Risks and Regulations 4

Biologically based technologies (BBTs) pose certain risks, some better documented than others. The significance of these risks depends on how well the regulatory structure prevents the high impacts. Scientists who study the ecology of natural systems are most concerned about the effects of introduced classical biological control agents on the population dynamics of native species and the functioning of ecosystems. Past regulatory review by the Animal and Plant Health Inspection Service (APHIS) in the U.S. Department of Agriculture (USDA) has been erratic and inconsistent. The U.S. Environmental Protection Agency (EPA) has done a better job in its oversight of microbial pesticides under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), but critics charge that previous thoroughness and concomitant expense to registrants kept useful products from entering the market. The evaluation of new risks from the release of genetically engineered microbial pesticides could pose a major challenge.

Chapter 4 begins with an examination of potential health and environmental effects from BBTs, summarized in table 4-1. The discussion then turns to some of the tools that scientists and regulators use to evaluate and rank those risks. The remainder of the chapter looks at how EPA, USDA, FDA, and state governments decide which BBT risks are acceptable.

RISKS FROM BBTS

BBTs generally receive favorable ratings from the perspective of public health and environmental safety. Many are relatively host specific, affecting primarily the targeted pest. Unlike conventional pesticides, most BBTs lack mammalian toxicity or pathogenicity. Moreover, the development of resistance by weed and insect pests appears significantly slower for most BBTs than for conventional pesticides. Despite these multiple advantages, the risks from BBTs occasionally may be substantial, and therefore their use deserves scrutiny and, in some cases, long-term monitoring.

Human Health Effects

Human exposures to certain BBTs may occur at many stages of production and application of the BBT and during use of the end product. For example, farm personnel and local residents may inhale microbial pesticides during aerial spraying; kitchen staffs and schoolchildren may work and study in facilities treated with tiny wasps and

CHAPTER 4 FINDINGS

- The environmental and public health risks from biologically based technologies for pest control (BBTs) are relatively low when compared to those from conventional chemical pesticides. Nevertheless, BBTs are not risk-free. The significance of the risks depends on how well the regulatory system screens out the high impacts.
- The relative absence of documented harmful ecological impacts attributable to BBTs may be misleading, however, given the lack of pre- and postrelease monitoring. Some of the most harmful ecological effects, such as declines in native insect populations, have probably gone unnoticed in past decades.
- The risks from certain BBTs cannot be accurately assessed; some scientists argue that they never will be. The wide variation in scientific opinion and the high degree of uncertainty concerning BBT efficacy and ecological impacts heighten the need for public participation in the regulatory process. One committee that would benefit from more diverse representation is the Animal and Plant Health Inspection Service's (APHIS) Technical Advisory Group on the Introduction of Biological Control Agents of Weeds.
- Past regulation of natural enemies by APHIS was inconsistent and incomplete. Proposed regulations were recently withdrawn after APHIS received 252 mostly critical public comments. The agency needs to devise a regulatory framework that ensures environmental safety while encouraging the development and use of BBTs.
- The regulated community gives the U.S. Environmental Protection Agency (EPA) high marks for the creation of its Biopesticides and Pollution Prevention Division. The division is developing some much-needed exemptions and expedited registration processes for certain classes or applications of microbial pesticides and pheromones. Ecologists warn, however, that EPA should not go too far in waiving its environmental testing requirements.
- Many genetically engineered microbial pesticides are making their way through the research and registration pipeline. Scientists are engineering these products to behave more like chemical pesticides, characterized by longer environmental persistence, expanded host range, more toxic mode of action, and faster kill rate. The tracking and evaluation of environmental fate and impacts may pose significant challenges.
- The Food and Drug Administration (FDA) plays a role that is as yet undefined in the regulation of biologically based technologies. The agency is still trying to identify the scope of its regulatory responsibilities regarding the use of BBTs in grain storage and food preparation areas. FDA involvement may increase significantly as application of these products in urban settings grows.
- Certain BBTs appear susceptible to resistance, but apparently at a rate slower than that for chemical pesticides. Widespread use of transgenic plants containing toxins from *Bacillus thuringiensis* (Bt), however, may speed the development of pest resistance to Bt and squander its value as a microbial pesticide.

nematodes; consumers may unknowingly consume microbial pesticides and fragments of arthropod natural enemies in foods, in addition to pieces of the pests themselves. Persons who work in facilities for rearing natural enemies may face occupational exposure to the insect predators and parasites.

Few human health risks from BBTs have been described in the scientific literature. Best documented are allergic reactions, particularly to fungal pathogens (411,420). Workers in insectaries have developed allergic asthma and rhinoconjunctivitis (nasal inflammatory disease) from contact with the eggs, scales, and waste of the arthropod pests and their natural enemies. Respiratory and dermal protection may help retard such effects (205). Another risk is that manufactured microbial pesticides could become contam-

TABLE 4-1: Examples of Potential Risks from BBTs

BBT examples	Potential environmental impacts	Potential human health effects
Conservation of natural enemies	Probably insignificant	No known risk[a]
Classical biological control/ introduction of new natural enemies	Some adverse impacts on nontarget organisms; destabilization of existing control by predators and parasites; habitat destruction; possible evolutionary changes. Many of these risks are shared by other BBTs	No known risk
Release of sterile fishes for biological control	Adverse effects on nontarget organisms; potential for hybridization with wild forms; possible development of resistance, self-reproducing strains, or selective mating patterns; potential transmission of parasites	No known risk
Augmentative releases of parasites and predators	Some risks similar to those for classical biological control; contamination of field-harvested natural enemies by parasites; depletion of natural enemies in collection sites	Allergic reactions among workers in insectaries
Pheromones	Potential adverse impacts on aquatic invertebrates and some fish from lepidopteran varieties,[b] but warning labels advise against such usage; other types of pheromones may have greater potential toxicity to mammals, fish, and birds; undocumented possibility for disruption of mating behavior of other insects; slight risk of resistance	Low oral or inhalation toxicity, possible dermal and eye irritation, from lepidopteran-active products; higher toxicity among other pheromone groups, but minimal human exposure
Bacterial pathogens (microbial pesticides)	Some adverse impacts on nontarget lepidoptera and their avian predators Short-term declines in certain nontarget insects; resistance documented in field populations of pests treated regularly with Bt	Minimal risk to general population; some data suggest possible infection of immunocompromised individuals
Viral pathogens (microbial pesticides)	Minimal effects on nontarget organisms; possibility of resistance in future as field use expands	No known risk
Fungal pathogens (microbial pesticides)	Possible effects on nontarget organisms; early evidence of resistance	Some established human allergens and toxic metabolites
Protozoan pathogens (microbial pesticides)	Possible effects on nontarget species	No known risk
Nematodes (microbial pesticides)	Possible effects on nontarget organisms, particularly those in the soil	No known risk
Release of sterile insects	Some adverse effects on nontarget organisms; possible development of resistance, self-reproducing strains, or selective mating patterns	No known risk

[a] "No known risk" indicates that risks have not been documented. In some cases, the absence of documented effects may be due to a lack of monitoring or observation.

[b] Lepidoptera is a large order of insects that includes butterflies and moths, some of which are considered pests.

SOURCE: Office of Technology Assessment, U.S. Congress, 1995.

inated with human pathogens such as *Shigella* and *Salmonella;* each production batch must be screened for the growth of unwanted organisms (314).

Health concerns arise more often from microbial pesticides than from other biologically based approaches. Bacteria, fungi, protozoans, and viruses all raise questions about infectivity; bacteria and fungi trigger toxicity concerns as well (311). Occasional medical case reports describe infection from certain microbial pesticides, although it is unclear whether the organisms have actually multiplied or caused any harm in patients' tissue (125).

Products based on *Bacillus thuringiensis* (Bt), by far the most widely used microbial pesticides, have been the focus of many animal experiments and some human studies. Isolated incidents of eye infection and inflammation of connective tissue have been reported. Some varieties of Bt (esp. israelensis, used for blackfly and mosquito control) are more toxic to mammals than others (e.g., kurstaki, primarily used for gypsy moth and other lepidopteran pests) (125).

Although there is minimal evidence of health risks to the general population, some researchers have suggested that immunocompromised individuals (e.g., people with AIDS) may exhibit heightened susceptibility to certain insect pathogens including Bt (125,311,346). Similar concerns apply to individuals undergoing immunosuppressive cancer therapies (see table 4-1).

A BBT use that may call for extra attention in the future is the application of microbial pesticides to agricultural products after harvest to prevent spoilage. To date, EPA has registered for postharvest use only microbial products that work by preferentially colonizing wounded tissue to the exclusion of microorganisms that cause rot. These microbial pesticides, such as Ecogen's Aspire (a yeast, *Candida oleophila*) and EcoScience's Bio-Save (a bacterium, *Pseudomonas syringae*), although still present in reduced numbers on citrus, apples, pears, and other fruits at time of consumption, are considered by EPA to be as safe as the microorganisms regularly residing on these foods (182). Another approach controls microorganisms by producing antibiotic substances that are toxic to a broad range of organisms. These fungal and bacterial agents, if ever applied to fresh fruits and vegetables, would require a detailed evaluation of toxicity and pathogenicity, especially to immunosuppressed people (81,426).

Minor impacts on mental well-being may result from at least one natural enemy. The Asian lady beetle, *Harmonia axyridis,* was released by USDA from 1916 to 1985 primarily in the southern United States to control pecan aphids (288). Despite the lady beetle's beneficial agricultural effects, some people have come to regard the insect as a nuisance: Lady beetles enter homes in large swarms, where they interfere with daily activities and emit a noxious-smelling secretion. Anecdotal accounts describe families collecting pints of lady beetles in their homes on a daily basis and finding lady beetles crawling on the ceiling, windows, walls, and beds, and in cups, bowls, coffee pots, and so forth. Many state agricultural experts urge homeowners not to kill the lady beetles, in light of the insects' important role as natural enemy of aphid pests (288,252).

Environmental Impacts from BBTs

Many of the effects of BBT use remain unknown (313). Natural enemy companies generally point to an exemplary record of safety (128), whereas conservation biologists argue that the dearth of documented impacts does not mean they have not occurred (220). There have only been occasional studies of environmental effects in the United States, and most of these efforts have been directed toward agricultural crops. The consequences for nontarget native insects, in particular, have been largely ignored (151). Some of these play important roles as natural enemies. Yet unlike native plants and commercial crops, insects (with the possible exception of butterflies, honeybees, and silkworms) have no constituency to advocate for their conservation (284,117).

Despite the incomplete and controversial record, at least a few documented releases of certain biological control agents have disrupted natural communities and brought about localized declines in native species. Some of the very characteristics that make many natural enemies effective in controlling pests (their capacity to harm other organisms, to survive, to reproduce, to disperse, and to evolve adaptations to new conditions) also make them potentially harmful invaders (219). Generalist natural enemies—those less choosy in selecting food sources, hosts, or mates—pose some of the more serious ecological risks. The level of risk depends also on such factors as the reversibility of the release, the potential of the agent to spread, the extent to which impacts may be mitigated, the availability of monitoring, and the predictability of impacts across life cycle and distribution. It is worth noting that some of the more significant adverse impacts that have resulted from biological control releases took place long ago, and many involved generalist predators on small island ecosystems in other countries. In the analysis that follows, OTA's emphasis is on documented impacts in the United States. Where there are no U.S. examples, the text also includes some potential risks based on experience in other countries, as well as some of the theoretical risks postulated by ecologists and other scientists. Many of the introductions of agents that are described would not stand up to scrutiny or be allowed today.

Although the potential consequences from the use of biological control agents and certain other BBTs are worrisome, it is worth remembering that the pests themselves—and the synthetic chemical methods of control—raise health and ecological concerns that at least equal and often exceed those presented by most BBTs (414). Consideration should also be given to other available options for controlling a particular pest situation. The following discussion describes the full range of documented and theoretical risks from BBTs and then puts these risks in context.

Impacts on Nontarget Organisms

Introduced natural enemies, sterile insects, certain microbial pesticides, and pheromones have sometimes affected not only the targeted pest species but also nontarget plants or insects. These nontarget organisms are often related to the pest species. Some serve important ecological roles; others are listed by the U.S. Fish and Wildlife Service as threatened or endangered. Many of the suspected or known impacts have occurred in habitats far and ecologically disparate from the original location of release, and at times long after the introduction or use of the BBT. The release of classical biological control agents raises the greatest ecological concerns, although the extent of risk is controversial. Vertebrate organisms and other generalist species pose many of the more important risks; some of these are addressed in greater detail in OTA's report, *Harmful Non-Indigenous Species in the United States* (338).

The best-documented nontarget impacts involve the release of vertebrate predators. For example, the barn owl (*Tyto alba*), imported in 1958 into Hawaii from California for rodent control, preys also on shearwaters, terns, petrels, and other organisms (313). The small Indian mongoose (*Herpestes auropunctatus*), released in the West Indies, Mauritius, Hawaiian Islands and Fiji, failed to control its target—rats in agricultural fields—but caused the decline of native birds and, in the West Indies, apparently contributed to the extinction of native snake and lizard species (313,284). A predatory snail, *Euglandina rosea*, introduced to many islands throughout the world for control of the giant African snail, *Achatina fulica*, may have helped bring about the extinction of several endemic snails (313).

In some instances, fishes introduced for biological control (including the two most widely used varieties, mosquito fish—*Gambusia* spp., and grass carp—*Ctenopharyngodon idella*) have caused substantial declines in local populations of native fishes (313,338). For example, the mosquito fish, introduced in many regions for mosquito control, has preyed on, and in some locations contributed to the decline of at least 35

other fish species (313). Seemingly innocuous predatory fishes may become harmful as they switch dietary preferences in later life stages. The use of fish-eating fishes to control pest fish species raises special concerns because native fishes are often highly valued resources (191).

Plant-eating (phytophagous) insects introduced for biological control of weeds have spread to other locations where they have contributed to the decline of related native plant species. A few such cases are documented, but others may have gone unnoticed. One example, that of the cactus moth (*Cactoblastis cactorum*), a native of Argentina, illustrates the need to evaluate the effects of a candidate biological control organism on all potential plant hosts. The moth, which feeds only on cacti of the genus *Opuntia,* was released with great success as a biological control agent in Australia (1925), on several Caribbean islands (1957, 1962, and 1970), and in other locations. Together with two scale insects (*Dactylopius* species), the moth effectively controls highly invasive weed species of the cactus, for which chemical pesticides, grazing, burning, and other approaches are economically and environmentally infeasible (75). The moth has had serious nontarget impacts on native *Opuntia* species on Nevis and Grand Cayman; at the time of its release, however, the value of these indigenous plants was not fully appreciated (74).

