

Attack of the Killer Tomatoes!

BY ROBERT LUHN

One of the newest American economic powerhouses, California's biotechnology industry, is a well-oiled machine. But so is a runaway train.

THE NIGHTMARE: With a bit of gene splicing, a biologist creates a microbe that gobbles up toxic waste the way a Teenage Mutant Ninja Turtle scarfs pizza. The Environmental Protection Agency, stuck with hundreds of toxic, oozing Superfund sites, drops the microbe into a contaminated wildlife refuge, and witnesses a miracle: a fouled marine ecosystem restored to pristine condition for a minimal cost. Unfortunately, this microbial toxic avenger also produces methane as a byproduct. And like sailors on leave, the microbes mix it up with local bacteria, passing their designer genes on to some tough germs that start pumping out methane like mini-volcanoes. The bacterial ecosystem—the one that supports all life—is hopelessly polluted and collapses, and with it, every other life form.

Possible? Yes. Probable? No. But even biotech advocates admit that genetic engineering may not necessarily bring good things to life. It's an issue a nervous public is confronting now that biotechnology firms are trotting out their first gene-spliced wares. Although most people would welcome any wonder drug that cures cancer or AIDS, the public—and environmentalists—are decidedly worried about the potentially disastrous effects of releasing artificially altered microbes, animals and plants in the open world.

Some of biotech's most vocal critics, such as Jeremy Rifkin's Foundation for Economic Progress, make it sound like a biotech Three Mile Island is just around the corner. Few of the regulators, scientists and biotech companies interviewed for this article take such claims seriously. Most feel the risks are acceptable. But many experts also admit that there's a lot we don't know about how genetically engineered organisms—especially microbes—will act outside of the petri dish.

There's a PR problem, too. "The [biotech] industry must contend with deep-seated public fears about genetic engineering," says Cynthia Robbins-Roth, editor in chief of San Mateo-based *BioWorld* magazine. "Heart attack

victims may not worry about how their anticlotting drug was made, but it's entirely different to ask them to feed their kids engineered tomatoes."

An attack of the Killer Tomatoes is hardly a threat, but even some biotech companies feel that a stronger regulatory system is needed—not only to allay public fears, but to ensure the success of the biotechnology. Genetic engineering is no longer confined to musty university labs—it's big business and a veritable flood of consumer and industrial products is about to spill into the marketplace. In the coming years you can expect pest-resistant fruits and vegetables, Arnold Schwarzeneggerlike trout, superpure drugs, tests for genetic disorders, frost-resistant bacteria for crops, gene-spliced microbes that can churn out everything from silk to biodegradable plastics, bacteria that can mop up toxic wastes, and a hundred other applications. Each new product promises to save lives, money or the environment. And each raises questions about privacy, property laws and, especially, environmental safety.

Biotechnology is nothing new. Humans have been tinkering with life since the first seed was planted in Mesopotamia nearly 10,000 years ago. Every grain you eat is a hybrid, every domesticated animal is the result of

centuries of selective breeding. But biotechnology lets scientists precisely rearrange the building blocks of life (proteins, carbohydrates, DNA) that make up viruses, bacteria, plants and animals. In short, it's the stuff of instant evolution.

To most people, biotechnology is synonymous with gene splicing—where, say, a gene in an animal cell that produces insulin used by diabetics is cut out and inserted into bacteria, which can in turn manufacture gallons of the stuff. It also includes modifying the end product itself, such as tomatoes engineered to ward off insects, or fish designed to grow extra fat.

But as biotech companies pursue cures, greater crop yields, cheaper raw materials and bigger profits, a growing cadre of scientists, environmentalists and lawmakers are asking: Is biotechnology safe? And can it be regulated?

Genetically engineered drugs are considered safe, because they're confined to the person being treated. But microbial pesticides, plants and animals that do their work outdoors can't be easily controlled—and therein lies the concern. Of course, microbes released in the environment must face a survival-of-the-fittest battle. "Most of the microbes we've released have been whomped on by

Coming Bio-Attractions

The fruits—and vegetables—of biotechnology may be some years in coming. But the promise is tantalizing. Consider some of the products that could be showing in the '90s and beyond.

