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"'Biotechnology' is a terrible term," says David Kingsbury of the National Science Foundation, who has been chairing the federal-wide effort to coordinate biotechnology regulations and guidelines (1). Although definitions of biotechnology have changed often during recent years, the word's meaning has seldom proved a serious stumbling block. However, in 1986, federal officials renewed the debate over how best to define the term because of a troublesome dilemma they find themselves facing. Indeed, even their reluctance to close this long-lived debate suggests a useful purpose is being served by keeping the definition of biotechnology from becoming too precise.

The dilemma over biotechnology arises because of the dual missions of research and regulation for which so many federal agencies are responsible. As interest in biotechnology grew rapidly during the past 5 to 10 years, members of Congress have pressed agency officials to show they were giving proper support to this emerging enterprise. Although its growth in the private sector has been fast and enormous, no one questions the impetus stemmed from federally sponsored research—originally, largely from basic biomedical research underwritten by the National Institutes of Health (NIH). Other agencies have been urged to join in supporting biotechnology and, wherever possible, to induce researchers whom they fund to modernize their own efforts by adopting its powerful tools.

Following that path has not proved a straightforward assignment, however. Because many of the same federal agencies also share a responsibility for regulating biotechnology research and its products, agency officials often find themselves faced with two very different agendas on the same topic. In particular, techniques used widely within biotechnology, especially manipulations involving recombinant DNA techniques, have come under close regulatory scrutiny.

Although this attention has been deemed critical for ensuring both public confidence and safety, it tends to slow progress. Some federal officials now are increasingly worried that the biotechnology regulatory net may be opening too widely. In the rush to redirect and reclassify agency research efforts, making them better attuned to biotechnology's promise, the scope of regulation may also have been inadvertently broadened too much.

Federal Panels Refining Biotechnology Regulatory Roles

During the January 1987 meeting of the interagency Biotechnology Science Coordinating Committee (BSCC), efforts were made to clarify lingering confusion about the committee's role in federal biotechnology policy-making. The upshot of the latest discussions is that BSCC is strictly a coordinating body—overseeing a scientific debate, albeit with many regulatory implications—but not a regulatory body. Although this role was set at BSCC's inception, the flurry of documents, discussions, and lawsuits surrounding proposed federal biotechnology policies in 1986 tended to obscure this circumscribed but not inconsequential charter.

Assembling information and arriving at a consensus are not proving easy tasks for federal officials dealing with biotechnology. At best, the defining of certain key terms, such as "pathogen" and the "deliberate release of genetically engineered organisms," is turning out to be a reiterative process. The proposals that were published in the Federal Register prompted an outpouring of critical and contradictory comments (4). Thus, not only are the proposals now not considered "enforceable" in a legal sense, they also are proving to be just another round in a continuing cycle among scientists from different disciplines who are seeking a purely scientific consensus.

In addition to the BSCC's efforts to massage that collective information, other federal agencies are going through a similar process. It could take most of 1987 before the details of this exercise are worked out.

For example, to the Recombinant DNA Advisory Committee (RAC) of the NIH, the issue of how to define the deliberate, or "planned," release of genetically engineered organisms into the environment has become a key but largely symbolic sticking point. At its February 1987 meeting, the committee urged a further easing on current restrictions, an abstract maneuver that can succeed only if other federal agencies evaluating actual plans for such experiments heed NIH's intellectual lead. Moreover, despite limiting its role reviewing most recombinant DNA proposals that go to federal regulatory agencies, the committee reaffirmed its intent to evaluate plans for human gene therapy experiments, which also fall under jurisdiction of the Food and Drug Administration (FDA).

Meanwhile at the Environmental Protection Agency (EPA), science advisory panels consisting of outside experts have been convened to help agency staff members develop a better definition of deliberate release. The improved definition is expected to serve as a guide for when projects involving a "significant new use" of a microbe in the environment, a release for research and development of a commercial product, or organisms falling under jurisdiction of the Toxic Substances Control Act should undergo review by the agency.

Fine tuning a definition to meet this goal is not proving a straightforward chore.

