The FDA and the Biotechnology Industry: A Symbiotic Relationship?

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Abstract: Food and Drug Administration (FDA) regulatory reform has become a controversial, politically charged issue of particular significance to the biotechnology industry. The fundamental factors driving the movement for FDA reform include the prohibitive costs associated with developing a product approved by the FDA and the pressure to participate in the international harmonization of biotechnology product regulations. Two recent Congressional bills, Senator Kassebaum's Food and Drug Administration Performance and Accountability Act of 1995, and Representative Burr's Drug and Biological Products Reform Act of 1996 provide vehicles for analyzing the direction and goals of FDA reform as they apply specifically to the biotechnology industry.

The 104th Congress has been avid in its examination of federal agencies. Among the agencies it has been reviewing are the Occupational Safety and Health Administration, the Environmental Protection Agency, and the Internal Revenue Service.¹ Not surprisingly, the United States Food and Drug Administration (FDA), with regulatory authority over products accounting for twenty-five cents of every consumer dollar, or over $1 trillion annually,² is also being closely examined in this atmosphere of regulatory reform.

This is not the first time Congress, trade associations, consumer groups, and the executive branch have focused on reforming the FDA. In the late 1970s a Congressional attempt to streamline the drug approval process failed when consumer and industry groups withdrew support for legislation advocated by Senator Edward Kennedy.³ In the 1980s, AIDS activists were successful in seeking FDA reform establishing fast tracks for experimental drugs that might help dying individuals.⁴ More recently, in the 1990s, Vice President Gore's program for reinventing government streamlined, to some extent, regulations governing biotechnology


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products. While changes to date have been applauded by some FDA critics, many want more.

Until recently, cries for reform did not meet with significant support from Congress, but with the Republican congressional election victories in November 1994, legislation to reform the FDA reappeared on the Capital Hill agenda. In conjunction with the legislative approach, other players involved with FDA regulation, including the Clinton Administration, the FDA itself, trade associations, consumer advocacy groups, and several think tanks, have become more active in proposing changes and voicing concerns. The biotechnology industry itself also has taken a high profile stance in the ensuing debate.

The biotechnology industry can make a substantial contribution to U.S. economic growth and quality of life. Therefore, biotechnology, as an industry, is sufficiently important to warrant development of a comprehensive regulatory plan that takes into account the industry’s, as well as the public’s, needs. If industry needs are not met, the threat exists that the industry will focus its attentions abroad, taking with it new discoveries and jobs.

This Comment explores the effects of market forces and pressure from the biotechnology industry on FDA reform with regard to the regulation of biotechnology products. It examines recently proposed measures of reform, their likelihood of success in the current political environment, and how these measures will shape the future of FDA reform. More specifically, it analyzes Senator Kassebaum’s bill, the Food and Drug Administration and Accountability Act of 1995, and Representative Burr’s bill, the Drug and Biological Products Reform Act of 1996, in terms of their effectiveness in responding to the problems which gave

8. Id. at 20.
10. Although biotechnology products may be regulated as drugs, biologics, devices, or any combination thereof, this Comment is limited to drugs and biologics. See Gary E. Gamerman, Regulation of Biologics Manufacturing: Questioning the Premise, 49 Food & Drug L.J. 213 (1994).
rise to the movement for FDA reform, and in terms of their impact on the long-term interests of the United States with respect to the global biotechnology industry. Emphasis is placed on these bills because they are relatively moderate proposals which, even if not enacted, are likely to provide a starting point for future legislative attempts at FDA reform, as well as guiding future internal FDA reform.

Part I of this Comment reviews the FDA laws governing biotechnology products and examines the biotechnology industry. Part II discusses the reasons for the current focus on FDA reform and identifies the primary actors involved in reforming the FDA. Part III examines the various types of reforms being proposed or implemented, and evaluates whether Senator Kassebaum's bill and Representative Burr's bill meet the needs of the biotechnology industry and promote the long-term economic interests of the United States in this industry. Part IV concludes with a discussion of the direction of future FDA reform.

I. INTRODUCTION TO FDA REGULATIONS AND THE BIOTECHNOLOGY INDUSTRY

A. FDA Regulation of Drugs and Biologics

Drugs and biologics are regulated differently by the FDA, although both may be produced through the use of biotechnology. Drugs are defined, in part, as "articles intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease," and are regulated by the Food, Drug, and Cosmetic Act of 1938 (FDCA) and the Drug Amendments of 1962. The FDCA imposes stringent restrictions against the adulteration or misbranding of drugs, and requires that companies file a new drug application before a drug can enter interstate commerce. The Drug Amendments of 1962 expand the scientific, technical, and

administrative requirements for obtaining drug approval.\textsuperscript{21} The amendments require drug sponsors to prove that new drugs are effective, as well as safe for their intended use.\textsuperscript{22} Additionally, under these amendments, drug sponsors must gain FDA approval before beginning clinical testing.\textsuperscript{23} The approval process for drugs currently includes preclinical testing,\textsuperscript{24} the Investigational Exemption for a New Drug (IND) stage testing,\textsuperscript{25} the New Drug Application (NDA) stage testing,\textsuperscript{26} and post marketing surveillance.\textsuperscript{27} The statutory time frame for drug approval under the FDCA is six to thirteen months.\textsuperscript{28}

Biologics include “any virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative . . . applicable to the prevention, treatment, or cure of diseases.”\textsuperscript{29} They are regulated under the Public Health Service Act (PHS Act) of 1944.\textsuperscript{30} Unlike the FDCA focus on the safety and efficacy of the final drug product, the PHS Act focuses on the rigid control of the manufacturing process of biologics.\textsuperscript{31}

