems.*** National Academy Press. Washington, D.C. 12 pp.

National Academy of Sciences. 1989. The Ecology of Plant-Associated Microorganisms. National Academy Press. Washington, D.C. 34 pp.

New Directions in Biological Control. R. Baker 8c P. Dunn, eds. UCLA Symposium Molecular Cellular Biology 1990.New Ser. Vol. 112. Alan Liss, NY.