Courts Playing Key Role in Shaping Regulations

The U.S. District Court late in 1986 dismissed two lawsuits brought by activist Jeremy Rifkin protesting how the federal government proposes to regulate biotechnology (2, 3). In both cases, Judge Gerhard A. Gesell concluded the issues were "not ripe" for litigation and that Rifkin and his Foundation on Economic Trends lack standing to oversee what are properly federal policy-making prerogatives (2). The judge's decisions could represent a serious setback to Rifkin's heretofore most effective tactic—taking legal action to slow the progress of genetic engineering. In a separate action also brought by Rifkin, the courts have ordered the Department of Defense (DoD) to prepare an environmental impact statement for its entire biotechnology-based biological warfare defense program.

In one of his lawsuits, Rifkin (3) was seeking to prevent the President's Office of Science and Technology Policy (OSTP) from implementing its "Coordinated Framework for Regulation of Biotechnology," proposed in the Federal Register in June 1986 (2, 4, 5). In the second suit, Rifkin was objecting to EPA's procedures for evaluating experiments involving deliberate release of genetically engineered organisms (3). In the third suit, Rifkin and the other plaintiffs alleged that the DoD was careless in conducting research on certain pathogens and thus the whole biological warfare program needed a thorough review for safety as well as improvements in security procedures (3).

Rifkin's action against EPA dates back to May 1986 when he petitioned the agency to change its procedures for evaluating and registering genetically engineered "pesticides" (3). Judge Gesell cited Supreme Court decisions indicating the court cannot settle grievances involving alleged injuries that are merely "abstract, conjectural, or hypothetical." Thus, he turned down Rifkin's lawsuit, calling its grievances "wholly abstract." Although Judge Gesell said that the issues brought up in Rifkin's lawsuit are not ripe for judicial review, he left open the possibility of conducting such review later, but "in a far more concrete factual setting" (2).

In the second lawsuit, Rifkin wanted the court to declare OSTP's proposed Coordinated Framework for Regulation of Biotechnology illegal. He argued that the inexactness of the definitions that are laid out in the framework could lead to incomplete and possibly dangerous regulation of genetically engineered products. He also said the document needed to be accompanied by an environmental impact statement (3).

Judge Gesell again rejected Rifkin's claims, saying in effect that Rifkin was accusing the framework of failing at something it is not intended to do. "While the document is not a model of clarity... [its contents] are...to guide policy-making, not to regulate," the judge says in his decision. Moreover, the framework is "merely a first effort to aid in formulation of agency policy... [and] the definitions do not authorize agency action that could not otherwise take place." Thus, the judge concludes that Rifkin's legal action was premature, based on "abstract speculation about what the agencies involved may do in the future" (2).

In yet another lawsuit, DoD was told in February 1987 by a U.S. District Court judge to prepare a comprehensive environmental impact statement for its biological defense research program, much of which involves applications of biotechnology warfare. Judging just who won this round ultimately reflects on an assessment of Rifkin and the military's intentions. Rifkin asserts there are hints of sinister activities within DoD's overall program. DoD scientists retort that their research aims are legitimate and that valuable efforts to combat dangerous, sometimes woefully neglected diseases may be hampered because of Rifkin's meddling. They also suggest that Rifkin's allegations are by now a familiar means for gaining publicity. Rifkin says it is his duty to slow DoD's progress, which he sees as leading inevitably towards weapons development, by being a "pain" (6).

The DoD programs include developing pathogen detection systems, vaccines, and biological safety suits to protect against potential biological warfare agents. Top Defense Department officials have maintained that the United States follows the Geneva Conventions forbidding development and production of biological weapons and thus all work being done is strictly for defensive purposes. DoD's research is conducted in many facilities across the country, with a sizable fraction of it being done under contract in university settings. (6).

Although some DoD scientists question the need for a comprehensive review because they believe their laboratory practices are safe and environmentally sound, they view it as potentially a "worthwhile exercise" for proving their case in "the eyes of the public." However, they also say the suit has been an "embarrassment" because of its "implications of wrong doings," which they vigorously deny. According to several observers, Rifkin's actions ironically could lead DoD into a more secretive posture. If DoD eventually insists on classifying much of the material in the environmental impact statement, notes another observer, later efforts to use that material for delaying particular components of biological warfare programs are that much more likely to prove fruitless (6).