\begin{itemize}
\item \textsuperscript{21} Jordan, \textit{supra} note 16, at 477.
\item \textsuperscript{22} \textit{Id.}
\item \textsuperscript{23} \textit{Id.} at 478.
\item \textsuperscript{24} During preclinical testing the drug sponsor tests the drug on laboratory animals in order to determine if it is reasonably safe for human beings. \textit{See id.} at 479.
\item \textsuperscript{25} IND stage testing includes three phases of clinical investigations in which the drug is tested on human beings. Data are gathered concerning the drug’s toxicity, effectiveness, and safety. \textit{See id.} at 480.
\item \textsuperscript{26} During the NDA stage extensive information must be filed with the FDA, whose staff review the information. \textit{See id.} at 481–82.
\item \textsuperscript{27} The goal of post market surveillance studies is to obtain further information on the drug’s safety and efficacy. \textit{See id.} at 483.
\item \textsuperscript{28} 21 U.S.C. § 355(c)(1). The time frame specifies a maximum 180 day limit for initial FDA review, a 120 day limit for hearing preparation if required, and a 90 day limit for application approval. According to these time limits, excluding voluntary extensions, new drugs must be approved within 180 to 390 days. However, statutory limitations are exceeded on a regular basis. \textit{See part II infra.}
\item \textsuperscript{29} 42 U.S.C. § 262 (1988 & Supp. 1994). Typically, biologics are more complex molecules than drugs. \textit{See Gamerman, \textit{supra} note 10, at 215.}
\item \textsuperscript{30} 42 U.S.C. § 262.
\item \textsuperscript{31} Gamerman, \textit{supra} note 10, at 213. The Center for Biologics Evaluation and Research (CBER) partially relaxed the manufacturing restriction with the November 1992 cooperative manufacturing policy, which formally recognized policy contract manufacturing as a manufacturing option. \textit{Id.} at 225. More recently the FDA announced a six-point plan aimed at easing biotechnology regulation. The six-point plan includes: eliminating the establishment license application for well-characterized therapeutic biotechnology drugs, abolishing the FDA’s lot-by-lot release for well-characterized and therapeutic biologic drugs, and a commitment from the FDA to respond within 30 days to information submitted in response to a clinical hold on a study of an investigational drug or biologic. \textit{BIO Welcomes U.S. FDA Proposals}, Biotechnology Bus. News 1, Nov. 22, 1995. Although these are
Emphasis is placed on the manufacturing process due to the historical nature of biologics, which were originally crude mixtures or biological extracts prone to contamination.\textsuperscript{32}

The FDA uses the definition of a drug, combined with the definition of a device,\textsuperscript{33} to trigger the application of the FDCA to biological products.\textsuperscript{34} In this way the FDA may apply the safety and efficacy requirements of the FDCA to biologics.\textsuperscript{35} Biologics, therefore, are often required to meet safety, potency, purity, and efficacy criteria, reflecting the literal requirements of both the PHS Act and the FDCA. This regulatory scheme imposes expensive and time consuming obstacles on the biotechnology industry.

Within the FDA infrastructure, biologics fall within the jurisdiction of the Center for Biologics Evaluation and Research, drugs fall within the jurisdiction of the Center for Drug Evaluation and Research, and devices fall within the jurisdiction of the Center for Devices and Radiological Health.\textsuperscript{36} Which center has jurisdiction, and hence which center's regulatory scheme is applied, depends on how a biotechnology product is classified.\textsuperscript{37} Because some biotechnology products have characteristics which meet multiple statutory and scientific definitions, both the FDA and industry have difficulty distinguishing the jurisdictional status of many biologics from traditional drugs.\textsuperscript{38} Furthermore, during the 1980s, the FDA began classifying biotechnology products on an ad hoc, rather than a principled, basis.\textsuperscript{39} For example, diagnostic kits for blood borne diseases are regulated as devices, with the exception of those kits used to screen for HIV and hepatitis, which are regulated as biologics.\textsuperscript{40} This important steps, they do not solve all the problems associated with getting a biotechnology product to market.

\textsuperscript{32} Gamerman, supra note 10, at 213.

\textsuperscript{33} Device is defined, in part, as an "instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article . . . which is intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals." 21 U.S.C. § 321(h).

\textsuperscript{34} Korwek, supra note 4, at 126.

\textsuperscript{35} Id. at 129.

\textsuperscript{36} See Gamerman, supra note 10, at 215.

\textsuperscript{37} In 1991 the FDA promulgated guidelines explaining the regulatory jurisdiction of each FDA Center. See 56 Fed. Reg. 58,756 (1991) (codified at 21 C.F.R. § 3).

\textsuperscript{38} Gamerman, supra note 10, at 221.

\textsuperscript{39} Id.

\textsuperscript{40} Id. at 228. Another example of ad hoc classification can be seen in the regulation of recombinant growth hormone and insulin as drugs, while recombinant erythropoietin is regulated as a biologic. Id. at 228 n.68.
method of product classification has resulted in a loss of the predictability needed by the industry to plan how products will be developed and brought to market.\footnote{41. Id. at 221.}

The FDA regulates biotechnology under laws that were enacted long before the emergence of today’s biotechnology industry.\footnote{42. Zachary Coile, Biotech Unbound Industry Welcomes Overhaul of Drug Approval Process, San Francisco Examiner, Nov. 27, 1995, at D1.} Although the agency has the authority to regulate biotechnology products under current statutes, the existence of such legitimacy does not necessarily translate into the most rational and effective means of regulating biotechnology.\footnote{43. Peter Mostow, Reassessing the Scope of Federal Biotechnology Oversight, 10 Pace Envtl. L. Rev. 227, 265 (1992).} As with most areas where science and law overlap, the science has outpaced the law. As a result, the law must move forward to meet the regulatory challenges posed by advancing biomedical technologies.