After dispersing on its own through Haiti, the Dominican Republic, Puerto Rico, the Bahamas, and Cuba, the cactus moth eventually entered the United States, possibly as a contaminant of horticultural stock (220). The moth was discovered in Florida in about 1989. In the Florida Keys it largely destroyed the few remaining stands of the semaphore cactus (*Opuntia spinosissima*), a candidate for listing under the Endangered Species Act. This development probably would have gone unnoticed had it not taken place on a closely monitored Nature Conservancy preserve (313,284). It is likely that the cactus moth will spread north through Florida and west into Texas and Mexico, where it may attack other *Opuntia* species, including weeds, food or feed crops, and ecologically valuable species (75).

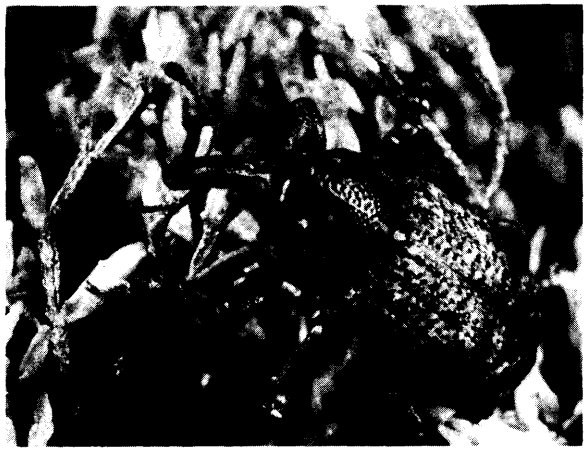
Numerous anecdotal accounts, intensely debated but often poorly documented, describe biological control agents that have parasitized nontarget insects in Hawaii, Fiji, and New Zealand (313). Most of these releases occurred in prior decades.

A documented example of nontarget effects from a microbial pesticide involves certain strains of Bt that can harm nontarget Lepidoptera[1] (313,220). Secondary effects on insect-eating bird species are possible: The decline in food may force them to change location or may depress successful reproduction (283). Some researchers suggest that the decline in nontarget Lepidoptera may be only temporary (411), possibly because the Bt does not form free-living populations (158).

One realm of particular concern involves potential risks in using plant pathogens for agricultural weed control. Farmers usually face a complex of broadleaf and grassy weeds. Development of a microbial pesticide containing sufficient variety of organisms to control several weed species would require a dauntingly complex set of tests to ensure safety. This situation contrasts with that of rangeland noxious weed control, in which land managers may target a particularly troublesome weed species individually (167).

The introduction of natural enemies to control native pests, however, raises concerns because the full ecological role of the pests may not be well understood. Certain native plants that are pests in one context may also be an important source of forage and may support numerous other native species. Debate about the desirability of using introduced biological control agents against native species rose to the surface in 1993. Plans by federal researchers to use a wasp parasite and a fungal disease against rangeland grasshoppers ground to a halt when entomologists

[1] Lepidoptera is the insect order that includes butterflies and moths.



Use of introduced natural enemies against native pests, such as this weevil (Heilipodus ventralis) *on snakeweed* (Gutierrezia sarothrae), *is controversial because of potential impacts on native ecosystems,*

Agricultural Research Service, USDA

pointed out that the control agents might also affect many of the over 280 nontarget native grasshoppers (122). Some may play important roles in native ecosystems, for example by suppressing native weeds such as snakeweed. The case continues to be highly contentious among scientists (204,43).

Interference with Existing Control Agents–Competition and Life-Cycle Disruption

Some evidence suggests that biological control agents have adversely affected native natural enemy populations by outcompeting them for food or other resources. Such competition is notoriously hard to document in the field, particularly among insects, the habitats and behavioral patterns of which are not well studied (313). A few such situations have been reported, one concerning the European lady beetle *(Coccinella septempunctata),* which has been released widely in the United States. The introduced lady beetle appears to be displacing other predatory insects such as the nine-spotted lady beetle (C. *novemnotata),* thereby potentially disrupting the control of pests by native insects (313). In fact, the European species is now the dominant lady beetle by far in many of the agricultural systems it has colonized (170).

Biological control agents can affect nontarget organisms also by interfering with their life cycles, ultimately resulting in the upsurge of pest populations. Reports from Fiji describe the life-cycle disruption of the coconut leaf-mining beetle *(Promecotheca reichei)* by an introduced mite *(Pediculoides ventricosus),* reducing the population of native parasites and thus enabling the beetle population to skyrocket (313).

Habitat Destruction

Damage to the habitats of nontarget species is an important yet underreported risk from the introduction of fishes for aquatic weed control. These fishes dramatically reduce local plant cover, potentially causing significant disruption to both plant and animal communities (313). In the case of grass carp, however, the negative impacts have been reduced somewhat by only using the fish in enclosed water bodies and by releasing sterile triploid fishes (191). The U.S. Fish and Wildlife Service operates a certification facility to ensure that grass carp for biological control are unable to produce viable offspring, and most states require permits and verification of triploidy for grass carp imports (191). The approach is impractical for many fish species, however, and generally not all fish in a treated lot become sterile (313). Although individual fish that are released harm nontarget vegetation, as do their fertile counterparts, the sterilized fish usually will not form reproductive populations that can spread.

Reproductive Effects

A little-documented potential risk from pheromones is the disruption of mating patterns. There is some evidence that the pheromone of bark beetles that stimulates them to flock together may influence the behavior of other beetles. Sex pheromones of Lepidoptera may possibly affect the behavior of certain parasites (313).

Another reproductive concern relates to the use of immunocontraceptive control for vertebrate pests, although these approaches have not yet been used in the United States. Australia

plans to use genetically engineered viruses to control foxes and rabbits by inducing the females' immune system to attack male sperm. The control plan will require simultaneous depression of both fox and rabbit populations: Controlling only the foxes would enable the rabbit population to explode; restricting only the rabbits would induce the foxes to switch to other prey, most likely endangered marsupials. Australian scientists are examining potential risks including the capacity of live infectious viruses to multiply, to attack other species including house pets, and to spread abroad.

The rabbit control involves a redesigned myxoma virus, which is specific to rabbits and hares. Lacking a virus specific to foxes, the Australians risk inadvertently sterilizing dingoes (wild dogs) and domestic dogs. Similar concerns have been raised by researchers at APHIS's Denver Wildlife Research Center, who are developing immunocontraceptive therapies with which to sterilize coyotes and deer in the United States (225).

Other Potential Risks

Evolutionary Change among BBTs

Evaluating genetic change among populations of biological control agents after their introduction is difficult and has rarely been attempted (171). Yet some ecologists argue that the conditions of such releases facilitate the rapid evolution of changes in a natural enemy's host range or other important characteristics. Evolved resistance to conventional pesticides occurs with some frequency among arthropods and has been demonstrated experimentally in certain natural enemies (see chapter 2). Introduced species might also evolve an expanded tolerance of physical factors, thereby increasing the range of habitats they may occupy and thus their impacts (313).

Some scientists speculate that biological control relationships could become less and less effective over time as the pest and its natural enemy evolve in response to one another (313), although data are lacking on the likelihood and on the rate at which this might occur. A further possibility is that introduced species might hybridize with native ones to the point that the native species no longer exist in their original form. Little research has addressed this phenomenon. The one documented case involved the introduction of mosquito fishes (*Gambusia affinis* and *G. holbrooki*) that hybridized with another related species (*Gambusia heterochir*) and now threaten the integrity of the latter's gene pool (313).

Inadvertent Introduction of Parasites of Natural Enemies

APHIS's screening of incoming biological control agents generally prevents accidental importations of hyperparasites (i.e., parasites of parasites) (236). A unique example of hyperparasitism among field-collected biological control organisms in the United States concerns the lady beetle (*Hippodamia convergens*). A parasitic wasp may contaminate up to 10 percent of these lady beetles. In the spring of 1994, APHIS decided to prohibit interstate shipment of field-collected lady beetles that had not been held in quarantine and cleared of parasites. Following strong public protests arguing that the collection and dispersal of California lady beetles has been a cottage industry for over 75 years and is thus unlikely to cause further adverse effects, APHIS overturned the decision. The agency continues to urge that field-collected lady beetles be held to identify and remove parasitized individuals (60).

Resistance to BBTs

Pest resistance to conventional insecticides has contributed to the growing interest in biologically based approaches. Initial findings suggest that pests may develop resistance to certain BBTs, particularly bacteria and viruses (9,411), and possibly fungi (420,281) and pheromones (40) as well. The likelihood of resistance or rate at which it might develop is unclear however. Compared with conventional pesticides, most BBTs appear less prone to stimulate resistance. Many biological approaches benefit from physiological modes of action (such as interference with photosynthesis, respiration, transpiration,

translocation, and seed production) that make it more difficult for pests to develop resistance to BBTs than to certain conventional pesticides that lack these properties (420).

If pests become resistant to BBTs, making these approaches no longer effective, agriculture will lose an important set of low-risk pest control tools. Indirect health and environmental risks could result if growers were forced to switch back to conventional pesticides, because BBTs offer significant advantages from an environmental and public health standpoint (274).

The bacterial insecticide Bt faces the greatest threat. Future large-scale use of crop plants genetically engineered to contain the Bt toxin could speed the development of resistance and put at risk its effectiveness as a microbial pesticide (112). Unlike Bt sprays, which are applied only intermittently, plants bred to contain Bt toxin in their tissues continuously expose pests to the toxin over the entire growing season. This increased exposure to Bt heightens the selective pressure on pests and may hasten the development of resistance (422,221,146,214). Some scientists believe that resistant pest populations will appear soon after the transgenic Bt crops are planted.

Thus far, evidence of Bt resistance in the United States has been seen only in field populations of the diamondback moth (*Plutella xylostella*). Resistance in the moth has been observed in the Pacific Rim, Florida, and New York (411,326). The Colorado potato beetle (*Leptinotarsa decemlineata*) on Long Island, New York, which was one of the first agricultural pests to develop insecticide resistance (to arsenicals in the 1940s and to DDT in 1952), now shows the potential for resistance to Bt tenebrionis. The silverleaf (sweet potato) whitefly (*Bemesia argentifolii*), another major pest that is notoriously difficult to control because of its expanding resistance toward organophosphate, carbamate, and pyrethroid insecticides, has developed resistance to Bt kurstaki in Taiwan, the Philippines, and Malaysia (112).

There is no published evidence of an insect developing resistance to a virus in the field. Microbial pesticides based on viruses have not yet been used extensively in the United States. Lab results indicate, however, that future large-scale use might result in resistance (411).

The potential that pests will develop resistance to other BBTs is only speculative at this time. Continuous exposure of susceptible insect pests to nematode products, for example, might encourage selection for resistance (411). Theoretically, pest populations might even evolve resistance to the sterile male technique by developing self-reproducing strains or the ability to recognize and mate only with fertile males (313).

Depletion of BBT Agents in Natural Areas

The mass collection of natural enemies impacts regional populations. Unlike most augmentatively released natural enemies, which are raised in insectaries, the lady beetle (*Hippodamia convergens*) and several natural enemies of rangeland weeds are collected from field sites. The lady beetles, for example, are harvested from locations in the California foothills to which the beetles migrate. Lady beetles dominate the biological control market for garden use because of their familiarity to the public, promising anecdotal stories, aesthetic appeal, and long history of commercial sale. Despite some doubts as to their effectiveness (see box 3-1 in chapter 3), the collection and sale of lady beetles continues to increase, with demand often exceeding supply. Supplies are finite, however, and there are increasing concerns about environmental costs associated with the commercial collection of the insect (60). In addition, the collection undermines natural control, which is free to the farmer (416), and interferes with publicly supported biological control programs.

Genetically Engineered BBT Organisms

The environmental repercussions of genetically enhanced microbial pesticides deserve special scrutiny. Scientists are using genetic engineering techniques to expand the target range (194), incorporate more toxic modes of action, increase kill rates, and extend environmental persis-

tence—in essence, to make microbial pesticides mimic their more heavily regulated chemical counterparts. Implications for nontarget species may grow in future years as these products move through EPA registration. University of Florida entomologist J.H. Frank (1995) raises concerns with respect to genetically engineered Bt products (108):

> Research is attempting to increase the range of targets that Bt will kill, to increase commercial profitability.... Where will it stop—how broad would commerce like the target range to be? Why should these commercial interests bother to look out for the welfare of nontarget organisms? Even more, why should they look out for the welfare of beneficial organisms that already exert partial control of some pests and complete control of others? It is not in their interests to do so, because they will be able to sell more product in the absence of these beneficial organisms....

The interests of commercial profitability and the protection of nontarget species may collide over the issue of target range. From an environmental perspective, a key advantage of many BBTs is their relatively narrow range of impacts. Yet products that kill or impair a wider range of species cater to a larger pest control market and hence generate higher profits. Producers of genetically engineered BBTs are developing microbial products with extended target range, although whether their breadth will ever rival that of conventional pesticides remains to be seen.

Some of the environmental effects from genetically engineered BBTs remain unclear. Depending on the properties of the toxins or hormones inserted into the microbe to achieve pesticidal activity, for example, symptomless infections by genetically modified viral insecticides in nontarget organisms could go undetected and later provide a reservoir of infection of other organisms (429).

Putting the Risks in Context

Almost every scientist contacted by OTA about BBT risks prefaced his or her comments by emphasizing that the occupational and environmental risks from conventional pesticides dwarf those from biologically based approaches. For example, chemical insecticides, herbicides, and fertilizers have caused documented adverse impacts on more than 90 species listed under the Endangered Species Act (89), as well as serious health and ecosystem effects. Although beyond the scope of this report, the risks from these synthetic pest control methods help put into perspective the relative safety of most BBT options.

The relative absence of effective low-risk pest control solutions—perhaps intercropping, crop rotation, field sanitation,[2] and row covers would fall in such a category—suggests that difficult choices must be made among suboptimal options, each of which implies an array of hazards for different organisms and population sectors. The risks differ both qualitatively and quantitatively: Chemical pesticides raise significant consumer and occupational health issues, in addition to environmental effects, whereas BBTs affect primarily native species, and native biodiversity is a relatively new category of concern in the United States.

Important risks derive also from failure to control the pests. These organisms, many of them invaders from foreign lands, can damage economic resources as well as native ecosystems. Our nation's food supply depends on efficient, low-cost agricultural technologies, and our environmental and aesthetic needs depend on the preservation of our national treasures such as parks and forests.

