ADVANCES IN APPLIED BIOTECHNOLOGY SERIES
Volume 10

BIOPHARMACEUTICALS IN TRANSITION

Industrial Biotechnology Association

PaineWebber Bio/Technology

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On the Cover

Sequencing of nucleic acids is one of the most important technologies affecting the future of biotechnology in particular as it relates to the Genome Project. On the cover is a photograph of a display on the Apple Macintosh® of automated DNA sequencing using software developed by Applied Biosystems. *Photograph reproduced with permission of Applied Biosystems.*

BIOPHARMACEUTICALS IN TRANSITION

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Foreword

The United States does not have an articulated, fully-integrated and supported national biotechnology policy. However, the actions necessary to promote the best interests of the United States biotechnology industry both here and abroad are easily discernable and are discussed in turn, below.

Support from the Top

Perhaps the closest we have come yet to the Bush Administration speaking out with force on behalf of biotechnology occurred when Vice President Quayle addressed the National Foreign Trade Council on June 20, 1989. He said:

"The key to our success in marketing new biotechnology products has been a sensible regulatory regime that applies basic competitiveness principles. Early Supreme Court decisions held that patents could be obtained for bio-engineered life forms. More importantly, the Federal Government steered away from simplistic policies that banned the testing and development of new products. Instead, the last administration wisely put in place regulatory principles that both ensured public safety and allowed development of new products.

"All these actions gave the United States a good lead, but important fundamental problems still must be addressed to ensure continued United States success in biotechnology. We need to avoid imposing unnecessary regulatory burdens on product development. We need to consider ways to improve incentives for private sector investment, such as reducing the capital gains tax rate and making the research and development tax credit permanent. And we need to reduce the backlog of patent applications and create greater certainty of property rights in new biotech products and processes. . ."

This paper will explore the issues noted, plus some additional, in an effort to demonstrate what the policy of the United States ought to be towards biotechnology and to set the stage for our discourse.

Capital Gains Tax

The capital gains tax needs to be lowered and whether it is a proposal sponsored by Representative Ed Jenkins (D-GA), which would cut the capital tax rate to 19.6 percent (from the current 28 percent) for two years, and thereafter index capital gains, or a Rostenkowski-sponsored alternative, is not the major issue—getting it done is. Small companies have traditionally depended on individual investment and bank loans to get started. However, in recent years, start-up companies have been faced with significant setbacks in opportunities to capture investors, due to the increase in capital gains taxes. This tax increase has discouraged investors from making long-term investments in the United States and at the same time bank loans have been nearly impossible to get because banks are unwilling to risk investment until a company's successful performance is evident. This unwillingness to invest or to loan has had a distinct adverse effect. Fewer people are reinvesting their money in the American economy. As a consequence, in many instances, those interested in starting up firms are forced to seek foreign investors and partners. Under such an arrangement, the overseas transfer of technology developed in the United States is a certainty. Equitable capital gains tax treatment would go far to alleviate the problem.

Research and Development (R&D) Credits

Proposals now before Congress, HR 1416 and S 570, would extend the R&D credit in modified form and encourage companies to increase their R&D expenditures. Such a move is vital for the growth of new biotechnology companies. In addition to extending the R&D tax credit, the provision which restricts coverage to a 100 percent increase over a given base period, is severely limiting for fast-growing biotechnology companies. It needs to be eliminated to provide maximum incentive for research. This would certainly benefit small companies rapidly increasing their R&D expenditures.

(To cite just one statistic about the powerful incentives supplied by an R&D tax credit, the 25-percent incremental credit enacted in 1981 clearly had value for the economy. A 1987 Brookings Institution study showed that the ratio of R&D to output grew more than twice as rapidly as it did in the five years prior to enactment of the credit. By 1985, American

manufacturing was 25 percent more R&D-intensive than it had been in 1980.)