\textbf{B. Biotechnology Industry}

Biotechnology, a broad term, is the “utilization of biologically derived molecules, structures, cells, or organisms to carry out a specific process.”\footnote{44. Peter B. Hutt & Richard A. Merrill, Food and Drug Law 971 (1991).} More specifically, biotechnology often refers to particular technologies such as recombinant DNA\footnote{45. Recombinant DNA, in general, refers to molecules developed outside living cells by incorporating DNA fragments in DNA that can replicate in a living cell. Guidelines for Recombinant DNA Research, 59 Fed. Reg. 34,496-97 (1994).} or cell fusion.\footnote{46. Cell fusion is the artificial joining of cells yielding one cell with characteristics of different types of cells. See Hutt & Merrill, supra note 44, at 965.} These technologies have commercial applications in various fields, including the development of human therapies, animal husbandry, agriculture, food production and environmental management.\footnote{47. Dianne E. Hoffmann, The Biotechnology Revolution and Its Regulatory Evolution, 38 Drake L. Rev. 471, 474 (1988/1989). These recent technological developments follow an ancient history of biotechnology. Biotechnology has been used to produce beer and wine and to selectively breed plants and livestock for over a millennium. See Mostow, supra note 43, at 229. This Comment is limited to the application of biotechnology to the development of human therapies.}
Although biotechnology was a relatively obscure science twenty years ago, it has since matured as an industry and a science.48 The United States biotechnology industry has grown to include more than 1300 companies.49 By the end of 1995, thirty-two biotechnology drugs and vaccines had been approved by the FDA and more than 230 were in clinical trials.50 Hundreds of dedicated biotechnology companies (DBCs) were formed during the early 1980s in the United States.51 DBCs are almost exclusively a U.S. phenomenon; they are created specifically to exploit the commercial potential of biotechnology.52 Typically, DBCs begin by focusing on specific technologies, particular products, and niche markets.53 Because these companies lack internally generated revenues during the development stage, start-up costs such as buildings, equipment, and employees are difficult to fund.54 To finance these costs DBCs rely on venture capital, stock offerings, and relationships with established companies.55

Commercial exploitation of biotechnology is not accomplished exclusively by DBCs. Both DBCs and established pharmaceutical companies utilize the methods and tools of biotechnology in their drug development efforts.56 Drug discovery research focuses on the use of biotechnology because of the unique approach it facilitates,57 allowing a molecular and cellular level approach to understanding disease, drug-disease interaction, and drug design.58

As biotechnology advances beyond the research stage, its products potentially are subject to numerous statutes designed to protect health and safety.59 The FDA holds life or death power over these companies, for they cannot market their products without approval from the FDA.

50. Coile, supra note 42, at D1.
52. Id. at 3–5.
53. Id. at 5.
54. Id.
55. Id.
56. Id. at 7.
57. Id.
58. Id.
59. Hutt & Merrill, supra note 44, at 973.
II. MAJOR FORCES DRIVING THE FDA REFORM MOVEMENT

A. Underlying Reasons for FDA Reform

The fundamental factors driving the movement for FDA reform are the expense, both in terms of money and time, involved in developing products that are approved by the FDA, and the movement toward international harmonization of biotechnology products. The FDA, with its "culture of caution," has resisted substantial change to its drug approval process. There are great disincentives for approving drugs that ultimately are determined to be unsafe. The FDA reviewer responsible may be subjected to intense congressional examination, professional criticism, and ultimately may lose his or her job.

I. Costs

Cross-national studies have indicated that the FDA's regulatory scheme is markedly more cumbersome than that of other countries. The FDA, functioning as a "gatekeeper" for the entry of biotechnologically derived products, creates significant cost barriers to product development. These barriers include the costs of testing to meet regulatory requirements, the likelihood of delay during the approval process, and the uncertainty associated with the possible disapproval of new biotechnology products.

The exact length of development time and associated costs are disputed by the various players in the FDA reform arena. Industry experts state that the total development time required for a new cure to reach the patient from the laboratory is fifteen years, with an average cost of $400 million. They estimate that delays by the FDA may

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60. This is not an exhaustive list of factors. Other factors include intimidation, whereby pharmaceuticals and biotechnology companies feel they cannot question the FDA's decisions without prejudicing future drug approval applications, and concerns that agency problems cost lives. See Green, supra note 6.


63. Note, supra note 2, at 2014.


65. Id.

account for as much as ninety percent of the average cost.\textsuperscript{67} The FDA, however, estimates that the total development time has remained at eleven and one-half years since 1980.\textsuperscript{68}

An example of the disparity between each group’s figures is the length of time needed to review new drug applications, the final step in the drug approval process. According to a recent Government Accounting Office (GAO) study of drug approval procedures, the FDA has reduced the time it takes to clear new drug applications before they reach the market by more than forty percent over five years.\textsuperscript{69} However, even in light of this positive statistic, the agency still takes nearly three times the limit set by federal law.\textsuperscript{70} By comparison, drug approval in the European Union (EU), depending on the member state, ranges from six months to three years,\textsuperscript{71} and in Japan the standard drug approval time is eighteen months for prescription drugs and ten months for nonprescription drugs.\textsuperscript{72} Furthermore, drug makers say the GAO report is misleading because it focuses only on new drug review time,\textsuperscript{73} while FDA regulatory authority extends over almost all of the drug development process.\textsuperscript{74}

Regardless of which party’s time estimate is the most accurate, the time and money needed to meet FDA requirements can serve as large

\textsuperscript{69} FDA Overhaul Is Sought Despite Some Improvement, supra note 66.
\textsuperscript{70} Id.
\textsuperscript{71} Rosemarie Kanusky, Comment, Pharmaceutical Harmonization: Standardizing Regulations Among the United States, the European Economic Community, and Japan, 16 Hous. J. Int’l. L. 665, 682 (1994).
\textsuperscript{72} Id. at 686.
\textsuperscript{73} FDA Overhaul Is Sought Despite Some Improvement, supra note 66. Another factor behind this apparent decrease in FDA drug review process time is the Prescription Drug User Fee Act of 1992. 21 U.S.C. § 310. This law requires pharmaceutical and biotechnology companies to pay a fee to the FDA for each drug submitted. The money, a projected total of $332 million, is being used to hire 600 more reviewers by 1997 and to speed up the drug review process with performance targets. Jennifer Reingold, Under Watchful Eyes: What’s Behind the Sudden Improvement in the FDA’s Notoriously Slow Drug Approval Process, 164 Fin. World 40, at 40 (1995).
\textsuperscript{74} FDA Overhaul Is Sought Despite Some Improvement, supra note 66. There are discrete phases through which a new product must pass before a new drug application (NDA) is sought for entry into the market. First, the company sponsoring the product must complete extensive laboratory and animal testing to collect preliminary data concerning the drug’s safety and biological activity. Then, the company must file an investigational new drug application, which, if not rejected by the FDA, enables the company to begin human clinical trials. These clinical trials occur in three distinct phases, the purpose of which is to evaluate safety and efficacy. After the clinical trials are completed, the NDA is filed for FDA review. See Rutherford, supra note 62, at 212–13.
obstacles to biotechnology companies. Regulatory delays may cause
cOMPANIES TO BURN UP THEIR CAPITAL BEFORE COMPLETING THEIR RESEARCH, OR
drive up the final cost of a new drug when it eventually reaches the
market. A delay of one year in marketing can represent a ten million
dollar loss to a company because of increased regulatory costs and lost sales.\textsuperscript{75} In addition, delays in drug approval affect small biotechnology
companies disproportionately because these companies depend on an
occasional or rare superstar drug to recoup research costs.\textsuperscript{76} FDA reforms
could free company time and money, previously spent on regulatory
issues, for increased research and capital investment. Reforms could also
bode well for venture capitalists, shareholders, and other investors.
Industry advocates are hopeful that the reforms will lure back venture
capitalists and strengthen investor interest in publicly held biotechnology
companies.\textsuperscript{77}