Most BBTs have a favorable health and environmental profile, and some provide solutions to pernicious health risks (box 4-1). A well-designed regulatory system could screen out the greater risks from BBTs while facilitating adoption of the vast majority of these technologies. The development of proper recordkeeping and

[2] Field sanitation involves the removal of crop residues that harbor pest stages.

monitoring systems could advance our base of knowledge, improve the development of new BBTs, and eventually allow for a tighter match between risks and regulatory testing requirements.

BOX 4-1: Controlling Public Health Scourges with BBTs

Biologically based approaches can sometimes control the disease vectors or intermediate hosts of malaria, schistosomiasis, and other afflictions of humans and livestock. Fishes, turtles, and fungi, for example, have all been used to control mosquitoes that transmit malaria and dengue fever in the tropics and veterinary diseases, such as heartworm and equine encephalitis, in the United States. The use of BBTs for public health purposes has certain advantages but also raises potential problems.

Over 200 fishes from around the world are known to eat mosquito larvae. In addition, fish that eat aquatic vegetation may modify their habitats, making them less suitable for mosquitoes. A big advantage of using fish for mosquito control is that they generally require little investment or infrastructure to produce an acceptable level of long-term control. In addition, the potential to evolve resistance to fish predators is much less than that to insecticides.

Although sometimes quite effective, however, fish do not completely eliminate mosquito populations; generally they do not provide the level or the rapidity of control achievable with insecticides. Their use is restricted to suitable bodies of water, leaving out many important mosquito habitats. Moreover, the nontarget impacts can be severe. The fish most commonly used for mosquito control in the United States, for example, is the mosquito fish, *Gambusia affinis,* from the southeastern United States. This fish often outcompetes other native fishes. Mosquito fish develop dense populations and may reduce the food sources or eat the eggs and young of native species.

Fungal species of the genus *Coelomyces* and *Lagenidium* are lethal to mosquitoes. The spores penetrate the insect and can cause mortality within a few days. Areas can be inoculated with fungal pathogens by transporting infected insects or sporangia to the target location. A significant advantage of fungal pathogens over the use of insecticides or Bt is that mosquitoes are less likely to evolve resistance to fungi. Moreover, since the fungi are already widely distributed worldwide, there may be less concern about unpredictable damage to nontarget species.

Fishes and fungi are not the only possible control agents for mosquitoes. Bats and some birds, such as swallows, consume an extraordinary number of mosquitoes, and juvenile turtles have reportedly provided successful control of mosquitoes in cisterns for drinking water in Honduras.

Schistosomiasis is another cause of considerable morbidity and mortality in the developing world. Certain predatory fishes can effectively control juvenile snails such as *Biomphalaria glabrata,* an intermediate host for the parasitic worm that causes the disease in the tropics. In addition, a competitor species of snail, *Marisa cornuarietis,* is used as a control agent in Puerto Rico and is considered to have contributed substantially to the sustained reduction of schistosomiasis on that island; adverse ecological impacts have not been documented. In Florida and other regions, however, the snail feeds indiscriminately on many native plant species.

SOURCES: A. Kuris, Department of Biological Sciences and Marine Science Institute, University of California, Santa Barbara, CA, "A Review of Biologically Based Technologies For Pest Control in Aquatic Habitats," unpublished contractor report prepared for the Office of Technology Assessment, U.S. Congress, Washington, DC, October, 1994; D. Simberloff, Department of Biological Sciences, Florida State University, Tallahassee, FL, letter to the Office of Technology Assessment, U.S. Congress, Washington, DC, July 16, 1995.

In the real world, moreover, many of the possible risks from BBTs pale in comparison with the benefits of use. For example, in the case of coddling moth control, although scientists have postulated theoretical risks with regard to future impacts of pheromones on the mating behavior of introduced natural enemies, in practice so far sex pheromones have proved to be highly effective in concert with augmentative releases of *Trichogramma* wasps. Studies on cotton bollworm and European corn borer suggest that the presence of certain pheromones actually enhances the searching behavior of the wasps (236).

Risks that deserve particular scrutiny in the near future include the growing resistance to Bt and the potential to rapidly reduce its effectiveness through large-scale use of crop plants containing Bt genes; the untested ecological repercussions from the use of genetically engineered microbial pesticides; and, more generally, the effects of BBTs on insect populations, organisms that often play valuable ecological roles and serve as natural enemies of many household and agricultural pests.

Minimizing the Risks

Regulatory agencies use several tools to sort out which BBTs bear more significant risks and to expedite registration of the safer technologies. Many of these tools have not yet been fully developed. A brief explanation of some of these approaches follows.

Establishing Priorities for Risk Evaluation and Testing

Risk depends on the level of hazard as well as the extent of the exposure. Evaluation of BBT risks should consider each of the possible adverse impacts plus the risk from the uncontrolled target pest and from other pest control approaches. Some scientists suggest that a ranking of BBTs along risk categories could help agencies set priorities and fast-track the permit applications of the most promising and least risky BBT candidates. By using more of a tiered testing system—in which more rigorous testing is only required when a potential risk is detected—agencies could streamline the data requirements for safer BBT products.

Developing a hierarchy among risks is controversial, often difficult, and sometimes impossible. It is not easy to generalize risk categories. The rankings may reflect scientific assumptions about the breadth of the host range, as well as broader assumptions about the value to be assigned particular classes of nontarget organisms (219). They could also include patterns of use and likely levels of human exposure.

Most scientists would place terrestrial vertebrates at the top of the risk hierarchy. Introductions of organisms such as the mongoose, myna bird, and giant toad have had severe and widespread adverse impacts due to their nonspecific feeding and their numerical abundance (219).

Many researchers would also designate as high risk those organisms that feed on a wide range of plants and animals (284). Generalist feeders such as the sevenspotted lady beetle (*Coccinella septempunctata*), which APHIS decided to mass-rear as a biological control agent in the late 1980s, have displaced native species in many environments (169). Even a nontarget organism that is rare or endangered—and therefore would not sustain a predator population—may still be vulnerable if related species in the vicinity that are more abundant attract the generalist agents (220).

Among control organisms used against arthropod pests, predators tend to be less host specific and less successful in biological control programs than parasites, suggesting that parasites deserve a lower place in the hierarchy of risks (219). Advantages of parasites include their greater specificity, searching ability, and ability to persist along with the pest at low population levels. Nonetheless, there may be reasons to use predators instead: Their lower specificity and their capacity to switch from one type of prey to another may produce more effective control of fluctuating pest populations (219). Also on the low end of the risk spectrum could be such approaches as the conservation of natural enemies or the use of pheromones in traps.

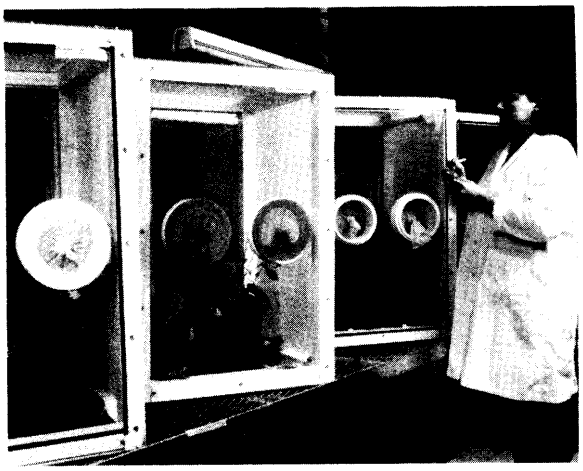
A major difficulty with attempting to order the levels of risk, of course, is that there will always be exceptions. Organisms within categories designated as high risk may prove relatively innocuous, while those that fulfill the criteria as low-risk BBTs may cause unexpected harm. A regulatory system that incorporates reliance on risk categories, therefore, must also include flexibility and substantial safeguards to ensure the recognition of such exceptions.

An advantage of a risk hierarchy is that it facilitates matching the required pre-use evaluations to the likely level of risk posed by a BBT. Evaluation schemes that take into account the variable levels of scrutiny required by different potential risks are called tiered testing. These systems preclude unnecessary testing and wasted resources. APHIS and EPA use tiered testing to varying degrees. The first tier provides maximum opportunity for the identification of any adverse effects. BBTs that pass the first tier are not subject to further testing. Second and third tier testing are used to reveal possible mitigating factors (21 9).

Testing for Host Specificity

Host specificity measures the degree to which a biological control agent is restricted to its target. It provides information on the range of organisms a biological control agent will affect through feeding, reproduction, or other interactions. Scientists use information on host specificity to try to identify the organisms likely to be attacked by candidate control agents in the release environment. Testing of host specificity began for biological control agents targeting weeds in the 1950s. Initially, the potential agent was tested only on the agricultural crops growing in the region into which the control organism was considered for introduction (21 9).

More predictive frameworks have since replaced the crop-testing method, often placing greater emphasis on nontarget threatened and endangered species and other plants of ecological value. Many biological control practitioners advocate use of the centrifugal/phylogenetic approach, which involves testing plants of increasingly distant relationship to the target until the host range is circumscribed. The centrifugal approach is not without its problems, however. For one, it assumes that related plants are more likely to be attacked, whereas, in reality, sometimes widely unrelated plants are attacked (220). This may be more a problem among pathogens than among insects (159). In addition, the centrifugal approach may overlook some important variations in resistance and susceptibility of individual hosts (328).



Natural enemies imported for research on the biological control of weeds are held in quarantine prior to release.

Agricultural Research Service, USDA

The relatedness procedure, the newest approach to host specificity, is a subtractive procedure that involves selecting plants to be tested on the basis of their evolutionary relationship to the target organism, as well as their distribution, climatic preferences, seasonal occurrence, regional weather patterns, life cycles, and other information available in the scientific literature (73). The approach is weighted to favor those potential hosts most closely related to the target organism, but it tests representatives from all other levels of relationship as well. The method has been applied successful y in Australia for the host-specificity testing of *Uromysces heliotropic,* a fungal agent for the biological control of the weed, common heliotrope, *Heliotropism europaeum (139,140,73).*

The relatedness procedure or other host-specificity approaches, if better developed in the future, may make possible the use of shorter, more predictive and reliable testing lists (73). To date, however, the science of host specificity has a long way to go, particularly given the complexity of ecological interactions and the difficulty of measuring them (360).

APHIS and EPA rely on these various testing procedures to varying degrees. APHIS evaluates the data on the basis of whatever approach the researcher uses. If a researcher asks for guidance on host range testing, the agency sends two sample papers, one from 1974 based on the centrifugal procedure and one from 1992 based on the relatedness procedure (360). In practice, however, the choice of nontarget test organisms depends more often on what the researchers happen to have available or readily accessible and know how to test (159,73). EPA's testing protocols emphasize the major agricultural crops.

Another problem is that researchers developing test lists for BBT registration applications often have little background in relevant biological disciplines. Entomologists petitioning to introduce an arthropod species that attacks weeds, for example, commonly lack the botanical training needed to identify likely host plants based on evolutionary relationships, life cycles, and other aspects of plant ecology (159).

Because of their potential to attack agricultural crops, pathogens of plants and plant-eating (phytophagous) arthropods have traditionally evoked the most thorough host-specificity studies. Host-specificity assessment for predators, parasites, and pathogens of insect pests, by contrast, remains in an early stage of development. This situation reflects the lower degree of social, economic, and environmental concern for arthropods than for plants as nontarget organisms. There are far fewer "domestic" arthropods (such as honeybees and silkworms) than there are agricultural crops, and plants are far more likely to be listed as threatened or endangered species, thus deserving special protection. Many scientists argue that the biological control agents used for control of arthropods deserve more careful attention than they receive today.

A single species that feeds on several organisms is often made up of numerous more specialized individuals. Such diverse populations may harbor enough genetic variation to evolve and eventually change hosts. Thus testing should sample as much genetic and geographic variation in the biological control agent as possible, to maximize chances of detecting the variation among individuals upon which natural selection might act (219).

Host Range

Host range refers to the number of different species that a given agent will attack. Although conceptually similar to host specificity, host range focuses on the biological control agent rather than the target. Often the terms are used interchangeably; they refer to overlapping subsets of risk (73).

Examination of a biological control agent in its site of origin provides a basis for predicting effects in the release area (256); so does information on the agent's biology, taxonomy, and ecology (415). To help approximate the range of organisms a biological control agent or microbial pesticide will affect in its proposed area of release, however, researchers also use laboratory and field tests. Lab tests aid in approximating the physiological host range of the control organism—the maximum extent to which an agent could impact potential hosts. Artificial testing conditions—such as use of starved biological control organisms and lack of dietary choice—may inflate the range results for many arthropods and pathogens (219). For example, if a candidate biological control agent does not feed on a test organism in laboratory conditions, it is nearly certain that it will not feed on the organism in field conditions. If the biological control agent does feed on the test organism in laboratory conditions, however, it does not necessarily follow that the same behavior will take place in the field (360).

The actual, or "ecological," host range is always less than the physiological host range

(74). Field tests give a more accurate picture of the extent to which control organisms can be expected to attack nontarget species upon release. The accuracy of extrapolation from the physiological host range (revealed in the lab) to the ecological host range (revealed in the field) needs improvement. Further development and testing of host specificity protocols may better establish what fraction of the potential host range is likely to be expressed in the field (219,73).

Host-specificity and host-range testing are no guarantees of environmental safety. The harmful effects of the biological control organism can include not only eating, parasitizing, or infecting a nontarget organism, but also indirect effects from interfering with shared natural enemies or shared hosts (219). There is also the risk of interspecies mating, especially with threatened or endangered species.

The relative specificity of BBTs requires that they be weighed on a case-by-case basis, each situation reflecting a unique set of potential interactions among the control organism, target organism, and potential nontarget organisms. No standard set of indicator species or single representative sample of nontarget species (e.g., rodent or other model organisms) or nontarget ecosystems will apply to all proposed agents. Moreover, when potential harm to ecosystems is weighed, there may be no easily defined endpoints to the analysis, a factor that makes development of protocols problematic (219).

Evaluating the Risks and Benefits of BBTs and Alternatives

Risk-benefit assessment of BBTs is exceedingly difficult, given the lack of accurate quantitative data on either risks or benefits. To date, much of the available information is unsubstantiated and anecdotal.

Moreover, risk implications may differ with the purpose of the BBT release. Natural area managers usually focus on protecting a large number of valued native species, and thus prefer narrowly targeted pest control methods. By contrast, an individual farmer, rancher, forester, or other producer focuses on the productivity of just a few species. The use of BBTs with lower host specificity may better meet these broad-spectrum needs, but at the same time may involve greater ecological risks (284).