Protection of Intellectual Property

The concept of a level playing field has been so overworked as a metaphor that we will not use it here. Let us just agree that United States intellectual property is not receiving fair or equal protection around the world. There are pirates at work. A pharmaceutical that required the work of hundreds of scientists and technicians and took years to make its way through the regulatory approval scheme can be copied in less than one month by a single chemist with perhaps no more training than a Masters degree. This kind of international theft is a wide-spread problem which costs the United States thousands of jobs, costs the Federal Government millions in lost tax revenues, and contributes to the unfavorable balance of trade.

The General Agreement on Tariffs and Trades (GATT) has the authority to tie the protection of intellectual property trade. If this connection is made then market access can be used as a leverage to ensure universal protection for intellectual property.

Patent Backlog

The United States Patent Office (PTO) has obtained a greater hiring authority from the Office of Personnel Management; they have gotten special engineering pay rates for examiners, they have reorganized groups 120, 130, and 150 into new group 180, and have just about completed hiring as many new biotechnology examiners as can be trained by existing senior staff.

They have also created a Biotechnology Institute, an idea originally proposed by the Industrial Biotechnology Association (IBA), by means of which industry, academia, and the private patent bar will make available resources to PTO. In this way, those actually examining biotechnology patents will have access to, and be conversant with, the latest technology available.

That is the positive side. Negatively, the backlog of biotechnology patents currently stands at approximately 15,000. Patent application pen-

dency is at 26.3 months and the number of months it takes the PTO to issue its first action on the merits of a biotechnology application is an average of 14.6. This situation is intolerable from everyone's point of view and most assuredly it will take bureaucratic agility, determination, and money to solve the problem. But solve the problem we must.

Animal Patents

Only one United States patent for a multi-cellular animal has been granted so far, that is, the patent which went to Harvard for Professor Philip Leder's transgenic mouse which can serve as a human model in cancer research. And there is trouble brewing. Legislation was introduced again in the 101st Congress which would effectively denude farm animal patents of their value. To be specific, HR 1556, introduced by Kastenmeier (D-Wisconsin) would not hold it an act of infringement for a farmer to reproduce a patented transgenic animal through breeding, use it in the farming operation, or sell it or its offspring.

The IBA, the American Bar Association, the American Intellectual Property Law association, along with American Farm Bureau Federation feel that such a "farmer's exemption" would reduce the rights of patent holders and thereby discourage investment in an area that promises to significantly benefit American agriculture. Both research gains and economic gains flow from the ability to patent animals. This right should not be interfered with or diminished in any way.

Bioagriculture

In 1987 the National Research Council publication entitled *Agricultural Biotechnology*, put it well when it stated:

"A national strategy for biotechnology and agriculture must focus on solving important scientific and agricultural problems, effectively using the funds and institutional structures available to support research, effectively transferring technology. . . .Thus far, government at both state and federal levels have responded with short-term, ad-hoc management approaches; it has not addressed the long-term needs and policy concerns of integrating biotechnology into agricultural research and technology."

Things have not changed much since 1987, except for the fact the

chairman of the Committee on a National Strategy for Biotechnology and Agriculture (which gave rise to the report just quoted), Dr. Charles E. Hess, late of the University of California at Davis, is currently Assistant Secretary of Agriculture for Science and Education. One anticipates that Congress will receive continuous, cogent arguments explaining why they need to move in the directions outlined, to alleviate the problems.

Deliberate Release of Genetically-Engineered Organisms

Up to this point, in the United States we have tested over three dozen genetically-engineered plants and microorganisms in the environment and have experienced no ill effects. Both the National Science Foundation and the Office of Technology Assessment state that there is no evidence of unique hazard when recombinant DNA technology is employed in this matter. And yet, the deliberate release issue continues to cause problems. At the European Forum on Risk Management in Biotechnology held in Grenoble, France, in April 1989, B. Haerlin, Deputy to the European Parliament, argued that it is simply not possible in the foreseeable future to calculate the ecological consequences of releasing large numbers of novel organisms into the environment. He called for an international moratorium on deliberate release. In Germany, under a basic law to regulate genetic engineering, individual experiments with genetically-modified organisms must be licensed. In Britain, the Royal Commission on Environmental Pollution advocated new legislation to back up a system of compulsory registration and licensing for any release in Britain of a genetically-engineered organism. The European Patent Office turned down an application for patenting of Professor Leder's oncogene mouse.