The biotechnology industry is an important part of the U.S. economy
and has improved America's quality of life.\textsuperscript{78} However, the extensive
cost of time and money needed to achieve FDA approval may push the
biotechnology industry to move their production, research, or both
abroad to avoid delays in getting their product to market.\textsuperscript{79} If American
companies locate abroad, such action may delay Americans' access to
new pharmaceuticals and hurt the American economy by shifting not
only jobs, but knowledge and technology out of the country.

\textsuperscript{75} John Patrick Dillman, Note, \textit{Prescription Drug Approval and Terminal Diseases: Desperate

\textsuperscript{76} Id. at 936 n.94.

\textsuperscript{77} In general, a biotechnology company requires more than $450 million to reach operating
profitability. Historically, public investment capital has been accessible for promising biotechnology
companies, beginning at a relatively early stage in their development. J. Casey McGlynn & Grant
Heidrich, \textit{Biotechnology Financing Remains a Tough Row to Hoe}, 13 Bio/Technology, 638, at 638
(1995). Major sections of the investment community have abandoned biotechnology due to
overselling and failed clinical trials. See Anderson, supra note 49, at 131. Now it is more difficult for
cOMPANIES TO RAISE THE NECESSARY FUNDING, WITHOUT WHICH THEY CANNOT SURVIVE. "Nineteen of the 100
companies in Cowen & Company's (Boston, MA) biotechnology-tracking universe now have less
than 1 year of cash reserves, based on their burn rate, while 33 of these firms have 1–2 years of cash,
and 18 of them have 2–3 years of cash." McGlynn & Heidrich, supra, at 638. After a large boom
period in the early 1990s, public-market financing for biotechnology decreased dramatically. Many
investors began to realize that promising science and research do not necessarily translate into
successful product development. Id. at 638–39.

\textsuperscript{78} \textit{Competitiveness of the U.S. Biotechnology Industry}, supra note 7, at 20.

\textsuperscript{79} Id. at 33. A Health Industry Manufacturing Association survey reported that 50% of the more
than 500 device makers surveyed had moved some clinical trials of new medical devices overseas
and 75% planned to move their trials to Europe. See Rick Henderson, \textit{Prescription Remedies},
Reason, Aug., 18, 1995, at 27. Although this survey was of medical device companies, it is likely
that biotechnology companies will take similar measures.
2.  International Harmonization

Global economic factors are also supplying pressure on the United States to change its regulatory process concerning biotechnology products. The major competitors in the international biotechnology industry are the United States, the EU, and Japan. These entities account for seventy-five percent of the world’s pharmaceutical market and generate ninety percent of all pharmaceutical research. Although the goal of drug regulatory agencies in foreign countries, as well as the United States, is to ensure that safe and effective drugs reach the market, these agencies typically act in a unilateral fashion. Differences in the approval process for marketing biotechnology products discourage international competition, to the detriment of both manufacturers and patients. This is because, at present, a new pharmaceutical product must be evaluated, tested, and approved in each potential market before it can be legally sold. Inconsistent international regulations tend to increase costs, both in terms of time and money.

Regulatory authorities worldwide continue to work together to create a more cooperative and complementary system of pharmaceutical regulation. Achievement of this goal is furthered by the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). Established in 1989, ICH is a tripartite effort between the United States, the EU, and Japan to address the regulatory issues of pharmaceutical drugs.

80. Buono, supra note 43. A nation’s competitiveness in biotechnology can be viewed in different ways. Competitiveness can be viewed in terms of who ultimately owns a company, or it can be viewed in terms of where jobs and skills are located. Biotechnology in a Global Economy, supra note 51, at 21. The competitiveness of U.S.-developed biotechnology products is also dependent on other issues such as fair trade practices, protection of intellectual property, and tax policies. Id. at 3.

81. Kanusky, supra note 71, at 667.
83. Buono, supra note 43.
84. Kanusky, supra note 71, at 667.
85. Id.
86. Id.
87. Buono, supra note 43. Although the ICH is open to worldwide participation, the emphasis is on the U.S., the EU, and Japan because of their importance in the biotechnology industry. See Kanusky, supra note 71, at 667. The general goals of the ICH are twofold. One goal is to decrease regulatory problems associated with pharmaceutical manufacturers’ compliance with the differing regulations of the various countries, lower research and development costs for manufacturers, and indirectly lower the cost of drugs to consumers of all countries. The second goal is to increase the safety, quality, and efficacy of pharmaceuticals for consumers of all nations. Joseph G. Contrera, Comment, The Food and Drug Administration and the International Conference on Harmonization:
A harmonized system would enable regulated industries, such as the biotechnology industry, to redirect time and financial resources to product development because of the reduction in regulatory costs. Consumers may also gain from harmonization through increased and earlier access to new medicines.

The formation of the European Medicines Evaluation Agency (EMEA), a centralized agency designed to standardize and accelerate the approval process for certain new drugs, may increase pressure on the FDA to reform. The EMEA will serve as a centralized approval agency and as an oversight body for a decentralized mutual recognition procedure. Through this system, when one EU member state approves a new drug, it will be approved in all member states, unless cause exists for disapproval. Because of this centralization of the European drug review process, the EU will be the largest single market for medicines. Combined with what may prove to be less stringent regulations, the U.S. biotechnology industry may be encouraged to target the EU for first-market approval.

International harmonization, to some degree, is an inevitable and worthy objective as the world progresses towards a more global economy. Various obstacles within the United States, however, currently confront this movement. These obstacles include constitutional difficulties with delegating decision making authority to a foreign government, concerns about safety risks to the American public, and unproven regulatory standards.