Many difficulties complicate the task of quantifying the relative risks posed by a BBT release and those posed by taking no action against the pest or using other control methods. Benefits and costs may be unevenly distributed socially, geographically, or across generations, and excessive uncertainty or questionable valuation techniques may undercut the analysis (219). A qualitative, multi-factoral comparison of BBTs with other control methods, however, might serve to elucidate some important differences in nontarget effects, impacts on groundwater, residues on crops, and occupational exposures, as well as short- and long-term effectiveness and resistance.

ADDRESSING THE RISKS

This section examines the regulatory structure for most BBTs. The agencies that regulate BBTs have a difficult dual mission: facilitating the development and registration of biologically based technologies while minimizing the risk of harmful environmental and public health impacts. The incongruous nature of these directives suggests that neither will be satisfied completely. The challenge is to incorporate a reasonable degree of ecological scrutiny into a more streamlined and efficient regulatory process.

Although there is no federal statute that directly deals with biologically based approaches, several federal agencies regulate BBTs. EPA oversees the commercial sale and use of microbial pesticides and pheromones. USDA's APHIS regulates the introduction and dissemination of biological control agents including arthropods, mites, nematodes, slugs, snails, and other macroorganisms. FDA monitors the use of BBTs that could become components of stored or prepared food, such as microbial products and fragments of insect natural enemies in stored grain. The U.S. Department of Inte-

rior's Fish and Wildlife Service (FWS) evaluates potential impacts of certain biological control organisms on threatened and endangered species. Some states regulate BBTs as well (box 4-2).

This section does not cover in detail regulations for the use of vertebrate animals and fishes as biological control agents. Such agents historically have posed some of the greatest risks, yet they are subject to very little scrutiny by federal agencies. Instead, most authority resides with the states (box 4-3).

BOX 4-2: Regulation of BBTs by Hawaii and Other States

Importation or interstate movement of biological control agents requires filing of APHIS's Application and Permit to Move Live Plant Pests and Noxious Weeds (PPQ form 526). Before APHIS issues a permit, state regulatory officials have the opportunity to review the APHIS recommendation. In addition, state officials may indicate special conditions of entry, containment, and release. In general, however, states lack resources to enforce additional requirements.

Seven states have statutes or regulations governing the entry, distribution or release of biological control organisms into or within their territories: California, Florida, Hawaii, Indiana, Nebraska, North Carolina, and Wisconsin. All of these states will accept PPQ form 526 in lieu of their own permit applications. Many of the specific state provisions are similar to those required by PPQ; California has explicit lists of biological control agents not subject to state permit requirements.

At least one state, Hawaii, imposes requirements more restrictive than federal APHIS regulations. Hawaii's special efforts to keep out certain species stem from that state's history of ecologically harmful introductions to its unique and vulnerable island ecosystems. Hawaii maintains lists of prohibited, restricted, and conditionally approved organisms.[a] Biological control agents not yet listed may be evaluated for host specificity and other characteristics in the state quarantine facility. Advisory subcommittees (on entomology, invertebrate and aquatic biota, land vertebrates, microorganisms, or plants) review applications for introduction of nondomestic animals and microorganisms for biological control and other purposes. The Advisory Committee on Plants and Animals holds bimonthly public meetings to decide whether to permit particular agents for biological control or other purposes.

Although Hawaii has instituted elaborate screening procedures, the state is unable to fully enforce its laws. The Alien Species Prevention and Enforcement Act[b] provides that USDA will inspect mail entering Hawaii from the mainland United States to prevent the entry of plant materials subject to U.S. quarantine laws. APHIS carries out inspections of incoming domestic mail for two hours each day; during the rest of the day, however, the mail just enters the state uninspected. Under the Fourth Amendment to the Constitution, APHIS can open first class mail only with a search warrant; to get one requires probable cause. If the inspectors feel or hear (by shaking the parcel) something that seems like plant material, they can use specially trained dogs to sniff it out. If the dogs react to something, that constitutes probable cause to obtain a search warrant.

The impetus behind the act was Hawaii's desire to keep out lizards, snakes, and other organisms from the mainland United States that could disrupt Hawaii's island ecosystem. Yet the act does not actually apply to these organisms, but only to those listed on U.S. quarantines for interstate commerce. The nonindigenous species of concern to Hawaii damage forests and other natural ecosystems, while U.S. quarantine lists focus on risks to agricultural crops. As a result, virtually none of the species of concern to Hawaii are included under the Alien Species legislation. APHIS lacks the legal authority to prevent the entry of these organisms.

(continued)

BOX 4-2: Regulation of BBTs by Hawaii and Other States (Cont'd.)

Hawaii's inability to enforce its inspection and quarantine laws illustrates a problem that is universal among the states: Although the laws are on the books, biological control agents may be shipped across the border illegally. Hawaii's situation underscores also the difficulties that any state might face in trying to enforce laws more restrictive than federal requirements for the importation and release of biological control agents.

[a] Chapter 4-71, Hawaii Administrative Rules.
[b] Public Law 102-393 (1992).

SOURCES: J. Levy, Operations Officer, Operational Support, Plant Protection and Quarantine, Animal and Plant Health Inspection Service, U.S. Department of Agriculture, Riverdale, MD, personal communication, April 5, 1995; W.W. Metterhouse, Cream Ridge, NJ, "The States' Roles in Biologically Based Technologies For Pest Control," unpublished contractor report prepared for the Office of Technology Assessment, U.S. Congress, Washington, DC, November 1994; "Plant and Non-Domestic Animal Quarantine" *Title 4, Subtitle 6, Chapter 71 (Non-Domestic Animal and Microorganism Import Rules), Hawaii Administrative Rules,* 1995; G. Takahashi, Maritime Supervisor, Plant Quarantine, Department of Agriculture, Hawaii, letter to the Office of Technology Assessment, U.S. Congress, Washington, DC, May, 26, 1995; 39 USCA Section 3015.

BOX 4-3: Oversight of Vertebrates as Biological Control Agents

A number of the most harmful past introductions for biological control have involved vertebrate animals. The small Indian mongoose (*Herpestes auropunctatus*), for example, is renowned for devastating ground-nesting bird populations, chickens, and lizard predators of insects when it was introduced to the West Indies, Puerto Rico, and Hawaii during the late 1800s. Its importation into the continental United States has been banned. Other vertebrate animals introduced for biological control in the past, including giant toads, ducks, geese, mynah birds, and water buffaloes, have likewise inflicted harm on native species, and many of these examples would probably not be repeated today.

Several species of fishes continue to be released regularly for biological control, with serious ecological impacts. The grass carp and common carp (*Ctenopharyngodon idella* and *Cyprinus carpio*) that have been introduced throughout the United States for weed control also destroy habitats for young fish and increase water turbidity. Introduction of mosquito fish (*Gambusia affinis*) not only results in the suppression of mosquitoes, but also has been associated with a decline in populations of certain native fishes.

The standards and mechanisms for regulation of vertebrate introductions differ markedly from those for arthropods and pathogens covered in most of this chapter. Under current law, the states retain almost unlimited power to make decisions about which vertebrate animals to import or release. Federal incursions in this area have been few and controversial. The state fish and game departments vary greatly in the rigor and comprehensiveness with which they regulate introductions of vertebrates.

A 1993 review of state laws and regulations revealed that although every state except Mississippi has laws governing fish releases, at least 15 states lack any legal standards for evaluating species prior to release. No state ties its releases to any scientifically based protocols, such as those produced by the American Fisheries Society and other organizations, in part because of the costs involved. A number of states, however, do specifically prohibit releases of grass carp, and many other states allow only releases of grass carp that have been sterilized to prevent their reproduction and spread. These provisions, of course, do not address the risks of the more than a half-dozen other fish species used for aquatic weed control in the United States.

SOURCES: Office of Technology Assessment, U.S. Congress, 1993; J.R. Coulson and R.S. Soper, "Protocols For the Introduction of Biological Control Agents in the U.S.," *Plant Protection and Quarantine, Volume III,* (R.P. Kahn, CRC Press, 1989); D. Simberloff and P. Stiling, Department of Biological Sciences, Florida State University, Tallahassee, FL and University of Southern Florida, Tampa, FL, "Biological Pest Control: Potential Hazards," unpublished contractor report prepared for the Office of Technology Assessment, U.S. Congress, Washington, DC, January 1994.

Animal and Plant Health Inspection Service

Past oversight of introduction of biological control agents by APHIS was unbalanced, incomplete, poorly documented, and difficult to understand for those seeking permits. The agency has taken some promising initiatives in recent years, however; these include increased attention to the environmental impacts of biological control agents of arthropod pests; an effort to consolidate the agency's multiple sources of jurisdiction; an attempt to centralize and make sense of the meager, vague, mixed-up records of past permitting decisions; the implementation of genus-level permitting; and an ongoing effort to adapt and clarify the permit system for environmental releases to better meet the requirements of the National Environmental Policy Act. APHIS staff deserve praise for these initiatives. Less successful, however, have been recent attempts to impose regulatory structure where none existed before (box 4-4). APHIS's proposed rule on the introduction of nonindigenous organisms attempted to screen out harmful organisms, but many people felt that the screen imposed was so fine-meshed as to be virtually impenetrable, thwarting the continued production, distribution, use, or research of biological control organisms.

Outside observers have commented that APHIS should not both regulate and promote biological control. It is difficult to know the significance of this dual role, although clearly it may lead to internal tensions and inconsistent missions within the agency (see chapter 5). The debate over the proposed rulemaking revealed some of these different perspectives. In 1992 the former APHIS Administrator asked the agency's National Biological Control Institute to examine the agency's authority in biological control, meet with interested parties, and propose guidelines for the importation, interstate movement, and release of biological control agents. The National Biological Control Institute developed protocols based on its two years of discussions with participants in the biological control community. Although, according to the APHIS Administrator's Office, this preliminary work was acknowledged in the rulemaking (216), it appears that few of the recommendations were actually incorporated into the final proposal. Following withdrawal of the proposed rule, APHIS formed a new task force that includes the National Biological Control Institute as a member.

Statutory Responsibilities

APHIS regulates the importation of biological control macroorganisms into the United States and their movement between states under the Federal Plant Pest Act[3] and the Plant Quarantine Act[4] (box 4-5) (360). Reliance on these plant pest statutes for jurisdiction often puts APHIS in the position of having to justify its intervention—or avoid action altogether—in matters of direct import to the use of biological control agents. Ongoing jurisdictional questions concern the granting of permits for *release* to the environment because the acts only cover the *movement* of agents; the control of "beneficial" organisms that are not generally considered "plant pests" or "noxious weeds" yet may indirectly cause harmful impacts; and the labeling and quality control of natural enemies. In addition, the statutes appear to suggest a zero-risk standard for introductions of biological control agents—a standard that is unrealistic and provides APHIS with little guidance.

Jurisdictional uncertainties arise also in the case of microbial pesticides based on nematodes. In accordance with the Federal Plant Pest Act, APHIS regulates the introduction and movement of nematodes in the United States. In light of APHIS's official role, EPA retains no jurisdiction over these products; the Federal Insecticide, Fungicide and Rodenticide Act authorizes the agency to exempt pest control products that are

[3] 7 U.S.C. §147a *et seq.* (1957).
[4] 7 U.S.C. §151 *et seq.*; 46 U.S.C. §103 *et seq*. (1967).

BOX 4-4: The Proposed APHIS Regulation for the Introduction of Nonindigenous Organisms

USDA's Animal and Plant Health Inspection Service (APHIS) currently grants permits for biological control agents under regulations that cover plant pests. Scientists and natural enemy companies have criticized APHIS's approach for years because it lumps "beneficial" natural enemies into the same category with agricultural pests. In 1992 the agency's Administrator instructed APHIS's National Biological Control Institute to meet with interested stakeholder groups to develop background information that would help in constructing a regulation more specific to biological control. But such a regulation never appeared.

Instead, in January 1995, APHIS published a much broader proposed rule that applied generally to nonindigenous species and superseded the agency's earlier development of a biological control rule. The proposed regulation was APHIS's attempt to address problems identified in the 1993 OTA assessment *Harmful Nonindigenous Species in the United States*. That report summarized the harmful economic and environmental impacts of organisms that enter the country or spread and then become agricultural pests, degrade parks and federal lands, or displace native species. The OTA report further specified that the piecemeal federal system for screening the importation or release of nonindigenous organisms contributed significantly to these continuing harmful impacts.

Unfortunately, APHIS's proposed rule did not do a good job of regulating both biological control (an area that is actively promoted by the agency and has little firm documentation of past harmful impacts) and other types of potentially harmful introductions. Furthermore, the agency's abandonment of its effort to write a regulation specifically addressing biological control aroused the ire of scientists and industry members who had participated in the earlier process. Such feelings were only compounded by the implied challenge in the rule to the deeply felt belief among many members of the biological control community that theirs is a benign practice with little if any potential for causing harmful environmental impacts.

Response to the nonindigenous organism regulation was swift and almost uniformly negative. Responses could be tracked by interested observers via an Internet listserver constructed solely for this purpose. A total of 252 responses came from biological control researchers, producers, practitioners, and distributors; university entomologists; farmers; weed control committees and districts; local, state and federal agencies; members of Congress; commercial laboratories; and industry associations. Most objected to how the regulation categorized biological control along with other potentially harmful introductions. Many also felt that the permit requirements would place unacceptable financial burdens and time constraints on the natural enemy industry, which already operates with a low profit margin.

Although most respondents expressed similar sentiments, they did not necessarily reflect an unbiased sampling of expert or public opinion. The vast majority were in some way affiliated with the practice of biological control, and the content of the regulation had been rapidly communicated throughout this group by way of several listservers and bulletin boards on the Internet. Jeffrey Lockwood, a scientist known for his concern about the potential ecological risks of biological control, was one of the few to express the opinion that the regulation was not strict enough. This view might have been better represented had other groups, such as conservation biologists, known about the regulation.

SOURCE: Office of Technology Assessment, U.S. Congress, 1995.

BOX 4-5: Pest Control Acts

- The **Federal Plant Pest Act of 1957** prohibits the movement of any plant pest from a foreign country into or through the United States without a permit from USDA. The definition of plant pest includes any living stage of "any insects, mites, nematodes, slugs, snails, protozoa, or other invertebrate animals, bacteria, fungi, other parasitic plants or reproductive parts thereof, viruses, or any organisms similar to or allied with any of the foregoing, or any infectious substances, which can directly or indirectly injure or cause disease or damage in any plants or parts thereof, or any processed, manufactured, or other products of plants." [7 U.S.C. §§150 aa *et seq*. (1957)].
- The **Plant Quarantine Act of 1912** bars the entry into the United States, without a permit, of any nursery stock—and under certain conditions, any other class of plants, fruits, vegetables, roots, bulbs, seeds, or other plant products—in order to prevent the introduction of any tree, plant, or fruit disease or any injurious insect not widely prevalent in the United States. The act also authorizes the Secretary of Agriculture to forbid importation of plants from particular areas and to quarantine any U.S. localities to prevent the spread of a dangerous plant disease or insect infestation. [7 U.S.C. §§151 *et seq*. (1967)].

