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FOREWORD

BIOTECHNOLOGY BUSINESS STRATEGY: A LAWYER'S PERSPECTIVE

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INTRODUCTION

Since the dawn of time, people have pondered which came first: the chicken or the egg. In biotechnology business planning, the analogous debate might focus on which must come first strategically: patents and proprietary rights issues or regulatory strategy for FDA approval. At least insofar as any attempt to analyze the problem quickly becomes hopelessly circular, the analogy to the chicken and egg holds up. Of course, without a strong patent position and proprietary rights to the technology being developed, no significant investment in the project can be justified. On the other hand, without a clear and plausible regulatory strategy to FDA approval for a significant market, no significant investment in the project can be justified. Furthermore, a company's patent strategy must accommodate its regulatory strategy. It is important to protect, if at all possible, the use of your technology in particular indications for which approval might be sought.[1] Thus, both patent strategy and FDA strategy are essential, and must fit

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1. For example, Acme Biotech may have filed an application for a newly discovered growth factor, which covers the composition of matter itself. Sometime later, it is discovered that this particular growth factor is essential for the differentiation and maturation of dopaminergic neurons, a cell-type that is central to and deficient in persons with Parkinson's disease, making Parkinson's an attractive first target (in FDA parlance, "indication") for the company's research and development plan. It is not only possible, but essential to file an additional patent application claiming a method for treating Parkinson's disease with the growth factor. This not only prevents anyone else from making the same discovery independently and potentially gaining patent rights in the U.S. or elsewhere that would block Acme from using its own compound for that indication, but also would start a new twenty-year patent term from the date of the second application, thereby extending the Acme's period of patent protection, at least for that new indication.

together. The intrinsic importance of patent and FDA issues to the biotechnology industry provided the impetus for the Twelfth Annual California Biotechnology Conference, which brought together an international panel of experts to discuss their views of recent developments in those crucial areas. That is why I am especially pleased to provide a foreword to this symposium focused on two cornerstones of today's biotechnology industry, patents and the new drug approval process of the FDA, and to provide some of my own "lawyer's view" of strategic planning for biotechnology.

Section I of this Article is a brief analysis of the market issues in the biotech business plan. Section II extends the analysis of market issues in relationship to regulatory strategy. Section III provides a synopsis of the financing issues that are involved in planning for a new biopharmaceutical in the context of a small dedicated biotechnology company,[2] as well as the interplay between financial strategy and other strategic issues. Section IV completes the overview of the process of developing biopharmaceuticals, with particular emphasis on the issues raised by the contributors to this symposium.

I. DEFINING AND CHOOSING A MARKET: THE ROLE OF THE FDA AND REGULATORY STRATEGY

Most business plans, whether for a cookie franchise or an Internet software venture, begin with an effort to predict the potential market for the potential product. For many products, this can be very difficult to ascertain. For most biotechnology-based health care products, the task of determining the size of the potential market is actually somewhat easier than predicting how many people will buy a new flavor of ice cream. This is because the market for most biotechnology products is determined by the disease or health-related condition for which the product might be used. In most cases, reasonable data as to the number of patients per year with a particular disease is readily available, whether for the U.S. market, the European Union member states, or Japan. In the United States, the Center for Disease Control is a major source of such epidemiological data. There are also patient advocacy groups that have fairly accurate data on the numbers of patients suffering

2. "Dedicated biotechnology company," or "DBC," is a term used to refer to small and emerging companies that have been founded with the exclusive intention of developing and applying biotechnology to produce a new product or products. Since biotechnology's techniques are now used throughout the pharmaceutical industry, as well as other industries such as agriculture, the term DBC is particularly useful in distinguishing small, exclusively biotechnology-focused companies from larger, well-established companies such as large pharmaceutical companies, that have now begun to incorporate biotechnology into their research and development. Business planning for a DBC involved in developing a new biopharmaceutical is, necessarily, significantly different than it is for a large pharmaceutical company such as Merck or Pfizer. Such large companies are easily able to finance development of new products from existing revenues, whereas DBCs generally are financed piecemeal, over time, with the status of the next planned funding always dependent on the success of the prior stage of development. It is impossible to overstate the significance of these funding constraints for the DBCs, particularly for strategic planning.

from a wide range of diseases. However, the role of the potential market variable in strategic planning for a new biotech product differs from market considerations for a consumer product in two very important ways.