89. Id.
90. Note, supra note 2, at 2018.
91. Rutherford, supra note 62, at 221.
93. Rutherford, supra note 62, at 222.
94. It is unclear yet whether the EMEA regulatory scheme is less stringent than that of the FDA. The EMEA seeks “adequate evidence of safety, efficacy and quality” when reviewing drug applications. However, “adequate” and “quality” are not clearly defined and may result in less demanding standards. See Rutherford, supra note 62, at 221. Additionally, some fear that American and European regulatory agencies could decrease regulatory standards in order to gain a competitive advantage. See Note, supra note 2, at 2024.
95. This is essentially an example of the nondelegation doctrine, which could be overcome as long as the FDA retained the final authority to object to, and thereby not approve, specific new products. See Note, supra note 2, at 2022.
96. Again, the fear behind this argument is that the risk of adverse reactions may increase if U.S. decisions about the safety and efficacy of new products are based on decisions made by foreign agencies. See id. at 2024.
cultural and demographic differences between populations.\textsuperscript{97} Any successful future reform must address these barriers.

\textbf{B. Key Players in the Movement for FDA Reform}

Almost everyone has become involved in the recent dispute over FDA reform. The Republican-controlled Congress has acted as a catalyst.\textsuperscript{98} Trade associations have joined the fray in an effort to benefit from the Republican emphasis on deregulation.\textsuperscript{99} The Clinton Administration and the FDA itself have also become involved in an attempt to stave off drastic legislative action. Even consumer groups have become more vocal in critiquing the FDA and proposed reforms.

Neither Congress, nor the Clinton Administration, is particularly capable of developing a rational regulatory policy for biotechnologically derived products because neither has the necessary expertise.\textsuperscript{100} The FDA, on the other hand, has technical competence and familiarity with the specialized subject area.\textsuperscript{101} Growing intolerance with the FDA's ability to self regulate, however, may cause Congress or the Administration to impose new regulatory schemes on the FDA.

The types of reform measures advocated by the various players can be categorized as either incremental or radical in nature. Incremental reform tends to build on the existing structural system, only making slight modifications. This type of reform can be seen in much of the pending legislation as well as in the changes proposed by the Administration. Incremental reforms stand a better chance of being adopted because

\textsuperscript{97} Different racial and ethnic groups may react differently to a new biotechnologically derived product, such that a drug shown to be safe and effective in one population may be less so in another. For a discussion of possible methods of mitigating these concerns with respect to the United States and Europe, see \textit{id.} at 2224–5.

\textsuperscript{98} Green, \textit{supra} note 6.

\textsuperscript{99} In addition to proposing methods of FDA reform, the regulated industries have contributed to members of Congress in an effort to further their cause. The Center for Responsive Politics reported that political action committees or individuals connected to pharmaceutical and health products companies donated more than $1 million to Congresspersons and Senators from January to June of 1995, 70\% of which went to Republicans. Robert Cohen, \textit{Fixing the FDA As Regulators Slow Medical Advances, Republicans Go on Offensive}, San Diego Union-Trib., Jan. 28, 1996, at G4.

\textsuperscript{100} Mostow, \textit{supra} note 43, at 266.

\textsuperscript{101} \textit{Id.} The FDA, as a federal agency, has the ability to formulate its own rules and procedures. Rules promulgated pursuant to § 701(a) of the FDCA are subject only to the informal notice and comment procedures of 5 U.S.C. § 553. Hutt & Merrill, \textit{supra} note 44, at 1245. Regulations, representing legal requirements, and guidelines, representing general principles, comprise the FDA's principal administrative rules. Kanusky, \textit{supra} note 71, at 695–96.
fewer competing interests exist than with dramatic reforms.\textsuperscript{102} Other suggestions for reform, put forth by various conservative organizations, are more radical, seeking to dramatically alter the current system, making it, in most cases, unrecognizable.\textsuperscript{103}

1. Consumer Group Organizations

Consumer groups are important players in the effort to change the regulatory process governing biotechnology products. As these organizations become more active, however, the lack of consensus among the groups concerning the type and degree of FDA reform to promote becomes apparent. Citizens for a Sound Economy, a grassroots organization formed to promote market-based solutions to public policy problems,\textsuperscript{104} believes Senator Kassebaum's bill does not provide enough change with regard to consumer access to drugs.\textsuperscript{105} Their reasoning, based on the FDA's inability to meet the statutory requirements for review times,\textsuperscript{106} leads them to advocate, among other options, a private approval process.\textsuperscript{107} The Patients' Coalition, a group of independent organizations representing Americans with various serious and life-threatening diseases, fears that proposed FDA changes may jeopardize


\textsuperscript{103} A unifying theme of many of the conservative proposals is an almost complete elimination of the FDA's authority to prevent a new drug from reaching the market. The Cato Institute, for instance, advocates restricting the agency to considerations of drug safety, leaving decisions on a medicine's effectiveness to the market. See Daniel Green, Obstacle Course for Drug Producers: Pressure for Reform of the U.S. Food and Drug Administration is Growing, Fin. Times, Aug. 21, 1995. The Competitive Enterprise Institution wants to turn the FDA into an advisory agency, allowing a never-approved drug to be used "pre-label," provided there is consent of the physician and disclosure to, and consent of, the patient. See Bruce Ramsey, Time to Consider Dramatic Change at FDA, Seattle Post-Intelligencer, Dec. 27, 1995, at B4. Under this scheme the drug developer would never have to get FDA approval, though they may seek it for other reasons such as marketing or because certain managed care organizations, or government funded medical programs, require it. The Progress and Freedom Foundation, a think tank associated with Speaker of the House of Representatives Newt Gingrich, wants to privatize the parts of the FDA that oversee drug and medical device testing. See Laurie McGinley, Group with Links to Gingrich Urges Broad FDA Reform, Wall St. J., Feb. 8, 1996, at B6. Under this scheme the drug developer would never have to get FDA approval, though they may seek it for other reasons such as marketing or because certain managed care organizations, or government funded medical programs, require it. The Progress and Freedom Foundation's FDA reform proposal, the FDA would retain final approval for product marketing, but its primary role would be certifying the quality of the private certification bodies. Id.


\textsuperscript{106} Citizens for a Sound Economy Scrutinizes FDA Review Times, supra note 104.