SOURCE: Office of Technology Assessment, U.S. Congress, 1995.

adequately regulated by other federal agencies. Although APHIS claims to regulate these products, and indeed the agency has processed a few nematode applications over the years, in practice most of these products go unregulated. Major nematode production companies contacted by OTA said they neither apply for APHIS permits nor interact with the agency in any other way. Among the states, moreover, only Hawaii controls the entry of incoming nematode products, which are allowed into the state only under specific research permits for greenhouse trials. Hawaii is evaluating nematode products in light of the state's long history of ecological harm by nonindigenous species (209).

The lack of oversight concerning nematodes has had benefits as well as potential drawbacks. It has contributed to the nematode industry's success in getting products on the market, particularly in light of the very low profit margins. What limited information has been generated about these organisms suggests that they are relatively innocuous and unlikely to cause harmful environmental impacts. At the same time, however, the taxonomy of these organisms is poorly understood; some are ubiquitous in nature; and many have a relatively broad host range. It is unclear whether the advantages from regulating nematodes would outweigh the costs, but this matter deserves more explicit deliberation and resolution.

APHIS proposed the Plant Protection Act and the Animal Health Protection Act in 1990 and again in 1995 to consolidate the provisions from 28 statutes under two laws (144). Although they do not completely resolve the mismatch between statutory authority and regulatory needs, these bills take steps to clarify certain jurisdictional questions. Specifically, the recently proposed Plant Protection Act adds to the definition of "plant pest" vertebrate and invertebrate animals, biological control organisms, and undesirable plant species (358). This last term replaces "noxious weeds," liberalizing current noxious weed laws by enabling port inspectors to quarantine unlisted plants even if those plants are not new to or widely prevalent in the United States. The law does not define "biological control organism," but leaves this term to be decided at a later date by rulemaking with public input (144).

APHIS's Permit System

The Plant Protection and Quarantine (PPQ) division serves as APHIS's principal regulator of biological control agents. Through its permitting system, PPQ seeks to protect U.S. agriculture from the introduction and interstate dispersal of harmful plant pests. APHIS includes biological control agents among these regulated pests, a source of contention because arguably most beneficial natural enemies do not fit that characterization. Enforcement by PPQ takes place at major U.S. ports of entry, while permitting is carried out by APHIS headquarters in consultation with the states.

PPQ grants several thousand permits each year for introduction and interstate movement of pathogens, invertebrate animals, and weeds. Pinning down exact information about types and numbers of permits for biological control and level of technical review is difficult; in response to OTA's inquiry regarding numbers of applications evaluated by agency entomologists each year, for example, APHIS supplied figures ranging from eight to 2,500 applications. In truth, most of the applications are processed by clerical staff, but the inconsistency of information supplied to OTA illustrates APHIS's recordkeeping problems and raises questions about its sense of accountability.

It appears that most of the first-time ("unprecedented") applications are reviewed either by one of APHIS's two entomologists or by the agency's plant pathologist. Each year these scientists evaluate about 10 (and sometimes as many as 20) applications for phytophagous (plant-eating) biological control organisms and a roughly comparable number for entomophagous (insect-eating) agents. Numbers of unprecedented applications appear higher in 1995 than in some of the previous years (143). Each application is usually reviewed by one scientist, who consults occasionally with colleagues when questions arise.

PPQ has no process by which to expedite the permitting of unprecedented, taxonomically promising species over those that may carry heightened capacity for ecological harm (such as organisms that attack a wide range of nontarget plants and animals). Rather, APHIS categorizes applications in accordance with the purpose of the introduction (movement or release), the purity of the organism, and, eventually, the outcome of the environmental assessment. Data requirements vary depending on whether the organism is to be imported from another country into quarantine, moved between containment facilities, or released to the environment (box 4-6). APHIS plans soon to address some of OTA's concerns about setting priorities; in particular, the agency is posting on the World Wide Web and APHIS gopher a list of arthropods commonly used for biological control of pest arthropods for which permits will be expedited (360).

Unprecedented releases of biological control organisms require the preparation of an environmental assessment. As part of this process, APHIS's Biological Assessment and Taxonomic Support (BATS) division is required to determine whether the candidate control agent "may affect" endangered or threatened species. Sometimes BATS contacts FWS, although some observers suggest that communication and coordination between the two agencies is not always adequate.

Some researchers have complained that issues regarding endangered and threatened species do not enter early enough into the decisionmaking process. When they were about to release their test organisms, researchers at the University of California had their APHIS permits challenged by local FWS field officers, leading to long, costly and counterproductive delays (24). Another example involved APHIS's evaluation of permits for five types of insects to be used for the control of purple loosestrife (two beetles to eat the flowers, two to eat the leaves, and one root weevil). APHIS approached FWS concerning three of these agents in June 1995, just two weeks before the intended release date. APHIS was completing the final stages of its assessment, and the beetles were unlikely to survive much longer, putting FWS in the difficult position of having to confirm, on very short notice, the introduction of biological control agents against a

BOX 4-6: Categories of Pest Organisms

APHIS divides permit applications into categories as follows:

- **A**—Foreign plant pests new to or not widely distributed in the United States; domestic plant pests of limited U.S. distribution, including program pests; state regulated pests; and exotic strains of domestic pests;
- **B**—Biological control agents and pollinators;

  B(1)—High risk: weed antagonists; shipments accompanied by prohibited plant material or Category A pests;

  B(2)—Low risk: pure cultures of known beneficial organisms; and
- **C**—Domestic pests that have attained their ecological range, nonpest organisms and other organisms for which courtesy permits may be issued.

All biologically-based pest control agents fall under category B, biological control agents and pollinators. APHIS has yet to examine the environmental impacts of organisms in subcategory B(1). Some of the B(1) organisms may include hyperparasites or other impurities; they may come from a particular strain never before introduced or from a new field site. Those organisms designated in subcategory B(2) are pure cultures that have been cleared for release to the environment; most of these have undergone some form of environmental assessment or administrative determination. Some were previously imported into quarantine as subcategory B(1) organisms.

SOURCES: D. Knott, Plant Protection and Quarantine, Animal and Plant Health Inspection Service, U.S. Department of Agriculture, Riverdale, MD, personal communication, May 4, 1995 and August 2, 1995; M. Royer, Biological Assessment and Taxonomic Support, Animal and Plant Health Inspection Service, U.S. Department of Agriculture, Riverdale, MD, personal communication, April 20, 1995; U.S. Department of Agriculture, Animal and Plant Health Inspection Service, *Safeguard Guidelines For Containment of Plant Pests Under Permit,* June 1993.

high-priority pest of natural areas. FWS scientists had many concerns, including possible effects on endangered or threatened nontarget species; the beetles' lack of native natural enemies, and the fact that, once released, the beetles would not be readily controllable. In July 1995, FWS acceded to the release of the beetles. APHIS's handling of these situations, however, raises questions about the timely incorporation of threatened and endangered species issues into the permitting process and the adequacy of coordination with FWS.

According to members of the natural enemy industry, much of the permitting process involves redundancy, delay, and unnecessary paperwork at both state and federal levels. Many of the permit applications are precedented, which means they concern the same biological control organism that was granted a permit previously, coming from the same state or country of origin, imported under the same conditions, and based on the same permit conditions and facilities. Often these repeated releases have been taking place for 10 or 20 years. According to the Association of Natural Bio-control Producers, a distributor selling 20 different products to customers in 40 states would need 800 permits which would have to be reviewed every two years (11). APHIS has somewhat simplified the approval process for pure cultures of precedented organisms, but further streamlining or permit waivers may be warranted.

Rather than waste time and resources renewing old permits, critics contend that APHIS needs a tiered, risk-based system with built-in waivers for repeated biological control releases, so that the agency can concentrate on the more high risk agents. Greater scrutiny may also be called for when the previous release has not become self-sustaining and was cleared before the agency instituted its data requirements (299).

In response to such criticism of its permit process, APHIS says that the agency has many innovations under development. These include new instruction sheets for preparing permit applications and environmental assessments, a customer satisfaction questionnaire, guidelines for containment facilities, optional electronic submission of application data, and plans to formulate categories of organisms excluded from permitting. APHIS hopes to offer some of these materials on the Internet, and eventually to adopt a computerized system, enabling customers to track the progress of their permit applications (360). These changes might address some of the problems identified by OTA. APHIS should be commended on these planned initiatives and encouraged to follow through with these improvements.

APHIS's Data Review

APHIS began doing rudimentary environmental assessments on biological control applications in 1970, upon passage of the National Environmental Policy Act. These early "administrative determinations" were often poorly documented and based on incomplete information. The system continued in place throughout the 1980s.

The new leaders at APHIS in the early 1990s inherited an arbitrary and nontransparent permitting system. In 1991 they revised the outline for prerelease environmental assessments. The new form requested much more extensive data including host specificity, hyperparasites, threatened native species, and effects on natural enemies. In 1993, APHIS again rewrote its requirements for environmental releases. This so-called "NIDR" format, which continues in use today, asks for a detailed description of the proposed action, biology of the target (host) organism and of the organism to be released (including both field and laboratory host range), status in North America, and expected environmental and human health impacts (359). While adding to the data requirements, PPQ has tried to streamline its permitting process in other ways, for example, by granting genus-level permits for *Aphytis* (September 1994), *Encarsia* (February 1995) and *Eretmocerus* (April 1995).

APHIS's review of applications for insect-feeding (entomophagous) biological control organisms has been particularly lax; APHIS had virtually no data requirements for such agents until 1991. Even today, the agency is struggling to develop scientific protocols for testing host specificity and other characteristics of the entomophagous agents. APHIS's environmental assessment for *Scelio parvicornis*, in April 1994, was considered a milestone in denying a permit for an entomophagous agent (299).

Technical Advisory Group

APHIS has a Technical Advisory Group on the Introduction of Biological Control Agents of Weeds (TAG) but lacks a similar body for biological control of insects. This independent voluntary committee was formed in 1957 primarily to provide advice to researchers. Today, TAG reviews applications for biological control of weeds and advises PPQ on whether to grant permission for quarantine or release.

Chaired by a member of the U.S. Army Corps of Engineers, TAG has up to 16 members, half of them from USDA and the U.S. Department of Interior (box 4-7). Usually TAG convenes without complete participation; only about five to nine representatives consistently participate in TAG recommendations (360,51,299). No particular number constitutes a quorum. Although foreigners are barred from voting, the Canadian reviewers participate actively, and there is interest in making them voting members (51). According to APHIS representatives, however, the Federal Advisory Committee Act[5] prohibits voting membership by nonfederal members on federal advisory committees like TAG. In fact, federal advisory committees *can* have nonfederal members so long as they follow the Act's procedural requirements, such as announcement of meetings in the *Federal Register* and formal

[5] Federal Advisory Committee Act, title 5, U.S.C.A., appendix 2, subsections 1-15 (1972), as amended.

BOX 4-7: Technical Advisory Group on the Introduction of Biological Control Agents of Weeds

Membership of TAG Committee

U.S. Army Corps of Engineers, Chair

U.S. Department of Agriculture:

- Animal and Plant Health Inspection Service
- Agricultural Research Service
- Cooperative State Research, Education and Extension Service
- Forest Service

U.S. Department of Interior:

- Bureau of Land Management
- Bureau of Reclamation
- Fish and Wildlife Service
- National Park Service

U.S. Environmental Protection Agency

Weed Science Society of America

National Plant Board

Members-at-Large

- Canada (nonvoting)
- Mexico (nonvoting)

Executive Secretary: (APHIS/PPQ employee)

Reviews by TAG

From 1987 through 1994, TAG reviewed 86 petitions for release or quarantine of organisms. Annual tallies varied from a high of 19 in 1989 to a low of seven in 1993. There were 71 different agents (some went through TAG as applications for quarantine and again for release) petitioned on 28 target plant species, mostly rangeland weeds. Four of the targets, leafy spurge (*Euphorbia escula*), diffuse knapweed (*Centaurea diffusa*), spotted knapweed, and yellow starthistle (*Centaurea solstitialis*), accounted for 43 percent of these petitions. Some 77 percent of the petitions received favorable recommendations from TAG.

SOURCE: A. Cofrancesco, U.S. Army Corps of Engineers, Vicksburg, MS, letter to the Office of Technology Assessment, U.S. Congress, Washington, DC, May 12, 1995; U.S. Department of Agriculture, Animal and Plant Health Inspection Service, "Charter for the Technical Advisory Group on the Introduction of Biological Control Agents of Weeds," unpublished draft guidelines, 1990.

recording of meeting minutes. Thus, any decision to restrict TAG membership to federal agencies should carefully weigh the desirability of broader representation against whatever costs these procedural requirements impose.

When PPQ receives petitions for the biological control of weeds, it sends them to the TAG secretary, who distributes them to the TAG representatives for comment. TAG reviews often take about three to four months because of scheduling difficulties of the TAG representatives. TAG conducts most of its business by mail; an annual meeting provides a forum to resolve controversial issues and to meet with weed control researchers. TAG is funded by member agencies, with APHIS paying only for the nongovernmental participation (51).

Although TAG is set up in an informal advisory capacity, in practice PPQ virtually always follows TAG's recommendations. Formally, PPQ makes the final decision, however, as is required by the Federal Advisory Committee Act. TAG reviews only about 10 petitions annually (50). Apparently this represents all of the

unprecedented petitions received by APHIS each year for biological control of weeds. Pre-quarantine review is less stringent than that for release but enables TAG to advise and monitor biological control activities in the early stages of development rather than first confronting petitioners years into their research (51). Pre-quarantine review is done only if requested by a researcher (366).

Despite the fact that the representatives often consult with outside sources (51), critics charge that TAG lacks scientific expertise, particularly in plant taxonomy, pathology, ecology and evolution (58). Another complaint is that, as strong proponents of biological control technologies, TAG members traditionally have disregarded some of the negative repercussions of biological control introductions. For example, TAG review may not always screen against harmful impacts on abundant species of native plants.

Although PPQ follows the TAG recommendations, TAG does not use the exact data requirements developed by PPQ. Nevertheless, PPQ generally accepts the TAG decision in lieu of its own data requirements (299). In the early 1980s TAG informally issued to researchers its own internal guidelines, which differed from the PPQ requirements in some important ways. TAG asked petitioners to submit, for example, "dollar figures concerning crop or other losses caused by the weed and costs of its control, versus, if applicable, dollar figures concerning its beneficial qualities" (177), something never required by PPQ. TAG no longer requests such information from petitioners. Nonetheless, researchers commonly submit economic data, which is then considered by TAG in its deliberations (51).