1. The Blue Rose

By any other name, this rose will smell as sweet, but it will also be royal blue—and it won't wilt nearly as fast.

2. Killer Cells

Like Patriot missiles, cellular hitmen will carry extremely toxic chemicals to specific cancerous tumors and kill them on the spot.

3. Bacteria Factories

The silkworm may soon be out of business. Genes spliced into bacteria will produce milady's stockings in a thrice.

4. Artificial Organs

Cloned skin grafts for burns may be available soon; manmade organs for transplants are farther in the future.

5. Killer Tomatoes

Calgene's genetically engineered tomato could make obsolete every other tomato in the produce department. It will be bigger, meatier, and won't spoil.

6. DNA Fingerprinting

New biotech forensic tests could finger a criminal using blood, hair or skin samples found at the scene.

7. Vaccines, Treatments and Cures

Alzheimer's, rheumatoid arthritis, Parkinson's disease, AIDS and other diseases may be felled—or held at bay—via genetically engineered silver bullets by decade's end.

8. Bacterial Gas Stations

Take sawdust, mix with the right microbe and voila!—butanol, ethanol and other fuels.

9. Quicker Picker Uppers

Designer microbes that mop up oil spills, toxic waste and other nasty chemicals may be among the first to be approved for outside release.

10. Biodegradable Plastics

That shampoo bottle—or diaper—may someday be made from a bacterial plastic that disintegrates in months.

natural predators," says Steven Witt, of the San Francisco-based Center for Science Information, and the author of *Biotechnology, Microbes and the Environment*. "Regulations aren't regulating biotechnology—nature is."

"Genes are very finicky creatures," adds Robbins-Roth, "You can't develop something pathogenic by accident. Of course, if some terrorist asshole wants to create Super Anthrax, there's not much you can do about it. But that's the risk with all technology."

In short, a biotech Three Mile Island probably isn't in the offing, but a biotech Valdez could be. The big threat, say environmentalists from the Environmental Defense Fund and the National Wildlife Federation, is biotech pollution—the headaches that result when *any* exotic organism is dumped into a new environment. For example, naturally occurring zebra mussels carried into the Great Lakes by European cargo ships several years ago now carpet the bottom of some lakes, sucking plankton out of the water and crippling the fishing industry. An infestation of Chinese clams in the San Francisco Bay could similarly disrupt marine life.

The problem of biotech pollution gets thornier when biologists create "transgenic" organisms that incorporate genes from totally different species, typically to ward off pests and disease. The ability to essentially inoculate plants against disease could stop an estimated \$2 billion in crop damage every year. "These products can actually benefit the environment because they decrease the use of chemical pesticides," says EDF's Dr. Rebecca Goldberg.

But some important questions must be resolved first. "For example, when you add a totally novel trait to a frost-fighting bacterium or a wheat plant, you may give it an advantage that lets it dominate over others," says Goldberg. "Worse, if there's a wild cousin of the organism nearby, they could cross-pollinate and the wild cousin would have an undue advantage." Herbicide-resistant wheat could, via cross-pollination, pass its designer genes on to its wild weedy cousins, making *them* harder to control. Not a pretty picture.

Corraling errant plants or animals in the outside world would be tough enough; controlling genetically engineered microbes would be impossible. Bacteria are also rather promiscuous, and swap genes at the drop of a hat. If the genes in question imparted to bacteria the ability to resist antibiotics, you could end up with whole new strains

of hard-to-kill bacteria—and a potentially big health problem.

Scientists stress that the above scenario is unlikely—transplanted genes usually either can't be "read" by an organism or they cripple it. "The chances of a disaster are very low. But as you go up in size and scale—when you spray millions of acres with a genetically engineered biopesticide over many years—something *could* happen," says Dr. Trevor Suslow, one of the California plant pathologists who worked on Frostban, the first genetically engineered bacteria released in the environment.

Keeping mistakes to a minimum—and allaying public fears—is the job of federal and state regulators. But in the Reagan-Bush era, where deregulation is de rigueur and America's sagging competitiveness is a growing worry, boosting America's already considerable lead in biotech takes precedence over environmental and public health concerns. The states—especially California—have largely followed this business-first approach.