\textsuperscript{107} Rutherford, supra note 62, at 206.
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safety and efficacy standards. They do not support setting arbitrary statutory deadlines, as appear in Senator Kassebaum’s bill. Such deadlines, they fear, would lead to either quick rejection of valuable drugs, or premature approval of dangerous or ineffective drugs. The Patients’ Coalition would rather see the FDA provided with additional resources dedicated exclusively to the agency’s approval process. These consumer groups may influence Congressional decisions, through lobbying, and should not be dismissed lightly.

2. The Biotechnology Industry

The biotechnology industry has been very vocal and aggressive in its attempts to generate FDA reform beneficial to its interests. One trade organization representing the industry, the Biotechnology Industry Organization (BIO), has been especially active in promoting the industry’s point of view. Although it would prefer legislative action creating a more industry-friendly regulatory environment, it is approaching FDA reform from both a legislative and administrative perspective. BIO has drafted legislation with the goal of having it introduced in Congress. The objectives of its legislation include increasing the industry’s ability to rely on agency standards of review, predictability of agency actions, adherence to time limitations, and acceptability of new drugs approved by the EMEA or the United Kingdom Medicines Control Agency.

Although overall the biotechnology industry supports improvement of the FDA regulatory process, different perspectives within the industry

109. Id.
110. The pharmaceutical industry has also been a significant player, namely through the Pharmaceutical Research and Manufacturers Association. See Sweeping FDA Reforms Gain Ground, 21 Health Legis. & Reg., June 7, 1995.
111. Legislation would provide a more reliable framework for the industry to operate within, because it could not be easily altered by future administrations. BIO Welcomes U.S. FDA Proposals, supra note 31.
114. Id. § 8.
115. Id. §§ 6(a)(4)(E), 8, 10 (4).
116. Id. § 10(2).
make cohesion difficult. The industry predominantly supports incremental reform. One reason trade associations are not supportive of dramatic change, such as large scale privatization of the FDA review responsibilities, may be the political unlikelihood of such measures being enacted. BIO, for instance, has stated that it does not support blanket third-party review and does not expect such proposals to be incorporated into legislation enacted in the near future.\footnote{117} Furthermore, it believes that such attempts at privatization of the agency would be too dramatic a change for many Americans, removing the element of acceptability currently found in FDA approved drugs. In its draft legislation, however, BIO advocates privatization of some FDA functions, such as review of a new drug application, where it is effective and efficient to do so.\footnote{118}

Many critics have suggested that established biotechnology and pharmaceutical companies want to retain some of the current FDA structure because of the potential advantages it offers these companies.\footnote{119} Established companies have expended years of effort and money cultivating relationships with the agency and they may use the system to their advantage, blocking smaller, newer companies from competing in the market.\footnote{120} This could be the industry’s rationale behind wanting to avoid extreme change and wanting to maintain the FDA’s stamp of approval for marketing purposes. Many younger biotechnology companies, however, also seek to retain the FDA approval, viewing it as essential in helping them establish an image of safety and credibility.\footnote{121}

The biotechnology industry’s stance on altering the FDA raises the specter of agency capture. Agency capture occurs when a regulated industry, such as the biotechnology industry, is able to use its political influence to force the agency to promulgate regulations that are preferential to the industry and perhaps contrary to the agency’s intended purpose.\footnote{122} The agency itself may be co-opted into acceding to capture. For instance, the FDA wants a vigorous drug industry to maintain its power and jurisdiction.\footnote{123} Additionally, FDA employees may want to work for the companies they are regulating once they leave the agency.\footnote{124}

\footnote{117}{Politics and Policy FDA Reform: Package of Bills to be Introduced in House, 4 APN-HE, Feb. 20, 1996.}
\footnote{118}{BIO Draft Legislation, supra note 113, § 6 (a)(4)(B).}
\footnote{119}{Green, supra note 6.}
\footnote{120}{Id.}
\footnote{121}{Glenn Hess, FDA Overhaul, Chemical Marketing Rep., Sept. 18, 1995, at SR28.}
\footnote{122}{C. Frederick Beckner, III, Note, The FDA’s War on Drugs, 82 Geo. L.J. 529, 540 (1993).}
\footnote{123}{Id. at 543.}
\footnote{124}{Id.}

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The agency, therefore, may choose to promote industry goodwill by altering its regulations to better meet the needs and demands of the biotechnology industry. Currently this does not seem to be a major concern, as relations between the FDA and the biotechnology industry have been adversarial.125

III. ANALYSIS OF PROPOSED REFORM MEASURES

A. Congressional Efforts

There are a number of bills in Congress aimed at FDA reform.126 National attention has been split between Representative Burr's bill127 and Senator Kassebaum's bill.128 Comparisons of these two bills, particularly in terms of their effectiveness in addressing the factors driving the reform movement provide insight into the direction of future reform and the hurdles that will have to be overcome.

1. Senator Kassebaum's Bill

Senator Kassebaum's bill has received much national attention. This bill, the Food and Drug Administration Performance and Accountability Act of 1995, has five major themes and nine distinct titles. The major themes, as stated by Senator Kassebaum,129 include altering the FDA mission statement to facilitate the development and availability of safe and effective products,130 imposing statutory deadlines for agency action,131 authorizing contracting with outside experts for product review under certain circumstances,132 expanding access to investigational new

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125. Hutt & Merrill, supra note 44, at 1240.


130. S. 1477 § 102(1).

131. Id. § 103.

132. Id. § 743(d)(1).
pharmaceuticals and medical devices,\textsuperscript{133} and establishing a collaborative clinical testing and review process.\textsuperscript{134} Because it is comprised of such distinct areas, Senator Kassebaum’s bill may be divided accordingly and voted on separately.\textsuperscript{135}

The reform proposal augments the FDA’s role as facilitator of the process by which the biotechnology industry places their products in the marketplace.\textsuperscript{136} While the bill is advantageous in that it attempts to address many of the problems currently plaguing the regulatory regime for drug and biologic approval, the bill does have potential flaws. Some of the problems apparent in Senator Kassebaum’s bill are the result of good intentions that lack either sufficient penalties or oversight and enforcement mechanisms to ensure that those intentions are implemented.