In the United States, there are problems as well. The state of North Carolina, in August 1989, adopted legislation which makes no provision exempting from state review those applications that are not reviewed at the federal level. The federal exemptions which do arise are developed over several years in consultation with nationally recognized scientific experts and this fact raises questions. What benefit is to be gained by insisting that industry comply with state regulations governing environmental or safety concerns which federal regulatory experts deem to have been satisfied? Surely, a model state law, which does not unnecessarily superimpose a state regulatory scheme on an already adequate federal regulatory mechanism, is necessary and desirable.

The Need to Revitalize Science Education

To strike a familiar theme, the decline of science education in the United States threatens the quality and quantity of industrial innovation. Without it, the American standard of living will most certainly decline as well as our chances to compete successfully in the world market. The fact that American students are not opting for science and engineering careers, coupled with the fact that foreign nationals are earning a greater proportion of graduate science degrees than ever before, should be read by all of us as ominous.

In order to bring about the needed revitalization, there is need for significantly increased federal support for basic research in universities and colleges. A system of federally supported scholarships and fellowships and other programs, to help attract more of our brightest students to science careers in research and teaching, is a vital necessity. The core curriculum in United States schools, colleges, and universities needs strengthening in the areas of science and mathematics. Just as importantly, academic research facilities, equipment, and instrumentation need to be restored and updated. Increasing faculty teaching skills and providing them the means to gain command of new technology needs to be accorded the highest priority. By way of illustration, in a measurement of pre-college science achievement in 17 countries, the following ranked above the United States: Australia, Poland, Norway, Singapore, Japan, Hungary, England, and Hong Kong.

Support for Research

Dr. James B. Wyngaarden, Director at National Institutes of Health (NIH), said:

"Research, by its nature, requires nurturing. It is a time-consuming process because it explores the unknown and moves cautiously to assure the public's safety. . . . But, the pack of research cannot be forced or hastened. . . . Success in any one instance is uncertain, yet overall progress is virtually guaranteed. . . . Even more certain is the fact that there remain diseases and health problems to conquer. The partnership between government, academia, and industry is the best guarantee that this vast research enterprise will continue to prosper. The NIH recognizes that 'the partnership' is a national treasure that must be guarded well."

The unfortunate fact is that the percentage of total federal R&D investment devoted to basic research has decreased in recent years. This can be attributed to the rather dramatic rise in the percentage of all federal research allocated to military R&D. That percentage has jumped from 48 percent in 1980 to approximately 67 percent in 1988. At the same time, government support for basic research in universities has declined as a portion of federal R&D spending. Only about 20 percent of the total federal civilian R&D funding is currently devoted to basic research in academia.

While not exclusively its province, the Federal Government must bear primary responsibility for funding and encouraging basic research, for accelerating a transfer of technology to the marketplace, and for expanding the nation's talent base in science and technology. These needs simply are not being adequately met. Not only must Congress strengthen the funding from basic research, it must ensure the stability and continuity of funding that basic research required.

Summing Up

As a nation, we must find a way to piece it all together without falling prey to central economic planning. Our long-term investment in basic research, the availability of investment capital, and a robust entrepreneurial spirit have produced a United States biotechnology industry which stands first in the world. There is no reason why we must, or should, accept second place.

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Acknowledgments

Taken from meetings of the Industrial Biotechnology Association and PaineWebber and *Bio/Technology* magazine, *Biopharmaceuticals in Transition* brings together in one volume the most comprehensive overview of the current state of the biotechnology industry in the United States. The book comprises both formal presentations and panel discussions touching on all aspects of the industry's well-being and a look into its future.

Papers presented in this book were delivered at the Eighth Annual Meeting of the Industrial Biotechnology Association on Biotechnology's Focus in the 1990s, held October 11-13, 1989.

The Panel Discussions were taken from transcripts of the PaineWebber-*Bio/Technology* Conference on Biopharmaceuticals Futures, held September 13-15, 1989.

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