Unfortunately, the administration's obsession with competitiveness and its determination to keep Congress out of the picture has produced a crazy-quilt regulatory system that serves neither safety nor commercialization of biotechnology. "It's a pastiche of different agencies working under different laws written long before biotechnology ever existed," says Steven Witt. "Biotech has given some statutes stretch marks." The problem is exacerbated by interagency turf battles and by the nature of the technology. Is an engineered tomato that releases a natural pesticide subject to approval of the Agriculture Department, which oversees plants; the EPA, which checks out pesticides; or the Food and Drug Administration, which regulates the grub on your plate? With big budgets on the line, which agency has primacy is being hotly disputed.

Worse, say critics, the safety net is so full of holes, and agencies so lacking clear statutory authority, that biotech regulation practically runs on the honor system. The USDA, for example,

has yet to turn down a permit for a single field test, and its current research guidelines for plant introductions are voluntary: hence, unenforceable. The EPA, 10 years after the first genetically engineered microbe was patented, has yet to issue guidelines covering large-scale field tests. It's



Roger H. Salquist, CEO of Davis' Calgene, Inc.: "If it ain't broke, don't fix it."

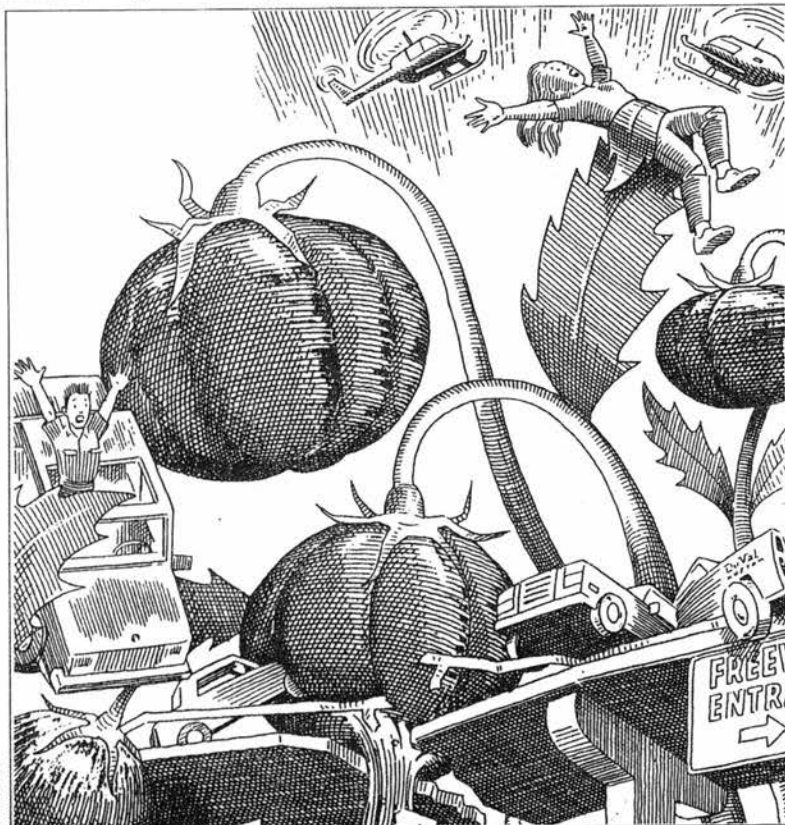
"a regulatory system based on a wink," says Margaret Mellon, director of the National Biotechnology Policy Center.

Some companies think that's just dandy. As Roger Salquist, CEO of Davis-based Calgene, Inc., booms: "If it ain't broke, don't fix it!" The company is one of the pioneers in genetically engineered tomatoes, cotton and tobacco, and is currently testing its products in a number of states. But Salquist admits that getting a product from field test to marketplace is still an unknown, because of the EPA's "meddling" and because the FDA hasn't laid down any rules. The solution, according to Salquist, would be "someone coordinating things—someone with the brains and balls to act as a federal traffic cop."