Although the bill provides for decreasing the time for product approval, it is hampered by the lack of enforcement mechanisms. For example, although the bill would require the establishment of standards for eliminating backlogs,\textsuperscript{137} it offers no good method of enforcement. What is lacking is an entity such as an external, independent performance panel with the power to discipline FDA officials.\textsuperscript{138}

Furthermore, the provision providing for the approval of a new drug in the United States, once it has been approved in the United Kingdom or EU,\textsuperscript{139} is also too relaxed to have significant impact on the agency’s approval process. This provision originally had the potential to increase the speed of approval for such a drug. If the Secretary did not act on an application within thirty days following the expiration of the time period, established in the standard, for a product that had met the marketing requirements of the EU or the United Kingdom, it would be deemed

\begin{thebibliography}{99}
\bibitem{133} Id. Title II.
\bibitem{134} Id. Title III and IV.
\bibitem{135} FDA Reform Should Focus on Consensus Issues First, Rep. Fox Urges House Leadership; Commerce Committee May Produce Several Separate Bills, Pink Sheet, Jan. 8, 1996, at 3.
\bibitem{136} Vogt, supra note 61, at CRS-9.
\bibitem{137} S. 1477 § 103(3)(B).
\bibitem{139} S. 1477 § 743(c)(1).
\end{thebibliography}

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approved by the FDA as well.\textsuperscript{140} In the committee approved bill, the provision was amended so that it only applies to drugs that offer "a significant improvement over existing approved products,"\textsuperscript{141} not to all drugs. Additionally, failure of the FDA to act on such a request would no longer result in the product being deemed approved.\textsuperscript{142}

In other areas where there are mechanisms in place to ensure adherence to the legislative provisions, the emphasis on compliance with statutory guidelines may be misplaced. For instance, the FDA Commissioner, Dr. David Kessler objects to the requirement in Senator Kassebaum's legislation that the FDA act on all new drug applications,\textsuperscript{143} not just those for treating life-threatening diseases, within 180 days.\textsuperscript{144} If the agency does not comply with the statutory deadlines by 1998, it must cede parts of the approval process to private companies.\textsuperscript{145} Kessler predicts that rather than striving to meet the deadline, the FDA will simply deny problematic applications.\textsuperscript{146} It remains unclear, however, whether the use of outside review panels would actually be more effective or efficient than merely hiring more FDA reviewers.\textsuperscript{147}

\paragraph{b. Harmonization Efforts Lack Strength}

The problem of unenforceable provisions also is inherent in how Senator Kassebaum's bill treats U.S. harmonization efforts. Under

\textsuperscript{140} Id. There was, however, a loophole which the FDA could have used to deny such approval. In order for foreign approval to have triggered approval in the United States, the FDA would have had to have already extended its review time beyond its statutory time limit. The approval could have been denied simply by notifying the applicant in writing that the application was disapproved. Id.

\textsuperscript{141} Revised Kassebaum FDA Reform Measure Greatly Scales Back EU/UK Device Approval Allowance; Senate Labor Mark-up Postponed Until Week of March 18, 22 Gray Sheet, Mar. 18, 1996.

\textsuperscript{142} Kassebaum FDA Reform Mark Allows More Discretion For FDA: Supplemental Approvals Based On Expert Opinion Would Be Allowed But Not Required In Latest Bill, 58 Pink Sheet, Mar. 18, 1996.

\textsuperscript{143} Statement by David A. Kessler before the Committee on Labor and Human Resources, United States Senate, Feb. 21, 1996, available in Westlaw 1996 WL 47135603.

\textsuperscript{144} Senator Kassebaum's bill would require the FDA to act within 120 days on applications for new drugs to treat life-threatening diseases or other disorders with no approved treatment. All other FDA regulated products would have a 180 day time line. S. 1477 § 103.

\textsuperscript{145} Id. § 743(d).

\textsuperscript{146} Hearing of the Senate Labor and Human Resources Committee, Changes at the FDA. 104th Cong., 2nd Sess, available in Westlaw 1996 WL 5508818 (statement of Dr. Kessler, Commissioner of the FDA).

section 302 of the bill, the Secretary is required to publish criteria for the type and amount of information relating to the safety of an investigation drug. The Secretary must, however, only take into account the recommendations of the ICH.\textsuperscript{148} This is a very loose requirement, as there is no mechanism to ensure that the FDA seriously considers these recommendations. In section 402 of the bill there is the same vague requirement that the Secretary consider recommendations of the ICH when determining reasonable data requirements for an application submitted to the FDA.\textsuperscript{149}

c. \textit{The Biotechnology Industry Will Seek Additional Reform}

While Senator Kassebaum's bill addresses many of the concerns of the biotechnology industry, the bill still allows for more deference to the agency than the industry feels is appropriate. The biotechnology industry applauds the attempt of Senator Kassebaum's bill to shift the FDA's orientation from that of a gatekeeper to that of a facilitator. However, it is not clear that merely changing the FDA's mission, from one of safeguarding safety and efficacy to one of pro-actively facilitating medical advances, can actually impact an agency steeped in risk aversion.\textsuperscript{150}

The biotechnology industry seeks the submission of less information on drugs and medical products, a reduction in the amount and type of testing required, and specific timetables for FDA responses to applications.\textsuperscript{151} Senator Kassebaum's bill, if enacted, will aid the biotechnology industry in achieving some of these goals. However, as is often the case with incremental reform measures, it will be but a stepping stone in a continuum of reform efforts.

2. \textit{Representative Burr's Bill}

The Drug and Biological Products Reform Act of 1996 has the advantage of specificity, allowing more precision to be incorporated into the bill with less left to be addressed at a later date. Divided into twenty-six sections, Representative Burr's bill differs notably from Senator Kassebaum's in its use of third-party reviewers to reduce approval
time. The House bill, regardless of dedicating a section to harmonization, does not, however, adequately promote international harmonization.

a. The Use of Third-Party Reviewers May Lower Product Approval Costs, But at What Price?

Representative Burr’s bill attempts to decrease the costs associated with bringing a new biotechnology product to market. For example, the bill provides for shorter FDA response periods in areas such as requests to begin clinical investigations and agency response to dispute resolution recommendations. The primary attempt to decrease the cost of product approval, at least in temporal terms, is seen in the option for third-party marketing approval.

