THE LAST WORD

By Robert B. Nicholas and Morris Levin

REGULATION AND BIOTECHNOLOGY

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To those involved in biotechnology, regulation has both genetic and legal implications. The goals and processes of each type of regulation need to be understood if the laboratory successes of biotechnology are to be readily translated into commercial success.

In the genetic world, regulation implies the control of cell functions governed by precursors, metabolites, and metabolic pathways. Researchers examine pathways in order to alter genetic control mechanisms and generate an easily recovered product. In this world, absence of knowledge means failure; success requires more research. The world of science involves primarily the researcher and his peers.

In the other world of biotechnology, regulation has an entirely different perspective. Here, regulation involves procedures to assess risks and benefits. Decision-making is based on avoiding potential negative impacts with the smallest cost to society. In this context, regulatory decisions (which could be decisions not to regulate) are frequently made in the absence of complete data. Ideally, scientists play a major role in the regulatory process. However, regulatory decisions, particularly in the absence of scientific certainty, are essentially public policy decisions guided by legislative mandates.

There are many successful examples of scientific regulation: alteration of biochemical pathways to produce Chakrabarty's microbe or reprogramming *Escherichia coli* to produce insulin are two examples. On the other hand, there are few examples of legal regulation of biotechnology. The guidelines of the NIH Recombinant DNA Advisory Committee (RAC) generally succeed in avoiding perceived negative impacts with minimum impediments to research, despite incomplete data and public and scientific pressure for regulation. The guidelines have been steadily relaxed as information from risk assessment studies and experience have accumulated. Today most research is conducted without any real restrictions.

The scientific progress made possible by these actions has rekindled public interest. As biotechnology enters a commercial stage, the public debate has shifted its focus from the laboratory to the environment. Current debate concerns release of genetically engineered organisms into the environment and human applications of biotechnology. That we have come so far without federal legislation, substantial regulation, or public concern is a tribute to the RAC and to the responsiveness of the scientific community. Now the challenge is how the scientific and public cooperation of the past decade can be extended. Of necessity, this challenge involves substantive or scientific questions as well as institutional ones.

Scientific questions of release of genetically engineered organisms into the environment can best be resolved by an interdisciplinary approach. We must address appropriate questions to molecular biologists, ecologists, and others, asking them to design experiments that answer specific questions. From the molecular biologist's standpoint, deliberate-release questions include stability and exchange of genetic material, pleiotrophic effects, and the positive influence of plasmids on the survival of modified microorganisms. For the ecologist the relevant questions address pathways to environmental effects (survival, growth, colonization, dissemination), and whether effects would be neutral, beneficial, or negative. As data accumulates, the probability and nature of the impact will be defined more realistically, as will the opportunities to modify potentially negative effects. A reasonable data base could reduce concern or promote adoption of new techniques, such as inclusion of a lysozyme-producing capacity that is repressed until the microbe's new environment changes, or the use of a gene designed to spontaneously inactivate the organism. Initial decisions—particularly for field-scale testing—will, of necessity, be made on less-than-complete data.

These questions are scientific, and the scientific community must take the lead in producing answers that will foster public and agency understanding. Failure will result in further public misunderstanding of biotechnology and, ultimately, will produce no winners.

Institutionally, the question now being discussed is which federal agencies—the Environmental Protection Agency (EPA), the Department of Agriculture, or NIH—have the legal responsibility for deciding environmental questions. Not just bureaucratic in-fighting is at stake, but real questions of the substantive standard that will be used to judge biotechnology. EPA has asserted jurisdiction under the Toxic Substance Control Act, but it does not have expertise in biotechnology. The RAC, on the other hand, has neither legal authority to review release on the commercial scale nor the institutional resources to review large numbers of applications. It is, however, the only agency with any real expertise in biotechnology.

No federal agency currently has both expertise in biotechnology and clear legal authority, so the waters are uncharted. Initial development of a successful regulatory regime for commercial biotechnology will depend upon agency cooperation. Clearly, a coordinating group is needed to prevent lapses, overlaps, and inconsistencies and to share out limited expertise and research. Given the potential conflicts, an interagency group, such as that called for in the staff report of the Investigations and Oversight Subcommittee, can succeed only with the leadership of the Executive Office. A non-regulatory presidential commission, such as the one recently proposed in legislation passed by the House of Representatives (H.R. 2350), would afford an opportunity to gather the talent needed to identify and debate these significant questions.

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