Of course, a runaway train "ain't broke"—but it can cause a hell of a pileup. Some biotech firms admit as much and agree that without meaningful regulation—and a quelling of public suspicion—biotechnology could go the way of the nuclear power industry. If nothing else, venture capital will simply flee to other countries. Dick Herrett, a lobbyist for ICI America Inc., which develops pharmaceutical and agricultural biotech products, notes that current regulations make it impossible to do any planning. "If you go to the agencies and say, 'I want to bring this product to market in five years,' they just throw up their hands," says Herrett. "After 10 years [of biotechnology research], we *still* haven't seen a genetically engineered plant make it from lab to consumer."

Dr. Susanne Huttner, who heads the University of California's Biotechnology Research and Education program, is blunter: "Agriculture] biotech has died in the U.S. because of the uncertainty of the regulatory structure and unreasonable restrictions on research."

For its part, California still lacks a streamlined, mandatory oversight program that serves both the public health and business. That doesn't mean the state has been asleep at the wheel, but business pressures have skewed the debate. In 1985, the Assembly formed an interagency task force to review existing state laws applying to biotechnology, clarify any fuzzy areas, and promote coordination among various state agencies. After months of poring over the statutes, the task force concluded, "the [existing] regulatory apparatus was sufficient," says Huttner, who served on the panel. The task force issued a detailed guidebook for biotech companies that included flow charts showing which agency to contact and when, and left it at that. "We felt the protocol [we established]



was enough," says Assemblyman Sam Farr, D-Carmel. "The burden is on the biotech industry to prove that its products are safe. It's also our burden not to distrust every new idea that comes down the pike."

With a philosophy like that, you'd think biotech companies would be rushing to test their products in California. But the state's regulatory roadmap has too many hairy twists and turns and not enough clear-cut authority. The result is a system that ignores some potentially ugly situations. For example, Selina Bendix, a San Francisco-based toxicologist and environmental impact consultant to public and private agencies, points out that there are no earthquake safety regulations for biotech companies. And can the state respond to a potentially pathogenic biotech spill? Michael Picker, of the National Toxics Campaign, thinks not. "How many sanitation districts have ordinances covering such spills? How many fire departments are trained for this?"

In some ways, California's thrashing about may be moot, since the federal government must grant final approval for any genetically engineered commercial product. But it's clear that California hasn't helped put local biotech companies at the starting gate.

Which brings us back to Washington. What's keeping uniform regulation at bay? Although big biotech firms like Monsanto and Lilly consider regulation and Congress anathema, the fingers mostly point to the President's Council on Competitiveness, led by Vice President Dan Quayle and the Office of Management and Budget. The council can issue policy statements that, in the absence of legislation, become de facto rules; the OMB can "review" proposed agency regulations out of existence.

"The political pressure has been incredible," says Margaret Mellon. "The overriding administration policy is to get on with the technology and avoid Congress. For example, the USDA admitted in congressional testimony that the Plant Pest Act had problems. The next day, the OMB changed the testimony." Later, when the USDA proposed tougher guidelines for plant introductions, the OMB gutted the provisions for government oversight. And a recent policy statement from the council opposes any "efforts to create new or modify existing regulatory structures for biotechnology through legislation."

This doesn't set well with Rep. George Brown, D-Riv-

erside, who heads the House Committee on Science, Space and Technology. Brown isn't wild about revising the laws that govern the EPA, FDA and USDA, since it could take the agencies years to recast their regulations. But current ambiguities could allow biotech firms—or environmentalists—to sue to prevent an agency from exercising its real or implied authority. "The only solu-

In short, the biotechnology industry probably isn't facing its version of the Three Mile Island disaster anytime soon.

On the other hand, it might well confront the bacterial equivalent of the Exxon Valdez oil spill.

tion," says Brown, "is creating a sound legal basis."

So given the spotty regulation, what keeps biotech companies in line? "Fear," says John Cohrsen, associate director of the Competitiveness Council and one of the key power brokers behind the scenes. "Simply due to liability, a company will want to jump through all the legal hoops," he says. But to critics like Andrew Kimbrell of Rifkin's Foundation for Economic Progress, this is economic madness. "This is biotech's Achilles heel. Their standard liability policies won't cover a disaster. All it takes is one small accident the industry can't cover and that's it for industry."