The first difference is that the market for a biopharmaceutical or diagnostic is more or less legally restricted to the precise use indicated on its product label[3] for which the FDA approved its marketing. Thus, a drug's label might state, for example, that it is indicated for use in the treatment of relapsing/remitting multiple sclerosis; or, alternatively, it might state that it is for use in the treatment of all forms of relapsing multiple sclerosis (a more broadly inclusive patient population than the former indication). Whereas a cookie baker may try to entice absolutely anyone to buy his wares, whether to eat as a snack or to break up and to use in a pie crust, a manufacturer of a new drug may not promote the use of its product for any indication which the FDA has not approved for its labeling.[4] Thus, even though it is perfectly proper (and commonly done) for a physician to prescribe a drug for a condition for which it has not been approved,[5] in most cases the market for a drug will be restricted to some share of the patient population with the indication for which FDA approval is obtained.[6]

II. REGULATORY STRATEGY (MARKETS AND PLANNING FOR THE FDA)

The second major difference between market analysis for a biotech strategic plan and that for other types of goods is that, unlike a business plan for most consumer products, which would assume that the bigger the potential market the better, making a similar assumption for a biopharmaceutical is often a mistake. The reason is that for biopharmaceuticals, different markets can require substantially different development costs, both in development time and in actual dollars expended on direct development costs. Most

3. Actually, "package insert" is more literally correct.

4. This particular position of the FDA is quite clearly set forth in the Draft Policy Statement on Industry-Supported Scientific & Educational Activities, 57 Fed. Reg. 56,412 (1992). It is reiterated by the FDA in Citizen Petition Regarding the Food & Drug Administration's Policy on Promotion of Unapproved Uses of Approved Drugs & Devices; Request for Comments, 59 Fed. Reg. 59, 820 (1994), which also reveals some of the important dimensions of the controversy surrounding this stance by the FDA. It has not, however, been statutorily codified, nor has it been the subject of a notice-and-comment rule-making by the FDA. *See* Boulding, *The Statutory Basis for FDA Regulation*, 4 J. PHARMACY & L. 123 (1995).

5. For example, prescribing human growth hormone for an extremely short child who is not suffering from a hypopituitary shortage of endogenous growth hormone, so that in some cases the market for a drug may in fact significantly exceed the total patient population for which it has been approved.

6. The ultimate share of the patient population that a drug will achieve will, obviously depend on its advantages over other therapeutics and its price, as well as other factors. However, for a breakthrough drug, that is one that offers significant efficacy for a serious disease which currently has no effective therapy, which is the goal that drives most biotechnology companies, the likely actual market for the drug may optimistically, yet reasonably, be conceived of as 60% or more of the patient population a few years after product launch.

biotechnology companies are in the research and development phase, spending significant amounts of money without yet having a product on the market, let alone earning a profit. Therefore, it may well make more sense to embark on a four-year, $25 million effort to win approval to enter a $100 million market, than to work on a six-to-eight-year, $120 million effort to enter a $500 million market.

These kinds of time and money differences can exist even when the same compound could be developed for multiple indications. For example, a company might have developed a compound which seems to have potential for protecting neurons from the damage which occurs in such differing neurodegenerative diseases as Parkinson's disease and Alzheimer's disease. An example is a neurotrophin, such as GDNF.[7] Of the two diseases, Alzheimer's is by far the larger market. Nevertheless, Parkinson's may well be the preferable clinical target because a variety of clinical considerations make Alzheimer's a much more difficult and expensive target, even if the compound ultimately works.

Alzheimer's is a very slowly progressing disease, with a highly variable course that can take from one to five years or more from diagnosis to a nearly complete loss of cognitive function.[8] Trials must therefore follow patients closely for a very long period of time, probably eighteen months to two years,[9] in an attempt to measure significant differences between the patients' rate of loss of function in the treatment group versus the control group.[10] Additionally, the extreme variability in the rate of progression

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7. *See e.g.*, Moore, Klein, Farinas, Sauer, et al.; *Renal and Neuronal Abnormalities in Mice Lacking GDNF*, NATURE, July 4, at 76-9, abstract *available in* LEXIS, Medline library (suggesting that glial-derived neurotrophic factor (GDNF) could be "considered a potential therapeutic agent for Parkinson's disease, amyotrophic lateral sclerosis, and Alzheimer's disease").

8. *See e.g.* Kraemer, Tinklenberg, Yesavage, *"How Far" vs. "How Fast" in Alzheimer's Disease*, 51 ARCH. NEUROLOGY. 275-9 (Mar. 1994), abstract *available in* LEXIS, Medline library.

