Biotechnology's Regulatory Tangle

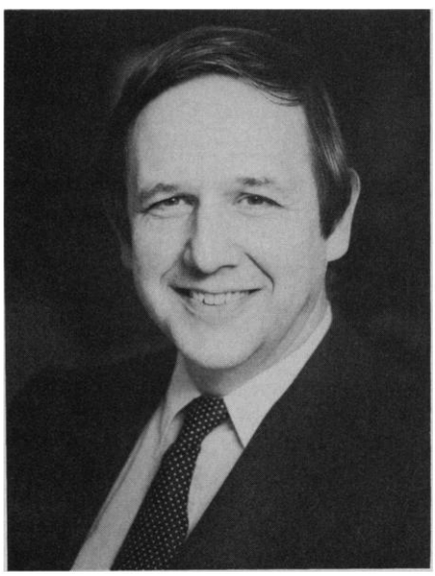
A Cabinet-level committee hopes to bring order out of the chaos; changes in RAC are contemplated

Government regulations are often adopted over a long period of time, leading frequently to a patchwork of cumbersome and contradictory laws. But the federal government hopes to do better in the regulation of genetic engineering. With research and development in genetic engineering beginning to bear fruit, a major effort is under way to forge a comprehensive and coherent regulatory policy concerning the biotechnology industry.

This effort will come to a head in the next few months. This fall, a Cabinet-level working group, headed by the White House Office of Science and Technology Policy, hopes to release a report that will set the tone for biotechnology regulation. Fifteen agencies are involved, including the Departments of State, Commerce, and Health and Human Services, and the Environmental Protection Agency (EPA). EPA itself plans to publish in September or October a set of guidelines that will lay out the agency's plans to regulate gene-splicing products, such as pesticides and toxic chemicals. In a separate but related matter, a federal court may deliver a final ruling on whether a federal advisory committee at the National Institutes of Health (NIH) has adequately reviewed gene-splicing experiments for their environmental impact.

Companies, particularly young biotechnology firms, are anxious about the outcome of these converging events, uneasy that the government may inhibit the industry with unnecessary regulation. Yet the need for a coordinated policy is already apparent in several ways:

- As commercialization nears, companies are asking individual regulatory agencies whether products produced by genetic engineering will be treated any differently from products made by conventional means. Agencies have responded in a piecemeal fashion.
- A federal judge recently issued a court order that highlights a gap in current regulations. As a result of a lawsuit brought by activist Jeremy Rifkin, U.S. District Judge John Sirica temporarily barred federally funded experiments which would involve the deliberate release of genetically engineered organisms. Sirica, however, ruled that because similar tests by private companies are not covered by the same laws, they can go ahead. The legal skirmishing continues (*Science*, 1 June, p. 962; 20 July, p. 297).
- For the past 8 years, the NIH Recombinant DNA Advisory Committee has exercised oversight of recombinant DNA research. The future role of this panel is now the subject of much discussion in the Cabinet council group. There is talk of significantly expanding the current committee. The panel now has authority to review only those recombinant DNA experiments conducted by federally funded researchers, but private companies voluntarily submit their research proposals for review. The Monsanto Company, however, which is gearing up to test a microbial pesticide on corn plants, plans to break with industry practice by bypassing the NIH committee's review and going straight to EPA for review under the law regulating pesticides.



Donald Clay

The man developing EPA's biotechnology regulation says the agency will "regulate with a light hand."

Although companies are somewhat nervous about the government's regulatory intentions, federal officials express a desire not to undermine the nation's international preeminence in biotechnology. NIH director James B. Wyngaarden says, "Biotechnology is coming to fruition." If the federal government is not careful, "we can create a chilling effect and drive the industry abroad." Says Donald R. Clay, deputy assistant administrator at EPA, who is directing the agency's development of the regulatory guidelines, "I'm looking to regulate with a light hand." Other officials say that additional legislation is not needed at the present time. Bernadine Bulkley, deputy director of the Office of Science and Technology Policy, said in a recent interview that it would be "premature to jump into new law."

The regulation issue was raised prominently a little more than a year ago by Representative Albert Gore, Jr. (D–Tenn.). Based on a hearing on the potential risks of releasing modified organisms into the environment, Gore concluded that current regulations do not adequately consider the possible ecological effects and recommended that an interagency task force be formed to review proposals for field test experiments. Interest in the issue spread rapidly, especially as EPA and the Department of Agriculture began to sort out their jurisdictional authority and hint of a turf battle surfaced. It is not clear which agency has the power to review tests of plants modified by gene splicing.

The Cabinet council working group has now taken up several issues raised by Gore. Its goal is to analyze existing law in terms of health and environmental protection, identify new gene-splicing products, and evaluate the jurisdictional problems. It plans to include in the fall report a regulatory road map that would help companies determine which agency has jurisdiction over a new product and what requirements they must satisfy to secure federal approval.

The group is also debating a larger role for the NIH's Recombinant DNA Advisory Committee, which is widely known as RAC, but the concept is amorphous at this point. As federal agencies seek ways to develop expertise in genetic engineering to evaluate new products, attention is turning to RAC because of its reputation and success. The creation of a larger NIH committee, which has been dubbed super-RAC, may be a solution. "RAC in its present form may not be adequate," says Bulkley. "It may need to be bigger and meet more frequently." She says its role would also have to be expanded to include the review of other types of

genetic engineering, not only recombinant DNA techniques. It is not clear whether super-RAC would lead to the termination of the NIH committee or whether it would be an interagency group.