One attempt to untangle the mess is the Omnibus Biotechnology Act of 1990, written by Greg Simon, staff director on Brown's technology committee. The bill doesn't create a new agency or dictate regulations to existing agencies. What it does, says Simon, is provide explicit legal authority for each agency, compel them to issue regulations, and make all biotech companies obtain standard research and commercial permits. The bill has its flaws, but environmentalists and legislators support it; most federal regulators, biotech companies and industry trade groups bitterly oppose it. Whether Brown will reintroduce it in the 1991 session is unclear.

Either way, the regulatory morass will continue until either Congress gets involved or a biotech accident draws national attention to the government's patchwork safety net. Biotechnology's most strident critics admit that a revamped regulatory system is no panacea, but a reasonable amount of oversight and regulation will at least let everyone get on with the job of making biotechnology work.

"We need to get this one right," says Andrew Kimbrell, echoing the concern of many environmentalists. "We need a full congressional review of the environmental problems, the insurance problems, the works—then we can arrive at some reasonable compromise legislation."

We may not be able to dawdle for very long. Our ability to compete internationally and to feed the world without drowning it in toxic chemicals may rely on it. "The world population is booming, and arable land is finite," says Terry Medley, director of biotechnology at the USDA. "Productivity via genetically engineered food production may be the only answer, and it's our responsibility to pursue these options."

The key is setting an agenda. "We're focusing on regulation and not on what we're trying to accomplish," says Steven Witt. "If we said, 'Let's reduce chemical pesticide use by 50 percent by 2010,' we'd have something to aim at. The Bush administration hasn't articulated what our national science policy is and that's why things are in disarray." Industry backer Dick Herrett, of ICI, can only nod his head in assent. "The current regulatory scheme isn't working," he says. "There's no traffic cop, no road map. The industry needs rational regulations so it can develop a timeline for products—or it's going to move offshore."

Expectations for high technology are sometimes exploited as excuses for avoiding bigger issues—like conservation and cutting back on pollution. But that is all the more reason, says Witt, that the United States should not only develop biotechnology, but be the world leader in its regulation. "We're so used to operating off catastrophes," says Margaret Mellon. "It's like Lake Erie has to catch on fire before we develop a clean water policy. We're not designing a regulatory process for the 40 products we know, but the 4,000 to come. We can't rush headlong into this technology without carefully assessing the risks." ♦

Bio-Regulation: Follow the Yellow Brick Rollercoaster

Let's say you want to field test a genetically engineered microbial pesticide. You notify the EPA and obtain an experimental use permit; you then turn to the California Department of Food and Agriculture. If you're a research farm, or academic institution like UC Berkeley, no permit is required. "The people at UC are big boys, and we feel they can control their experiments," says Tobi Jones, the state's branch chief of pesticide registration. And if you're a private sector company? The CDFA recommends a permit.

At this point the CDFA notifies affected state agencies and counties, who in turn notify various local counterparts, and comments are solicited. "[For a company], it's like mounting a political campaign," says Trevor Suslow, who went through the process in the 1980s with Frostban. "It's a cascading notification process that forces you to talk with everyone from state agencies to state legislators to local officials. There's no way to gauge the costs. It's one reason a lot of companies have gone out of state."

Another catch? There's no time limit from application to approval for a field test. "There are enough impediments that even a simple test is daunting," says Suslow. "And even if you get an OK, not everyone agrees that the agency has authority to issue it." The company Suslow works for has since canceled all projects involving genetically engineered microbes, opting instead for naturally occurring strains. Although Jones maintains "the system works ... we're just waiting for someone to use it," she also admits that wading through the state's regulatory maze is probably too costly for most small biotech firms.

Even if CDFA's regulations had more bite, critics claim it wouldn't make much difference. "The CDFA is a classic captive agency. There's no sense of their safeguarding the public health or environment," says David Roe, a senior attorney with the San Francisco office of the Environmental Defense Fund. One source of conflict? Like the USDA, the CDFA is expected to both promote agriculture and regulate it.



State pesticide regulator Tobi Jones: No permit required.