

CRUMBLING OBSTACLES TO ENGINEERED BUGS

By Russ Hoyle

The most cursory chat with executives in the bioremediation business often leads to solemn colloquies about the strategic disadvantages of genetically engineered microorganisms. Since they do not occur in nature, the mantra begins, the public harbors irrational fears that they will harm or alter the environment. Next it is usually noted that environmentalists oppose the bugs, and, with the cooperation of the press, have raised public opposition to their release into the environment to an insidious art form. Someone always points out, correctly, that not a single recombinant organism yet has proved effective for environmental remediation. Finally, there is the Environmental Protection Agency (EPA, Washington, DC), which has made it all too clear it prefers natural microbes and thus has raised the specter of fire-breathing regulators lying in wait to throw themselves into the path of new recombinant technologies.

All that seems to add up to a reasonable case for prudent businesses to focus exclusively on naturally occurring microbes. Right? Dead wrong. Or at least that is the view of Ron Unterman, a former chief of environmental biology at General Electric (Schenectady, NY) who now heads up research and development for Envirogen (Lawrenceville, NJ), a three-and-a-half year old bioremediation company. With \$7 million on tap in private-placement funds, Envirogen stands alone among the handful of new bioremediation firms for its wide-open public commitment to genetic engineering. Without so much as a blink, Unterman estimates that 25 percent of Envirogen's development resources now go into engineering improved microbes for cleaning up the environment. Why is Envirogen so confident about leaping into a black hole where others fear to tread?

"Because in many cases genetically engineered microorganisms are technically superior," says Unterman bluntly. "There's a cost advantage, and we know there's low risk. We've got to prove that to the public. Once you accept that, it's only a matter of timing. How can you not go ahead? If you don't, somebody—the Japanese, the Germans—is going to do it."

Armed with that straightforward, if controversial, coda, Envirogen is preparing to wade into the regulatory fray as early as next year to seek approval for testing a recombinant *Escherichia coli* said to be capable of reducing 20 part-per-million concentrations of trichloroethylene (TCE), a common industrial degreaser and solvent found at many Superfund sites, to less than two parts per billion. Initially researchers at Amgen (Thousand Oaks, CA) isolated a strain of toluene-oxidizing *Pseudomonas mendocina* that degraded TCE at significant rates. The problem with the naturally occurring strain was that it required a constant source of toluene to stimulate the degradation process. However, toluene also competed with TCE for the bug's attention and, in the absence of precise process controls, sharply reduced the efficiency of the microorganism. By adding the *P. mendocina* gene that produces the critical TCE-metabolizing enzyme, toluene monooxygenase, to *E. coli*, researchers constructed a recombinant organism that effectively degraded TCEs, leaving behind carbon dioxide, cellular constituents, and soluble metabolites (B.D. Ensley, *Bio/Technology* March 1989, 7). Envirogen bought the process from Amgen,

which is now a minority shareholder in the firm.

Although Envirogen's plans sensibly call for field-testing the engineered organism in contained reactors, its TCE microbe is likely to be the first bioremediation product of its kind to be scrutinized by EPA under the as-yet-unfinalized biotechnology provisions of the Toxic Substances Control Act. Unterman is well aware that Envirogen may be on a collision course with the environmental community and a potentially skittish public. "We're going to be pioneers in this," he acknowledges. "We will get the arrows in our back."

Perhaps. But then, again, perhaps not. There is method to Envirogen's apparent madness—in the person of David Glass, a consultant who will be responsible for shepherding Envirogen's TCE bug through the regulatory process. Glass argues that, practically speaking, the posture of the EPA, most environmentalists, and public opinion toward genetic engineering has changed dramatically in the past decade. A former executive at BioTechnica International (Cambridge, MA), he is one of a handful of people who have considerable experience guiding new microbial products through the EPA review process. Glass deplores the level of misinformation and paranoia that he says plagues the bioremediation field. "People in the industry are petrified," he says. "People think that it is five years ago and Jeremy Rifkin is on every street corner. Nothing could be further from the truth."

"The best-kept secret around," Glass asserts, "is how much is going on in the field." In the past two years, he estimates, some 60 field-tests have been approved by the EPA for new recombinant or genetically altered microorganisms, most of them pesticides. Glass, who personally handled five successful EPA reviews for BioTechnica, notes that as far as the agency screening process is concerned, there is no special presumption of risk attached to recombinants. What is more, just as exclusions are made for naturally occurring microbes, EPA rules may not require as extensive data on recombinant systems contained in well-founded bioreactors as they would for a full-fledged release. Assuming the scientific data are in order, Glass figures it will take six to eight months to move Envirogen's new TCE technology through the regulatory review. In two or three years, with data from the bioreactor tests, Envirogen will be ready to seek approval for actual small-scale releases into the environment.

True to Glass's predictions, the prospect of a release of genetically engineered microorganisms for cleaning up toxic waste does not rattle Margaret Mellon, who spearheads the National Wildlife Federation's (Washington, DC) biotechnology program. Mellon notes that recombinant microorganisms are unproven. She would prefer the use of naturally occurring microbes where the benefits are clear and effective. But she is critical of current regulations that favor the incinerator and landfill industries and the resultant bias against microbial technologies. "We're not going to oppose genetically engineered microorganisms across the board, as long as they are regulated for risk, efficacy, and sound science," says Mellon. As for Jeremy Rifkin, well, one environmental biotech researcher says she has "not seen him in this arena for two years." And his office did not bother to return telephone calls.