Under provisions in Representative Burr’s bill, companies seeking marketing approval could choose to hire third-party reviewers instead of the FDA. These reviewers would be accredited by the FDA, with the FDA retaining final approval authority. However, the use of such third-party reviewers is prone to conflicts of interest. Objectivity will be lost when the future business of an organization, paid to review products, depends on the organization’s previous history of granting favorable decisions.

b. The Section Dedicated to Harmonization Is Ineffective

Section 19 of Representative Burr’s bill, specifically addressing harmonization, suffers from the same vagueness and lack of sufficient enforcement mechanisms as Senator Kassebaum’s bill. The Secretary, under Representative Burr’s bill, is required to participate in meetings with other countries to discuss harmonization efforts. Such a provision, is not, however, particularly demanding or likely to induce serious harmonization efforts.

153. Id. § 3.
154. Id. § 9. The Secretary has thirty days to respond to recommendations, otherwise the recommendations of the person or panel are deemed to be those of the Secretary. Id.
155. Id. § 7.
156. Id. § 8(a).
157. Id.
158. Id. § 7.
159. Id. § 19.
The Biotechnology Industry Is Likely To Favor Burr's Bill

The option of seeking third-party market approval may be desired by members of the biotechnology industry. Such a system could increase the speed with which biotechnology products are reviewed. The discretion allowed by this provision to the company seeking market approval may enable the biotechnology industry to achieve faster approval times without sacrificing the element of public trust derived from the FDA stamp of approval.

B. Reform Promoted by the Clinton Administration and the FDA.

As efforts to enact legislative reform of the FDA have intensified, administrative solutions have been proffered in an attempt to prevent radical reform by Congress. The Clinton Administration, through Vice President Gore's "Reinventing Government" program for streamlining the federal bureaucracy, has announced regulatory reforms aimed at simplifying the FDA regulations. At least two of these reforms have been directed toward the FDA's treatment of biotechnology products. These reforms are intended to ease the manufacturing requirements, allow for development of a pilot program to experiment with third-party review of low to moderate risk medical devices, and harmonize the FDA's drug and device testing requirements with those of other countries.


162. In April of 1995, the White House released a National Performance Review by President Clinton and Vice President Gore describing a 13-point plan for reinventing drug and medical device regulation. Clinton, Wyden Offer FDA Reforms; Several Match BIO Recommendations, supra note 5. Another plan, "Reinventing the Regulation of Drugs made from Biotechnology," was issued in November 1995. Rhein, supra note 5. A third plan introduced by the Clinton Administration serves to increase the speed with which cancer drugs, potentially products of biotechnology, are approved. Politics & Policy FDA: To Speed up Cancer Drug Approval Times, 4 APN-HE. Mar. 29, 1996.

163. More specifically, the plans would allow manufacturers of drugs and biologies to, under certain circumstances, change the way they manufacture an approved drug without prior authorization from the FDA, and would allow manufacturers of biological drugs to get licenses for pilot facilities instead of requiring them to build full-scale manufacturing plants. Clinton, Wyden Offer FDA Reforms; Several Match BIO Recommendations, supra note 5.

164. Id.

165. Id. One recent plan, "Reinventing the Regulation of Drugs Made from Biotechnology," would, among other things, eliminate the requirement for establishment license applications for "well-characterized therapeutic biotech drugs," and eliminate FDA's lot-by-lot release for such drugs. Rhein, supra note 5.
The FDA, while actively participating in the incremental reforms proposed by the Clinton Administration, stresses that it can meet Congress' expectations on its own without radical FDA reform. Many critics, however, think that by instituting self reform, the FDA has shifted the focus of debate from the question of whether reform is necessary, to how far the reforms will go.

Many commentators have questioned whether administrative solutions are legally adequate or desirable, because such approaches tend to be more susceptible to the whims of changes in administration. Legislative solutions, although even more political in nature, may be the only relatively permanent and legally defensible option because legislation is more difficult to overrule and subject to greater input from the affected parties.

IV. CONCLUSION: THE FUTURE OF THE FDA

Any effective emerging FDA reform must balance the industry's interest in time and cost efficiency, the government's interest in assuring the safety and efficacy of new products, and the public interest in access to new potentially life-saving, yet safe and effective products. FDA reform, however, has become such a contentious issue, with so many players, that is difficult to predict a precise outcome, let alone recommend one.

Numerous problems await FDA reformers. One problem is the simple fact that the general public does not perceive a crisis in drug approval so there is no populist groundswell for systemic change. Yet congressional interest has been increasing, as demonstrated by the growing number of bills which have been introduced. This surge in congressional activity, however, may be too late. Election year politics may stymie any comprehensive reform movement. It is unlikely the

167. Green, supra note 6. The FDA Commissioner, Dr. David Kessler, objects, however, to the proposals that the FDA contract out portions of the drug approval process to private companies. Kessler Says Some FDA Reforms Could Slow Process, Cong. Daily, Feb. 21, 1996. Kessler fears contracting out will result in problems with conflicts of interest, inconsistency of reviews, and potential disclosure of proprietary information. Hearing of the Senate Labor and Human Resources Committee, Changes at the FDA, supra note 146.
168. Korwek, supra note 4, at 150.
169. Id.
170. Henderson, supra note 79.
momentum which has been generated can rapidly resolve the conflict between the House and Senate bills, or result in the passage of a bill acceptable to President Clinton.

Regardless of the outcome of the presidential election, the movement for FDA reform will reemerge in 1997, following the election. Consumer groups, with a large and tangible stake in the outcome, may provide some of the momentum necessary to make FDA reform an important issue in the years following the 1996 Presidential election. Economic pressures and the ever increasing business stakes of the biotechnology industry will also contribute significantly to the momentum for reform.

Regardless of the status of the Kassebaum and Burr bills at the end of this year, the controversy concerning FDA reform as it pertains to the biotechnology industry illustrates what some of the objectives and goals will be for future reform efforts. Foremost among these goals is the fundamental need to decrease the time and cost of product approval and increase the United States' involvement in international harmonization. It is important, therefore, that the law be flexible and applicable to new, rapidly developing biomedical technologies. Until these goals are realized, the FDA will remain unacceptably cumbersome and unresponsive to the ever changing advances of the biotechnology industry.