TAG has discontinued its use of published data requirements. Instead, the group has loose guidelines indicating its main areas of review:

- taxonomy of the target weed;
- test plant list;
- host-range testing and impact on nontargets;
- taxonomy of the agent;
- biology of the agent; and
- other issues raised by the researchers.

These guidelines and other information about TAG are not available to researchers in printed form, although experts in the biological control of weeds generally know what TAG expects. A more formal review document could help researchers gauge where to focus their attention and resources. TAG recognizes this problem and is awaiting the development of a final rule by PPQ. At that time TAG will review the incoming PPQ applications for biological control of weeds.

Proposed Rule

As mentioned earlier, APHIS's proposed rule on the introduction of nonindigenous organisms encountered widespread criticism and eventually was withdrawn. Although biological control practitioners considered the proposal heavy-handed, conservation biologists applauded certain of its provisions.

Compared with current protocols, the proposed rule paid more explicit attention to genetic variation in the control organism, recognizing that different genotypes may require independent assessment of their potential for ecological harm. Rather than focusing solely on weeds, the proposal called for the careful appraisal of biological control agents of arthropod pests. In addition, it recognized that there are potential hazards from movement of control organisms between different biogeographic regions of the United States. Finally, the proposal acknowledged that a control agent can harm a nontarget organism not only by eating or parasitizing it, but also by interacting via intermediate organisms (219).

Although many of the data elements in the proposal have been required on a more informal basis since 1991, the proposal extended the agency's regulatory control in a number of realms. Its broad definition of *nonindigenous organism* included any organism proposed for introduction into an area of the United States beyond its established range. Its list of species subject to the rule included organisms which have long been in widespread use as biological control agents throughout the United States.

The proposed rule combined an odd mix of management approaches. On one extreme was

the micromanagement of such features as the thickness of plastic bags (0.1270 millimeters) for seeds, the particular taxonomic groups listed to be regulated, and specifications for the submission of samples to three museums. Other provisions, however, suggested a much looser, more fluid approach to APHIS's regulatory oversight responsibilities; examples are the lack of clear standards on purity; the lack of specific protocols for host-specificity testing, and the absence of any reference to pre- and postrelease monitoring of nontarget effects.

That the proposed regulation failed to incorporate any provisions for postrelease monitoring, even for higher risk releases, suggests a possible reluctance by APHIS to confront the impacts of its permitting activities. Over time, without any monitoring, standards for successive applications cannot benefit from knowledge gained about the impact of prior releases (235). Until now PPQ did not even maintain in a usable form the basic records and databases on past releases. The PPQ form 526 database was unable to locate precedented permitting decisions except by the applicant's name (299). The computerized NIDR system instituted in early 1994 for environmental assessment data was redesigned in summer 1995 to enable PPQ to locate precedented permitting decisions by organism (360).

Environmental Protection Agency

In the early 1980s EPA developed special data requirements for biologically based products, but not until fall 1994 did the agency separate out its regulatory review of microbial pesticides and biochemicals from that for conventional chemical pesticides.

Today the regulated community generally gives EPA high marks for its actions on the registration of microbial pesticides and pheromones. The new Biopesticides and Pollution Prevention Division (BPPD) has consolidated the agency's BBT-related activities, streamlined the data requirements, and provided registrants with faster, less costly, more accommodating registration services. Critics charge, however, that the agency is waiving too many environmental data requirements and should pay closer attention to the effects on ecosystems and on insects and other nontarget organisms. EPA's protocols for host-specificity testing, moreover, focus almost entirely on commercial species such as agricultural crops and honeybees, with little regard for native organisms. Finally, a major challenge lies ahead for the agency as genetically engineered microbial pesticides raise unprecedented risk considerations that may require different regulatory approaches.

Statutory Responsibilities

Although EPA oversees the use of pesticides marketed in the United States, the agency has exempted from its jurisdiction all BBTs except those derived from microbes used in pesticide formulations (e.g., bacteria, algae, fungi, viruses, and protozoans) or biochemicals (including pheromones). A further exemption covers pheromones used in traps. BBTs remaining within EPA's jurisdiction are shown in table 4-2.

This arrangement derives from section 25(b) of the Federal Insecticide, Fungicide and Rodenticide Act, which authorizes EPA to exempt pesticides that are adequately regulated by other federal agencies or are of a character not requiring regulation under FIFRA[6]. Detailed testing protocols to accompany the regulatory requirements listed in 40 CFR Part 158 have been spelled out by EPA in its nonregulatory Pesticide Testing Guidelines, Subdivision M (393,394).[7]

[6] In 40 CFR Part 152, Subpart B, EPA exempts all BBTs except eucaryotic and procaryotic microorganisms (cellular organisms with and without a distinct nucleus, respectively) and viruses.

[7] Biologically based pesticides are also regulated under the food additive provisions of the Federal Food, Drug and Cosmetic Act (FFDCA). Section 402 designates as adulterated any food or feed that contains residues of any pest control agent unless such residue is covered by a tolerance under sections 408 or 409 or an exemption from tolerance. To date, however, all microbial pesticides and most biochemical pesticides registered for use on food crops have been exempted from the requirement of a tolerance (223).

TABLE 4-2: Categories Regulated by EPA

Microbial pesticides
Natural and engineered:
■ Algae[a]
■ Bacteria[a]
■ Fungi[a]
■ Protozoans[a]
■ Viruses[a]
Biochemical products
■ Enzymes
■ Hormones
■ Natural plant and insect regulators
■ Semiochemicals (including pheromones)[a]

[a] These categories are included in OTA's scope of BBTs.

SOURCE: Office of Technology Assessment, U.S. Congress, 1995.

Biopesticides and Pollution Prevention Division

Within EPA's Office of Pesticide Programs, BPPD coordinates the registration, development, and promotion of biologically based pesticides. Formed in November 1994, BPPD aims to expedite the registration process for microbial and biochemical pest control products, serve as an advocate for the use of safer pesticides, and facilitate cooperative programs with state and federal agencies, universities, and agricultural groups. In creating BPPD, EPA brought together from other divisions scientists experienced with the evaluation and registration of biologically based products. BPPD has established two multidisciplinary teams whose staffs work together in a shared office and are authorized to skip some of the many bureaucratic steps that normally add weeks to the registration process of pest control products (402).

Although BPPD was created as a one-year pilot division, the White House recently approved EPA's decision to make BPPD a permanent division. The division is serving as the model for the restructuring of the Office of Pesticide Programs as a whole. It illustrates the advantages of bringing together into a single group those responsible for the multiple scientific and regulatory steps in the registration process. By speeding the availability of pesticide alternatives, BPPD could play a key role in the Clinton Administration's current initiative to expand use of integrated pest management and reduce reliance on conventional pesticides.

As of April 27, 1995, EPA had registered 43 biochemicals (mostly pheromones) and 45 microbial pesticides (more than half of them bacteria). Seven of these were registered by BPPD in its first six months of operation, and the others by the Office of Pesticide Programs in present and past years. According to BPPD, its turnaround time for registering pheromones and other biochemicals is 30 to 50 percent less than the time required by other EPA divisions for equivalent processing (47). Whether the registration of microbial pesticides will be similarly expedited remains unclear. In general the registration of microbial pesticides is much faster than that of chemicals because of substantially different data requirements and frequent use of data waivers.

Like the new administrators in APHIS's PPQ division, EPA's BPPD staff have inherited a difficult recordkeeping task. EPA's prior decisions are scattered among multiple offices in a variety of formats. At the same time, only rarely does EPA require pre- and postrelease monitoring of effects on nontarget organisms (305). This failure to evaluate impacts, combined with the challenge of consistent recordkeeping, suggests that the agency may not adequately build on past decisions and learn from prior mistakes. This shortcoming will become increasingly important as the number of BBT products submitted for registration grows. Rather than require that registrants take affirmative steps to evaluate impacts, EPA relies on FIFRA section 6(a)(2), which states that if pesticide registrants come across information on unreasonable adverse effects, they must submit that information to EPA. This directive may sometimes prove counterproductive: Legally bound to notify EPA of negative results, producers may be disinclined to thoroughly investigate risks from registered products.

Registration Requirements

BPPD is working to revise and update EPA's data requirements for microbial pesticides and biochemicals. The agency first developed its pesticide testing guidelines for "biorational" pesticides in 1982; those guidelines were rewritten for the microbial products in 1989. Guidelines for the biochemicals remain outdated and not in keeping with current EPA practices.

Producers of microbial pesticides and pheromones contend that compliance with the full product testing requirements can be prohibitively expensive. Although costs of testing are much lower than those for chemical pesticides, the revenue generated by BBTs is much smaller as well. BPPD waives many tests, however, and sometimes some of its fees. To fully test and register a BBT today costs between several hundred dollars and a half-million dollars. EPA's annual maintenance fees are $700 for the first product and $1,400 for subsequent products; the maximum limits or "caps" on the total annual maintenance fees payable by any registrant are usually between $55,000 and $95,000 (less for small businesses) (404). Tolerance fees for food-use BBTs generally range from $20,000 to $25,000, most of which is refunded if EPA grants an exemption (274).

BPPD has been seriously investigating the possibility of waiving both the maintenance and the tolerance fees for microbial pesticides and pheromones. The laws currently allow EPA to reduce or waive these fees for minor crop registrations where the fee is likely to significantly affect the availability of the pesticide. EPA hopes that the elimination of fees for BBT registration will spark an increase in applications (274).

BPPD calls for a customized data package for each active ingredient registered, based on a multi-tier system of data requirements; in contrast, a full set of data are usually required for conventional pesticides (217). EPA requires approval also for all large-scale field tests (more than 10 acres, or 250 acres for certain pheromones) of BBTs. In addition, the agency requires notification before small-scale field testing of genetically engineered organisms.

EPA requires registrants to submit data on efficacy for pesticide products used to control pests that threaten the public health (e.g., disease-carrying mosquitoes). The agency retains authority to order additional data where necessary. Some of the data are only conditionally required; others are waived in specific circumstances. For example, the use of microbial products in packinghouses and other indoor spaces commonly triggers an exemption to the nontarget testing requirements because no outdoor exposure is expected (224).

Pheromones and other biochemicals

EPA is about to publish in the *Federal Register* new exemptions for pheromone products. All straight-chained lepidopteran pheromones, regardless of application mode, are now exempt from the requirement of a tolerance and may undergo field testing on up to 250 acres without an experimental use permit. Past testing on small field plots has been extremely difficult because of the high volatility and specificity of the pheromones. This measure allows for testing of broadcast and sprayable applications of pheromone products over a wide area. Similar regulatory relief measures were provided earlier for all arthropod pheromones in polymeric dispensers (274).

Registrants of pheromones and other biochemicals must submit data on product identity, analysis, and manufacture; chemical residues; toxicology, and impacts on nontarget organisms (389). Often EPA waives most of these requirements. As in the case of microbial products, the toxicology and nontarget organism data are tiered; if the initial testing yields significant adverse effects, additional data points are added (218). Testing only rarely moves to subsequent tiers (305). Moreover, in light of the low toxicity and minimal expected human exposure to pheromone products, EPA, in 1986, waived certain requirements for mammalian toxicology studies on pheromones (218).

Microbial pesticides

Testing for microbial products covers the same general areas: product analysis, toxicology, residue analysis on food crops, and ecological effects. In calculating experimental dosage, registrants must take into account that environmental levels of the microbial agent and associated toxins often increase after application, at least temporarily—unlike environmental levels of chemical pesticides, which decrease over time (394). Toxicology data are set forth in three tiers, but EPA has never required data beyond the first tier (217), which involves short-term tests for toxicity, infectivity, and pathogenicity. Ecological effects testing is tiered as well, with the first tier consisting of maximum-dose, single-species hazard testing on nontarget organisms (394). For genetically engineered microbes, similar data are required on both the complete microbial product and the inserted DNA construct (224).

Environmental Effects

EPA's principles for review of microbial pesticides emphasize the importance of selecting susceptible, nontarget species (including insects, plants, wildlife) when testing for host specificity (394). In its actual testing protocols, however, the agency points to the specific organisms to be tested, chosen by EPA in part for their sensitivity to the test products (304) but mainly for their economic importance, commercial availability, laboratory experience with the organisms, and the fact that researchers "know how to run a good experiment" with them (223,305,394). This approach contrasts with the more unstructured approach employed by APHIS in its host-specificity requirements. Although EPA officials emphasize the flexibility of their system and the ease with which data requirements may be added or subtracted, the extra effort needed to design customized lists of nontarget species and to develop new testing methods for these organisms may well take a back seat to other agency priorities.

EPA focuses heavily on the effects on nontarget agricultural crops, an approach developed with APHIS for the 1982 Subdivision M report.[8] The agency rationalizes that cultivated crops are uniquely vulnerable because they are monocultures, nonmobile (unlike birds and insects), and commonly nonindigenous. Although such thinking may have been fashionable 14 years ago, the potential harmful impacts on nontarget insects and other organisms have since come to be appreciated. Moreover, declines in native natural enemies ultimately may affect agricultural plants by enabling pest populations to grow.

A related concern focuses on the lack of ecosystem testing for microbial and biochemical products. EPA relies primarily on observed impacts (such as unusual persistence in host organs) following administration to the isolated test organism of massive quantities (the "maximum hazard dosage level") of the pest control agent. Such focused testing protocols have procedural advantages, but they overlook the complexity of natural systems and the possibility for harmful ecological repercussions beyond those immediately apparent from short-term laboratory testing on isolated specimens. EPA is spending $1,224,000 in fiscal year 1995 researching ecosystem approaches for testing effects of biochemicals and microbial pesticides.

Genetically Engineered Products

BPPD deals with genetically engineered microbial pesticides on a case-by-case basis. Agency review resembles in most respects that for other microbial products but places increased attention on exposure and effects on nontarget species (305).

[8] Pesticide Assessment Guidelines, Subdivision M: Biorational Pesticides (1982) (393). This document provides guidance on developing data on biochemical and microbial pest control agents. Many of the provisions are obsolete. EPA has rewritten subdivision M only for microbial pesticides (1989) (394).

Recent developments

The first field testing of genetically engineered products took place a decade ago with release of the "ice minus" variant of the bacterium *Pseudomonas syringae*, designed to prevent frost damage on potatoes and strawberries (234).