Public Interest Groups Revising Their Biotechnology Agenda

Besides Rifkin, other members of the public interest community, including Barry Commoner and Ralph Nader, convened in November 1986 at a meeting, "Creating a Public Agenda for Biotechnology: Health, Food, and the Environment," sponsored by the Boston-based Committee for Responsible Genetics (CRG). Also attending the meeting were activists from West Germany, including members of the Green Party, who provided a flavor for the militant opposition to biotechnology that is developing in parts of Western Europe.

Commoner and Nader, although comparative newcomers to the biotechnology scene, seem eager to match Rifkin in their accusations against the new industry. Indeed, they offered strong and dire warnings of biotechnology's future misdeeds, based mainly on their appraisals of other technology-based industries.

Other elements of the public interest community showed themselves eager to join Rifkin, Nader, and Commoner in their watchdog roles. Just where they want to go, or why, is not so easy to say, however. Is biotechnology to be blocked altogether, or do the activists see themselves correcting the young industry's "exploitative" tendencies and putting it onto a track that better meets with their approval? No clear consensus has emerged.

Some efforts within biotechnology seem to have members of the public interest community especially perplexed. For instance, factions from among groups represented at the CRG meeting declared themselves interested in developing particular biotechnology-based products, especially vaccines, to benefit countries of the developing world. Vaccines are quite appealing to many members of the public interest commun-

ity, who recognize their value as a preventive, cost-effective means for tackling difficult disease problems in both industrialized and developing countries. They claim, however, that current profit-minded companies are failing to supply that need, and will continue to fail unless invested with social consciences.

Important Developments but also Frustrations for Farm Sector

In response, some industrial biotechnologists are calling upon leaders from the academic community to come forward and "demystify" genetic engineering. "We should not let a handful of idealogues set public policy," says Howard Schneiderman, senior vice president for research and development at Monsanto Corp. in St. Louis. "The new technology will hasten the change of U.S. agriculture—whether or not it is adopted by U.S. farmers," he adds. "[They must] either become innovative farmers or compete with one." (7).

Biotechnology's most ardent critic, Jeremy Rifkin, has argued that some of the first agricultural products of genetic engineering should be rejected, among other reasons, on economic grounds. For example, administering growth hormone (also called somatotropin) to dairy cows to increase milk production when there already is a milk glut would drive many small dairy farmers out of business, he argues. Such reasoning is the basis of one of his many legal actions to block biotechnology.

Proponents of this new hormone-based technology have developed several counterarguments. For example, according to economist Robert Kalter of Cornell University in Ithaca, New York, genetically engineered growth hormone could prove relatively cheap for small dairy farmers because its use entails no capital cost, but only the added cost of buying and administering the hormone. Moreover, its use would reduce feed, land, and numbers of cows needed per unit of production—all of which may benefit small farm operations. Because the diets of hormone-treated animals would need substantial adjusting, the biggest changes might be expected in land use, with demand increasing for land to grow high-protein soybeans but decreasing for land for other feed, such as corn (7).

Still other arguments are being advanced on behalf of growth hormone's use in agriculture. Not only does it boost milk production and feed efficiency in dairy cattle, it also improves productivity in hogs and cattle being raised for meat. Perhaps more significantly, the hormone dramatically decreases the fat content of meat, and it leaves no residues, according to Thomas Wagner of Ohio University in Athens. Thus, it could be a safer alternative to both antibiotics used in subtherapeutic doses and steroid hormones for boosting production in livestock, he says. Moreover, lowering fat content of meat could prove more healthful to consumers, who have been urged by health authorities to eat less animal fat to help prevent heart disease and cancer.

If the foodstuffs of the genetic engineering era are being portrayed as beneficial to consumers, other biotechnology wares are being called "friendly to the environment." Moreover, sometimes industrial successes may come by following "mid-level" instead of high technology, according to David Reed of Molecular Genetics Inc. in Minnetonka, Minn. (7). Although Reed did not say as much, another advantage of such a strategy, besides the often faster development of useful technologies, is a lower regulatory profile to the industry's critics. Rifkin, for instance, seldom has strayed from matters that directly involve recombinant DNA techniques. Other novel biotechnologies usually are spared his obstructionism.