Clay of EPA says that he favors the creation of a super-RAC in principle. "EPA has a credibility problem," he says, because it lacks a sufficient number of biotechnology experts. A super-RAC could provide the necessary scientific expertise to assess the potential hazards of new products. "The regulatory agencies would go to super-RAC for risk assessment, not risk management," Clay says. This would probably suit industry just fine, which has come to rely on the expertise of RAC.

Despite the attractions of a super-RAC, federal officials cite several problems. Changing the present committee may be tampering with a good thing, according to NIH official Bernard Talbot. Talbot, who is acting director of the National Institute of Allergy and Infectious Diseases, which provides a home for RAC, observes that the committee "has attracted good scientists to serve as members and their decisions are relatively prompt. If it were to become unwieldy and bureaucratic and researchers had to come to that body, then it could be a setback for science." Talbot and others also question whether enough scientists would be willing to volunteer their services if the committee is expanded and the workload increased. Clay is concerned about potential problems with confidentiality as more commercial products are reviewed. And he asks, "How will the results of the advisory committee be used? Will they be binding?"

EPA's draft report on its regulatory guidelines is now before an agency committee for review before it is presented to administrator William Ruckelshaus. The draft policy statement contains no surprises, since agency officials have been widely discussing the agency's intent during the past year. EPA, for example, plans to regulate microbial pesticides modified by genetic engineering under current pesticide law. Modified organisms which are not pesticides will be treated as "new chemicals" under the Toxic Substances Control Act, an interpretation that might be subject to legal challenge, according to the draft document.

Against this backdrop of federal activity, Rifkin has persisted in raising the issue of potential environmental hazards of genetic engineering, asserting that the risks have not been adequately evaluated. Rifkin is now trying to stop companies, as well as universities, from conducting experiments involving deliberate release into the environment of organisms modified by gene splicing.

He has filed yet another petition in federal court to bolster his argument that the two companies planning such experiments are bound by Sirica's decision. Rifkin's attorney Edward Lee Rogers argues that Advanced Genetic Sciences and Cetus Corporation agreed to abide by NIH guidelines when they signed a licensing agreement with Stanford University and the University of California concerning a key biotechnology patent.

In 1978, NIH stated in the *Federal Register* that university licensing agreements arising from federally funded research must include the following language in the contract: the licensee "specifically expresses its intent to comply with the physical and biological containment standards set forth in the NIH Guidelines. . . ." Rogers argues that NIH, by requiring these assurances, treats licensees the same as university researchers who apply for approval.

Monsanto is planning to break with industry practice by bypassing RAC and seeking permission from EPA to test a genetically modified microbial pesticide on corn.

Talbot of NIH says that deliberate release was not a consideration when the *Federal Register* notice was published. Furthermore, the guidelines only cover experiments conducted in a laboratory, not in the environment, he says. Harvey Price, director of the Industrial Biotechnology Association, says of Rogers's argument, "It's almost frivolous."

Meanwhile, NIH director Wyngaarden faces a difficult situation. He must now choose whether to accept a recommendation made by RAC that the experiment planned by Advanced Genetic Sciences should be allowed to go ahead. The experiment is virtually identical to a University of California experiment that was barred by Sirica. It involves testing bacteria modified to help prevent frost damage to crops. To be scientifically consistent, Wyngaarden would have to approve the company experiment, since NIH previously approved the University of California experiment, Talbot says. "If Wyngaarden were *not* to approve the company experiment [then], there would be a double standard."

At the heart of the regulatory agencies' work and the issues raised by Rifkin is whether scientists can adequately assess the potential environmental risk posed by genetic engineering products. Rifkin himself said in a recent interview, "I tend to doubt you can develop a way to conduct an adequate risk assessment." Even so, he says, "I think it's worth the effort." But the bottom line for Rifkin is that without more knowledge of the ecological consequences, "don't go ahead with deliberate release." He says, "The onus is not on me to explain that the experiments are unsafe. The onus is on NIH to prove that they're safe."

But this may be asking the impossible. "There is no systematic way to understand which of [a multiplicity of factors] contributes to the success or failure of an exotic [organism] in a new environment," ecologist Frances Sharples of Oak Ridge National Laboratory testified last year before Gore's subcommittee based on a 2-year study for EPA. "[T]he outcome of an introduction is not predictable. Rather, most ecologists refer to what can happen with an introduced species as a gamble, a game of chance, biological roulette. . . . I would like to emphasize that the terms 'unpredictable' and 'hazardous' are not necessarily synonymous." Wyngaarden says with frustration, "Zero risk isn't possible."

Companies are growing impatient with the delays. John Bendrook, Advanced Genetic Sciences' research director, says, "We're trying to do a limited scale test that will tell us the environmental impact. We can all sit around and theorize, but that's not going to tell us anything." Bendrook said that the company is seeking to test the frost-preventing bacteria in Canada and has approached various growers' associations there in hopes of ultimately gaining government permission for testing. Cetus, which wants to test genetically modified plants, has also considered conducting its experiments in other countries, according to Winston Brill of Cetus Madison who heads the research team.

But the federal government seems intent on creating a regulatory climate that will foster the industry and maintain its international preeminence. "For once we're trying to get ahead of the game," says a staff aide to Gore.

—MARJORIE SUN