To date, EPA has registered two types of genetically engineered microbial products, one involving Bt genes inserted into Bt, and the other involving Bt placed in a killed bacterium (305). Raven, registered in January 1995, is a strain of *Bacillus thuringiensis* kurstaki into which the Ecogen Company has incorporated genes of another Bt strain. With respect to environmental implications, EPA views the product as an insignificant departure from standard Bt products, and hopes in the future to exempt from notification requirements similar Bt products with inserted Bt genes. The other products, registered in 1991, use Bt in killed *Pseudomonas fluorescens*. The Mycogen Corporation killed the *Pseudomonas*, which can survive in a wide range of conditions, to prevent it from spreading the Bt genes to new locations. The killed bacterium protects from ultraviolet radiation the encapsulated Bt toxin, allowing for longer field persistence (239). EPA's main concern is to ensure that all the bacteria are dead; the agency requires the monitoring of every batch produced (305).

Other genetically engineered products are undergoing testing. For example, the agency recently approved the field testing of a genetically engineered baculovirus containing an inserted scorpion toxin gene that facilitates a faster kill rate. The scorpion toxin used is only a fraction of the full toxin and does not affect mammals. It may affect some Lepidoptera and other insects.

Notification requirements

EPA's final rule for field testing of genetically engineered microbial agents, published in September 1994, amends 40 CFR Part 172 to require notification of EPA, and preliminary data submission, prior to small-scale environmental testing of microbial agents modified through recombinant DNA technology. The rule applies also to nonindigenous microbial pesticides not acted on by USDA (390).

Some scientists criticize the rule for targeting genetic modification techniques rather than high-risk organisms or outcomes. They argue that the new molecular techniques that manipulate DNA and transfer genes are potentially even safer and more precise and predictable than their traditional counterparts. This view ignores the fact that many efforts to genetically engineer microbial pesticides have thus far focused on expanding target range, altering kill level and rate, and prolonging field persistence—characteristics that could affect environmental impacts in important ways. The critics also say that EPA should worry instead about agents manipulated by other means, such as chemical or radiation mutagenesis, transduction, transformation, or conjugation, which pose greater environmental risks and could pollute waterways (234).

Other scientists counter that gene-splicing techniques are a valid trigger for EPA review; elevated risks stem from the introduction of new living forms that have never had an opportunity to evolve any checks and balances in nature. Scientists' understanding of microbial communities and of the full import of particular species in the functioning of ecosystems is limited. Consequently, genetically engineered microbial pesticides may have wide-ranging consequences that may be difficult to evaluate (172).

Whatever the outcome of this debate, a prudent response by EPA requires scrutiny and flexibility, given the types of characteristics being engineered into microbial products and the paucity of information on potential environmental effects.

Resistance

One of the most significant challenges facing BPPD is the prevention of resistance to Bt. Some scientists believe that large-scale squandering of this microbial pesticide may result from the widespread use of crops engineered to contain the genes for Bt toxin. The use of these transgenic plants is expected to create tremendous selection pressure among lepidopteran and other

pest species, resulting in the rapid development of resistance to Bt. The susceptibility of Bt to resistance has already been documented, with early evidence emerging from certain regions of New York, Florida, and Asia. Potential loss of microbial Bt products poses a serious threat to agriculture in locations where pests have evolved resistance to chemical controls. In parts of Mexico, for example, Bt products are among the only options left against the tomato pinworm; the pest has become resistant to other pesticides (40). Campbell and other growers in that region rely on the availability of effective Bt-based pesticides.

Although EPA is working with manufacturers to develop strategies to manage resistance, it is unclear that any of these ad hoc attempts will actually work. Clearly, resistance has not been successfully prevented in the case of chemical pesticides (see chapter 2); EPA has no real track record in this arena (156). Some scientists argue that the effective management of resistance to Bt will require the concerted efforts of multiple parties. A recent article in *Science*, for example, urges development of a national research agenda, with full cooperation of industries, universities, and government, to develop and implement resistance management strategies for conventionally applied and transgenic Bt toxins (221).

To date, EPA has registered only transgenic potato (May 1995) and field corn (August 1995), although other crops genetically engineered for pesticidal properties are coming through the research and registration pipeline (182,156). As part of the registration process for these products, EPA has developed cooperative agreements with producers dealing with tactics to manage resistance (156,214).

Exactly how Monsanto will prevent the development of resistance to Bt from its potato product remains unclear; thus far, the company's resistance management strategy includes few clearly defined elements (402). In some respects, however, EPA views the Bt potato resistance management activities as a test case: Inasmuch as Bt is only partially effective against the Colorado potato beetle, loss of the microbial pesticide against this pest, hastened by its use in transgenic crops, will not create a major new gap in the pest control arsenal. Because the beetle has already developed resistance to many chemical pesticides, however, it is important to try to prolong the effectiveness of every control method available.

Resistance management for Bt field corn—and eventually for transgenic sweet corn and cotton plants—will present greater challenges for EPA. The pests that feed on cotton and sweet corn, and to a lesser extent on field corn, attack a number of vegetable crops and ornamental plants as well (404). Therefore, pest resistance induced by large-scale use of Bt in transgenic cultivars of these crops may make ineffectual the use of Bt-based pesticides against pests that attack not only corn and cotton but also a range of other crops (156).

The resistance management plan for Bt field corn includes: a Bt dosage meant to be high enough to kill all susceptible pests; annual monitoring for development of resistance; farmer education programs; and, once use of Bt corn becomes widespread in three to five years, the required planting of non-Bt corn as a certain percentage of acreage on each farm that uses Bt corn. The effectiveness of these approaches remains uncertain. EPA's agreement requires the Mycogen and Ciba-Geigy corporations to carry out research on many related issues; their resistance management strategies are likely to change as new evidence emerges (404).

Food and Drug Administration

U.S. Food and Drug Administration (FDA), a relative newcomer to the regulation of BBTs, has yet to identify exactly what roles it will play. The agency may face increasing responsibilities in the future, however, as BBTs become more prominent in food-related industries and postharvest uses.

FDA has authority to regulate the BBT uses that are not subject to EPA or USDA jurisdiction. To date, however, the agency has chosen only to advise state and local health officials; to enforce

grading standards for natural enemy and other insect fragments in stored grain; and to contemplate possible oversight of the use of BBTs, specifically, insects and nematodes in food service establishments and other food-handling institutions.

FDA could assume a greater role if it desired. It would need to designate EPA-exempted BBTs (i.e., natural enemies) as food additives in cases when the BBTs could become a component of stored or prepared food and USDA lacks regulatory jurisdiction. FDA could then establish and enforce tolerances for BBTs under section 409 of the Federal Food, Drug and Cosmetic Act (FFDCA). Although authorized to develop standards for BBTs (195), however, FDA would prefer to remain responsible only for enforcement of the BBT-related regulations set by EPA.

Two recent controversies may help elucidate FDA's current and future roles in regulating BBTs.

Postharvest Grain Storage

Until 1993, FDA, EPA, and USDA struggled to resolve the question of which agency had statutory jurisdiction over BBTs used for postharvest grain storage (195). Previously, EPA had prohibited such BBT use. Following extensive interagency discussion, FDA was chosen to shoulder the responsibilities.

FDA has determined that nematodes and predatory and parasitic insects released into grain storage areas for pest control purposes are unlikely to become a component of food. Therefore FDA, in conjunction with USDA's Federal Grain Inspection Service, will continue grading grain according to the existing standards for whole insects, fragments, parts and other residues, without special requirements for BBTs (1).

In setting these maximum allowable levels, commonly referred to as defect action levels (DALs), FDA recognizes that some foods will contain insects and insect parts at low levels that are not hazardous to the consumer. FDA designates as adulterated, however, those products found to exceed the DAL for insect fragments. Adulterated products are seized by FDA and, if they cannot be cleaned by further processing, destroyed.

Food Service Areas

The release of parasitic and predatory insects and nematodes into food service establishments and food-handling institutions has also created confusion over statutory jurisdiction. Unlike the controversy surrounding postharvest grain storage, this issue has been only partly resolved despite extensive discussions among USDA, EPA, FDA, and members of Congress.

After 11 months of indecision, the agencies decided that neither EPA nor USDA would regulate BBTs when used in food preparation areas. The task of how or whether to regulate BBTs for these uses has been left to FDA. FDA, however, has no formal policy or procedure to date (147) and has not assumed responsibility for conditions in restaurants and other institutions with food preparation areas (195). FDA restricts its activities to the manufacturing side of food products and leaves food preparation areas to state and local health officials. The agency issues recommendations, for the sake of uniformity, which the local and state offices can independently choose to adopt. On the assumption that introduced insects might find their way into food, putting the consumer at risk, FDA has recommended against the use of insects and nematodes as a pest control practice in food preparation areas (195).

The agency is now considering whether to regulate these insects and nematodes as food additives under section 409 of the FFDCA or to leave the decisions up to state health departments. Under section 409 (104) any substance must be an approved food additive or generally recognized as safe (GRAS) for its intended use, if its intended use results in its becoming a component of food. FDA does not consider these insects to be GRAS for their intended use and therefore has the authority to regulate them as food additives (148). It may decide to do so if data show that the insects may become a component of food.

FDA is currently reviewing its position and is willing to receive and review any valid data showing that there is no reasonable expectation that the insects will become a component of the food (147). It is unclear what further action the agency will take. In all probability, FDA will not assume a greater role unless forced to do so, enabling state or local health officials to make their own decisions (box 4-8).

BOX 4-8: Chronology of the Praxis Company's Experience with FDA

For two years, Praxis Integrated Biological Cybernetics, a small company in Allegan, Michigan, has been corresponding with local, state, and federal officials in hopes of obtaining permission to resume its use of parasitic wasps and nematodes for cockroach control in food service areas (restaurants, schools, nursing homes). Despite congressional intervention on behalf of Praxis, an agreeable solution has come only with considerable difficulty, years of delay, and great expense to the company.

In 1993, a Detroit bakery solicited Praxis's help in controlling cockroaches. Uncertain about regulatory requirements, the bakery contacted the Michigan Department of Public Health. Knowing little about these natural enemy products but concerned about their potential effects, the department director prohibited Praxis from any further releases of wasps and nematodes as of October 1993 and recommended that an advisory group be assembled with representatives from EPA and USDA to determine the appropriate regulatory response.

Weary of the inability of state and local officials to come to a conclusion, Praxis's owners sought the help of their representative in the U.S. Congress, the Honorable Peter Hoekstra, who wrote to EPA requesting its assistance in resolving the issue. In response to Congressman Hoekstra's letter, EPA replied that while "EPA registers pesticides and regulates their use, parasites, predators, or *macro*biological agents (including nematodes) are not required to be registered." Because EPA considered these organisms to fall under APHIS's jurisdiction, EPA would not make a determination as to their safety. Congressman Hoekstra proceeded to contact both USDA and FDA requesting an expedited determination on the safety of Praxis's products.

In a letter to the Michigan Department of Public Health dated January 13, 1994, FDA stated that while eating establishments are principally regulated by local and state agencies, FDA felt that the EPA exemption did not cover use in retail food establishments—thus implying that EPA was responsible for making the decision. The letter also stated that FDA would not recommend or condone the use of biological control agents in a public eating facility. The following month, USDA-APHIS responded to Congressman Hoekstra's inquiry, concluding that APHIS, like EPA and FDA, was not responsible for regulating the biological control agents for these specific uses.

In March 1994, FDA reiterated its belief that EPA was responsible and that, if so requested, FDA would assist EPA in making the determination. The contradictory agency responses prompted Congressman Hoekstra to request a telephone conference with the appropriate individuals at EPA, FDA, and USDA. In May, Praxis was notified that these agencies were holding preliminary conferences to decide how to handle the situation. By October 1994, however, neither Praxis nor Congressman Hoekstra had been contacted regarding a solution. Congressman Hoekstra sent a letter in October and a fax in December of 1994 expressing his concern about the delay.

In January of 1995, FDA responded to Praxis in a letter stating that "extensive discussions" had been held to determine statutory authority. It was decided that neither EPA nor USDA-APHIS would regulate the wasps and nematodes. The letter concluded that FDA would be willing to review data supporting the safety claims made by Praxis, but that any action on the part of FDA would not override regulatory actions by the state or other local agencies.

(continued)

BOX 4-8: Chronology of the Praxis Company's Experience with FDA (Cont'd.)

Although frustrated by the 16-month delay, Praxis agreed to send FDA copies of information that had previously been provided. Praxis's owners made another request for the phone conference that had been promised 10 months earlier. In February, after several delays, the phone conference was held. Praxis was asked to provide additional data to enable FDA to determine the safety of the products. At the conclusion of the meeting, FDA promised a final decision within 90 days.

The state of Michigan, meanwhile, convened an advisory group (Michigan Human Living Environment Pest Management Advisory Group) in the summer of 1994 to examine possible human health risks and to recommend safety procedures for the indoor use of biological control agents. In the absence of an FDA ruling, the group submitted its findings and recommendations in June of 1995. The group decided in favor of Praxis, resolving that the Michigan Department of Public Health should allow the use of biological control agents in food service establishments as part of an IPM plan.

FDA's final decision in August of 1995 also supported Praxis. FDA decided not to recommend that the State of Michigan prohibit Praxis from marketing parasitic wasps and nematodes for cockroach control.

Praxis is now free to move forward with its parasitic wasps and nematodes, but the two year delay has considerably drained the company's resources. The company continues to struggle to market its products. According to Praxis representatives, Cooperative Extension agents and university scientists insist that if the company wishes to gain their support, Praxis not only must submit to them proprietary information but also must allow them to publish that material. Convincing Extension Agents to recommend the company's biological control products—or at least not to dissuade potential customers—may prove to be another uphill battle for Praxis.

Source: Office of Technology Assessment, 1995.

REGULATING THE RISKS FROM BBTS: ISSUES AND OPTIONS

Regulatory Structure for Natural Enemy Industry and Biological Control Research

The current regulatory system under APHIS has a number of important flaws. Its requirements and permitting process for the natural enemy industry lack balance, transparency, and efficiency. Small companies must comply with often useless paperwork and critical delays in shipping organisms that have a long history of repeated introduction and widespread use.

Past permitting of classical biological control introductions by researchers has been uneven, with the greatest focus on biological control agents targeting weeds, and relatively little scrutiny of agents affecting insect pests. The existence of an advisory group (TAG) only for weeds demonstrates the varying levels of evaluation. To improve the agency's regulatory decisionmaking, APHIS needs to give more complete coverage to all biological control introductions, and to develop better documentation of nontarget impacts from past introductions.