Confidence in Other Industry Sectors Growing

Although experts are frustrated by current regulatory uncertainties now retarding biotechnology's application, particularly in the agriculture and food industries, they also evince confidence in their own growing scientific and technical know-how. They claim that biotechnology not only will benefit farmers and food processors but also consumers, whose food will become cheaper and more nutritious. And growth in the pharmaceutical industry already is having an impressive impact.

The biotechnology industry has reached "young adulthood," according to financial analyst Linda I. Miller, who follows its commercial developments for Paine Webber Inc. in New York City. According to her financial overview of the industry, it is youthful but apparently thriving (8). Moreover, the pharmaceutical industry, in offering an overview of its 1986 performance, is emphasizing how much money is being poured into research by the industry. Representatives from the industry point with pride to four biotechnology-based pharmaceutical products approved by the Food and Drug Administration (FDA) last year and say they expect this segment of the industry also to continue growing. Incremental changes for biotechnology research support also are embedded in the Administration's budget for fiscal year (FY) 1988. (Also, see Table 1, which indicates comprehensive federal budget figures for FY 1985.)

Table 1. GAO report summarizes biotechnology research support among selected federal agencies in Fy 85*

Agency	Total R&D $ millions/number projects	Biotechnology R&D $ millions/number projec s
USDA		
ARS	470/2300	25/NA
CSRS	284/12,250	48/750
EPA	320/NA	1/19
FDA	82/NA	3/17
NIH	4,824/30,000	1849/NA
NSF	1,346/14,157	82/1,621 to 1,773

*Source: "Biotechnology: Analysis of Federally Funded Research," U.S. General Accounting Office Report RCED-86-187.
Abbreviations: R&D = research and development; FY = fiscal year; USDA = U.S. Department of Agriculture; ARS = Agricultural Research Service; CSRS = Cooperative State Research Service; EPA = Environmental Protection Agency; FDA = Food and Drug Administration; NIH = National Institutes of Health; NSF = National Science Foundation; NA = not available

The biotechnology industry has grown to an impressive size in the past few years, according to Miller. Wall Street now accords the 50 or 60 publicly held companies an overall value of $9 to $10 billion, based on the selling price of the available aggregate stocks. Last year was a healthy year in terms of how much new money was put into the industry by investors, she notes. Marketplace funding accounted for about $800 million worth of investment in 1986, and private placements pushed last year's total private sector investment over $1 billion (8).

All this money is pouring into companies whose promises for products and profits are largely still to be realized. Nonetheless, more and more products are making their way into the marketplace, with estimates for total sales in 1986 of

almost $500 million, which could double this year, Miller says. The industry still is reporting overall losses but may break even in 1987, particularly if several promising drugs are approved for use in humans (8).

Most of the biotechnology-based products now being sold are medical diagnostic devices, with only a handful of human therapeutic products yet approved. Thus, although about two-thirds of the private-sector biotechnology investment supports research and development of products for human therapy, they still represent a much smaller fraction of sales—reflecting the relatively more complicated approval process for them. Diagnostic products, by contrast, receive only about 10% of the overall investment but currently account for about 55% of all sales.

So far, at least, the development costs for biotechnology-based products have been lower than those typical for new chemical drugs, Miller continues. The new industry has had relative good fortune with regulators, she says, particularly in receiving expeditious review by the FDA. Patent fights, state and local regulations, the effect of federal efforts to reduce hospital costs (hence, possibly also to lower the costs of drugs and diagnostic products), and the return of inflation are among the issues that could prove to cause difficulties in the future (8).

From the group of pharmaceuticals approved in 1986, four products were derived from biotechnology: a monoclonal antibody for preventing immune rejection of kidney transplants (Orthoclone, developed by Ortho Pharmaceutical Corp.), two versions of alpha interferon for treating hairy cell leukemia (Intron A. developed by Schering-Plough Corp.) and Roferon A, developed by Hoffmann-La Roche Inc., and a recombinant DNA-based vaccine for preventing hepatitis B (Recombivax HB, developed by Merck Sharp & Dohme).

According to Pharmaceutical Manufacturers Association (PMA) president Gerald Mossinghoff and his colleague William Szkrybalo, 1, 232 U.S. biotechnology patents were issued in 1986, an increase of 14% over 1985. Although about half those patents were for pharmaceutical and healthcare products, nearly two-thirds of the patents in this subgroup were awarded to individuals not at U.S. firms (9).

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