Significant environmental risk issues exist that APHIS needs to identify and evaluate. The agency's recently proposed (and subsequently withdrawn) regulation on the introduction of nonindigenous species, however, was clear evidence that APHIS has not yet succeeded in assigning priorities and addressing these risks. The proposal was exceedingly stringent in some areas and overly lax in others.

OPTION *Congress could, through its oversight functions, instruct APHIS to streamline its permitting process and to design a more balanced regulatory system for biological control. Components of these changes might include the following:*

- *Developing a more even-handed regulation for biological control with broader input from*

all stakeholders (researchers, natural enemy companies, farmers and other users, wildland managers, state agencies, conservation biologists, etc.).

- *Formulating an explicit policy concerning the regulation of nematodes. Although formally within APHIS's jurisdiction, nematode products rarely go through APHIS review. The agency needs to carefully consider whether this leaves any significant risk issues unaddressed. Potential impacts on companies producing nematode-based products must weigh into the development of a more formal policy.*
- *Instituting a technical advisory group (TAG) to evaluate proposed introductions of unprecedented biological control agents targeted at insect pests (entomophagous agents), and improving the science underlying the regulatory decisionmaking for these agents by developing appropriate host-specificity testing protocols. The different standards of review for biological control agents targeting plant and insect pests are based on historical concerns about agricultural crop protection and ignore our scientific understanding of the importance of native biodiversity and the value to agriculture of conserving native natural enemies. Enhanced review of entomophagous species may provoke objection from entomologists who are not used to this level of scrutiny.*
- *Developing mechanisms through which to include input from a cross section of nongovernmental organizations, including those concerned with environmental risk and conservation issues, in APHIS's decisions about biological control agents. The Federal Advisory Committee Act allows membership on advisory committees by nonfederal agencies so long as the committees adhere to certain procedural requirements. If APHIS chooses not to expand TAG membership, other channels may be available for nonfederal input.*
- *Requiring post-release monitoring of the nontarget impacts from the highest risk introductions as a condition of the permitting process. The challenge is to develop a mechanism for funding such research, so as not to place undue burdens on a low-profit industry that produces a valuable set of low-risk pest control tools.*
- *Maintaining clearer records of permitted releases, the basis for these decisions, and any subsequent impacts, to improve future decisionmaking. According to APHIS, some of these changes are already in progress; these efforts deserve support and encouragement.*
- *Convening a panel of scientific experts to evaluate APHIS's past regulatory precedents as a basis for future permitting decisions. This review could help APHIS identify some of the high-risk releases and facilitate agency streamlining of other permitting activities.*

OPTION *An opportunity to address some of the flaws in APHIS's regulatory system may present itself in the agency's efforts to consolidate all of its plant protection statutes into a single package.*

EPA's Regulation of Microbial Pesticides and Pheromone Products

Recent actions by EPA's Biopesticides and Pollution Prevention Division to expedite the permitting of pheromones and microbial pesticides have received high marks by the regulated industry. The division's strides in streamlining BBT registrations will need to retain some balance in the long run, especially regarding granting of waivers for environmental testing. Microbial products that have been genetically engineered to behave like conventional pesticides (see chapters 3 and 6) will need to be handled with care, because some will pose risks similar to those associated with conventional pesticides rather than having the relatively benign environmental profile of microbial pesticides registered to date.

OPTION *Congress could, either by amendment to FIFRA or through its oversight functions, instruct BPPD to pay closer attention to possible nontarget impacts on native insects and other noneconomic species, and to begin considering how it will deal with microbes genetically engineered for broader spectrum impacts and faster and higher kill rates. (One option would be to pass these on to other EPA divi-*

sions to be dealt with as conventional pesticides, but such action could substantially thwart development of genetically engineered microbial pesticides by removing the cost incentive to produce such products—see chapter 6.)

Consistency in the Regulatory Structure

Some analysts have identified as an important problem the lack of consistency among APHIS, EPA, and FDA in the agencies' regulatory oversight of natural enemies and microbial pesticides. They suggest that both types of BBTs pose similar questions of nontarget effects and other environmental risks (e.g., 235). They argue that these two categories of BBTs need an overall regulatory umbrella, a single law or a single agency to give microbial pesticides and natural enemies equal coverage.

OPTION *Congress could pass a new law embracing uses of natural enemies and microbial pesticides that would give more similar coverage to these two categories, but OTA does not find sufficient justification for this option. EPA, FDA, and APHIS all have expertise in different areas, which corresponds at least roughly with their current regulatory responsibilities. It is important, for example, that EPA continue toxicity studies on certain microbial products; the other agencies are unequipped to take over that function. Certainly regulatory gaps exist, but these can be addressed within the current institutional framework (see previous options).*

Anticipating the Occurrence of Pest Resistance to BBTs

Scientists believe that resistance is probable for bacteria- and virus-based microbial pesticides and possible for several other categories of BBTs. The rates at which resistance appears are likely to be slower than those for conventional pesticides. Of particular concern, however, is the threat of more rapid development of resistance to Bt-based microbial pesticides from the anticipated large-scale use of crop plants genetically engineered to contain the Bt toxin.

OPTION *The problem of managing resistance to Bt is exacerbated by the lack of clear understanding of its scientific underpinnings and the paucity of demonstrated successes in countering this phenomenon. EPA is requiring the development of resistance management plans as a condition for its registrations of Bt-containing crops, but the effectiveness of these provisions remains uncertain. To prevent the loss of this valuable tool in the pest control arsenal, Congress might consider funding research on mechanisms to halt or reduce the development of resistance (e.g., specific use patterns for the transgenic plants), possibly as part of a cost-sharing program with potentially impacted commodity groups.*

Recent deliberations in Congress have centered on whether EPA should keep or transfer to APHIS its regulatory oversight of plants genetically engineered for pesticidal properties. OTA has identified several technical and institutional factors that favor retention of jurisdiction by EPA. Crops that are manipulated to express the Bt toxin raise many of the same issues (resistance, toxicology, etc.) that EPA has addressed in the context of microbial pesticides. Only EPA has the experience, scientific capacity and infrastructure with which to tackle these difficult problems with any hope of success. Moreover, the agency has the necessary authority to designate specific use patterns, labeling requirements, and training programs that could help prevent resistance and thus the loss of Bt-based pest control tools. APHIS lacks the relevant experience and statutory authority to adequately address the Bt resistance problem.

Adjusting Regulatory Requirements for Chemical Pesticides

Integrated pest management (IPM) involves the combined use of multiple pest control approaches. Conventional pesticides often are used in concert with augmentation or conservation of natural enemies. However, many pesticides kill the natural enemies as well as the pests. Information on such effects could enable pesticide applicators to reduce or eliminate applications of certain conventional pesticides to protect populations of natural enemies.

OPTION *Congress could amend the Federal Insecticide, Fungicide and Rodenticide Act to include product labeling requirements that alert users to the impacts of pesticides on populations of natural enemies. Currently, Germany requires that pesticide labels indicate the level of harmfulness to beneficial arthropods. A U.S. system could incorporate similar provisions. For example, a German label reads:*

> This product is 'harmful' for populations of *Aphidius rhopalosiphi* (parasitic wasp), 'slightly harmful' for populations of *Coccinella septempunctata* (ladybird beetle), 'not harmful' for populations of *Poccilus cupreus* (carabid beetle).

The species listed are chosen based on such factors as sensitivity to the product and likelihood of exposure (106). Although no other countries presently require such a labeling system, the European Union may consider adopting a similar program as part of its efforts to harmonize requirements. (For other regulatory examples from abroad, see box 4-9.)

Anticipating Food Safety Issues

Pressures on FDA to play a role in BBT regulation will grow as applications of these technologies to control postharvest diseases in food-related industries increase. Current ambiguity about the agency's role has had negative repercussions for at least one BBT company and its clients, who need a more predictable and workable system.

OPTION *Congress could instruct FDA to analyze and firm up its current and future role in this area. In view of FDA's recent experience with the state of Michigan and the Praxis Company, a small investment of resources into workshops or policy sessions to review the important issues now would preclude significant bureaucratic entanglements and the resources they consume down the line.*

BOX 4-9: Other Regulatory Systems

The Australian Biological Control Act and the draft code of conduct of the United Nations' Food and Agriculture Organization (FAO) are often cited as regulatory models deserving consideration or emulation by policymakers in the United States. These systems are described here. Also included is the International Convention on Biological Diversity, which raises ownership issues that may affect future prospecting for biological control agents in other countries.

Regulation of BBTs Down Under

Australia relies on a combination of BBT-related laws. The Quarantine Act (1908) and the Wildlife Protection Act (1984) control the importation of exotic organisms into quarantine and for release. The Genetic Manipulation Advisory Committee, which lacks legal authority but wields considerable power regardless, oversees the release of genetically modified BBTs (a mandatory rule is under development). And the National Registration Authority has responsibility for approving commercial biological pesticides such as Bt, in addition to chemical products. The use of non-exotic organisms is not regulated unless they are genetically modified or they merit examination in a manner similar to that of agricultural and veterinary chemicals. The Australians invoke their widely acclaimed Biological Control Act (1984) only as a last resort, when the choice of a target or the use of a particular control agent is likely to be controversial. To date, the act has been summoned only for two programs, controlling the annual weed Paterson's curse (*Echium planatagineum*) and the blackberry (*Rubus fruticosus*). In the latter case the use of the law was threatened but never executed.

(continued)

BOX 4-9: Other Regulatory Systems (Cont'd.)

Australia's Biological Control Act is the only biological control legislation ever adopted by a national government. Several features of the act deserve attention. First, the act directly addresses biological control, unlike laws in the United States which apply to BBTs only secondarily in the context of noxious weeds, conventional pesticides, or other concerns. Second, compliance with the act is not mandatory. It is there to be invoked only if needed. Third, the act places considerable emphasis on the inclusion of all issues and public comments, but where a decision to proceed is then made, the individuals or organizations involved are freed from liability. Fourth, although the Biological Control Act offers a valuable mechanism on certain occasions, it may be used only rarely in light of the substantial time and expenditure involved. Fifth, in contrast to U.S. approaches, the Biological Control Act includes serious consideration of the target organism. When the Agriculture and Resource Management Council of Australia and New Zealand recommends declaration of a target pest, the Biological Control Authority must publish its intention in widely circulating newspapers and journals, giving relevant information and inviting comment. If further information is needed, the Biological Control Authority may initiate an inquiry by the Industries Commission or under the Environmental Protection Act or a specially constituted body, depending on the issues at stake. Decisions on individual biological control agents with which to control the target organism follow much the same course, although publication in the *Commonwealth Gazette* (*Federal Register*) is deemed sufficient.

FAO Draft Code of Conduct for the Import and Release of Biological Control Agents

The U.S. government is participating in the completion of the FAO code of conduct, a voluntary set of standards for the importation of BBTs capable of self-replication—parasites, predators, nematode parasites, plant-eating arthropods, and pathogens. The code will cover agents imported for research as well as for field release, including those used in classical biological control and those packaged or formulated as commercial products. The recommendations of the code do not distinguish between different kinds of BBTs, in contrast to the U.S. regulatory approach which addresses separately biological control importations and the use of microbial pesticides. Pheromones and resistant host plants fall outside the scope of the code. Toxic products of microbes that are used as pesticides, which cannot reproduce and which behave like conventional pesticides, are covered instead by the International Code of Conduct on the Distribution and Use of Pesticides (1990). In the future, the biological control code may apply also to genetically engineered BBTs.

The FAO code describes the responsibilities of governments and of importers and exporters of BBTs before, during, and after importation. Its provisions include, for example, the designation by each government of a competent authority to oversee BBT imports and releases; the use of precautions against the export of BBTs adulterated with their own natural enemies or with other contaminants; and the preparation of dossiers on the pest to be controlled (to justify the importation of a control agent) and on the candidate biologically based control agent (to document its identity and potential human and environmental risks). The draft code emphasizes that every effort should be made to transport the BBT at a life-cycle stage during which it can survive without its host pest (the entry of which could present an additional quarantine risk). The code also stresses the importance of proper labeling, post-release monitoring, deposition of voucher specimens, education and training of users, and other procedures.

(continued)

BOX 4-9: Other Regulatory Systems (Cont'd.)

Convention on Biological Diversity

The United States is a signatory to the Convention on Biological Diversity, an international agreement promoting the conservation of biological diversity and the equitable sharing of benefits arising from the use of genetic resources. The convention does not specifically mention biological control, but it touches upon related issues such as the commitment of countries to control alien pests (Article 8.h) and the creation of conditions facilitating access to genetic resources for environmentally sound uses (Article15.2).

Several countries, most notably China, India, Brazil and Mexico, have interpreted the convention to suggest that the nation importing the biological control agents from abroad must reimburse the country of origin. Article 15.7 calls for "sharing in a fair and equitable way the results of research and development and the benefits arising from the commercial and other utilization of genetic resources with the Contracting Party providing such resources." Article 19.2 addresses specifically the benefits arising from biotechnologies based upon genetic resources, and emphasizes developing countries' special need for access. Article 15.1 acknowledges state sovereignty over resources: "...the authority to determine access to genetic resources rests with the national governments and is subject to national legislation." These passages could imply the development of a fee system for the collection of natural enemies from abroad. Undoubtedly this option is controversial, however, particularly because the pests themselves commonly originate from those same countries and because the international exchange of natural enemies can be a mutually beneficial enterprise.

At least 98 countries worldwide have been the source of biological control agents for one or more programs, and 121 countries have introduced at least one agent. Countries in the developing world have been the source of 57 percent of all biological control introductions against alien insect pests worldwide and the recipient of 52 percent of all such biological control introductions.

SOURCES: Office of Technology Assessment, U.S. Congress, 1995, compiled from Centre For Agriculture and Biosciences International, *Using Biodiversity to Protect Biodiversity: Biological Control, Conservation and the Biodiversity Convention* (Wallingford, Oxon, UK: 1994); J.M. Cullen and T.E. Bellas, Division of Entomology, CSIRO, Canberra, Australia, "Australian Laws, Policies and Programs Related to Biologically-Based Technologies for Pest Control," unpublished contractor report prepared for the Office of Technology Assessment, U.S. Congress, Washington, DC, March 1995; United Nations Environment Programme, *Convention on Biological Diversity,* June 5, 1992 (as of July 20, 1995: URL=gopher:\\Gopher.UNDP.Org:70/00/Unconfs/English/Biodiv.Txt, no date); United Nations Food and Agriculture Organization, *Draft Code of Conduct for the Import and Release of Biological Control Agents* (Rome, Italy: November 1994); J.K. Waage, Director, International Institute of Biological Control, Ascot Berks, UK, letter to the Office of Technology Assessment, U.S. Congress, Washington, DC, July, 1995.