9. Morris, Edland, et al., *The Consortium to Establish a Registry for Alzheimer's Disease (CERAD), Part IV. Rates of Cognitive Change in the Longitudinal Assessment of Probable Alzheimer's Disease*, 43 NEUROLOGY 2457-65 (Dec. 1993)(". . . there is need for an accurate analysis of large numbers of persons with the disorder studied over long periods. . . . We found that rate-of-change determinations are less reliable when the observation period is 1 year or less, that dementia progression may be nonlinear when described by certain measures, and that simple change scores do not accurately characterize the rate of decline.") (quotation from abstrasct *available in* LEXIS, Medline library).

10. A difference in the rate of disease progression, rather than a measure of improvement over time, would be the goal in any Alzheimer's disease trial that is now foreseeable for such neurotrophins as GDNF. Alzheimer's disease is produced by the death of neurons involved in cognitive functions. Once dead, the neurons and their functions cannot be restored with any technology that is now within the realm of contemplation. At best, a treatment would completely arrest the progression by preventing any more neurons from dying, or, more likely, slow the rate of further neuronal death. This having been said, however, the only currently approved drug for Alzheimer's (trade name Cognex, composition name tacrine) is designed to improve function over placebo on tests of cognitive functioning, primarily by getting a bit more action from the remaining neurons while the drug is active, in much the same way that a non-Alzheimer's patient may do better on some short-term memory tests after a small dose of caffeine or other stimulant. In our hypothetical, GDNF would not be likely to act via short-term stimulation, but rather by

among patients makes larger groups necessary to provide statistical significance to the differences between groups in order to overcome the random "noise" of the underlying variations which can mask the treatment's effect in smaller groups.[11]

Parkinson's disease, on the other hand, progresses differently. Though the disease itself is caused by a progressive loss of dopamine-producing neurons of the substantia nigra region of the brain, at least in the earlier stages of the disease, the loss of function is reversible if the dopamine levels in the affected areas of the brain are raised. Thus, a treatment for Parkinson's that results in sufficient endogenous dopamine production either from a new source[12] or from protection and stimulation of the remaining dopaminergic neurons of the substantia nigra could result in the improvement of Parkinson's patients, rather than a mere slowing of the disease's progression. As a result, one would expect that an effective Parkinson's therapeutic would make its effect clear in a smaller group of patients and over a shorter period of time.[13]

For example, assume that the time from initial animal tests to FDA approval for an Alzheimer's indication will be eight years, with clinical trials on two thousand patients for Phases II and III combined, and a per patient cost of $12,000.00.[14] This Alzheimer's market entry will carry with it direct clinical trial costs of $24 million. We might also estimate that the time to FDA approval for a Parkinson's indication will be six years, with a total of 1000 patients for Phases II and III combined, and a cost of $6000 per patient or $6 million in direct clinical costs. For most biotech companies, the shorter and cheaper route to an approved Parkinson's indication makes much more sense; this is true even if the ultimate annual sales never exceed $300 million rather than the approximate $1.5 billion an effective Alzheimer's drug might command. After all, the profits on the first indication (and the money that can be raised as its likelihood of success increases) can easily fund the longer, more expensive effort to enter the larger market. The choice of the initial

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actually (potentially significantly) slowing the rate of neuronal death over a long period of time, requiring a clinical trial to show differences in rates of change over time, rather than short-term improvements in cognition over placebo.

11. *See supra* note 5.

12. For example, the sometimes successful efforts to transplant fetal neurons into the brains of Parkinson's disease patients.

13. A cinematic depiction of the dramatic effect (although it is unfortunately short-lived) of medication on advanced Parkinson's disease is the film *Awakenings* based on the book of the same name by neurologist Oliver Sachs.

14. This discussion assumes that which is generally true, *i.e.* that longer clinical trials not only are more expensive by virtue of the continuing indirect costs (rent, depreciation, patent life amortization, general payroll, etc.) that are consumed during the trial, but also in direct costs. This is generally true because the longer trials typically require a proportionately greater number of patient observations, laboratory analyses, and physician examinations. If, for example, the protocol requires blood to be drawn from each patient every month for complete analysis, a two-year trial requires 18 more such tests than a six-month trial. The same logic affects each of the major components of direct clinical costs. Additionally, the more data, the more difficult and expensive the process of data analysis and FDA filing.

target then helps define not only the product development pathway, but goes a long way towards defining the financing pathway.

III. FINANCING BIOPHARMACEUTICAL DEVELOPMENT: CONSIDERATIONS AND STRATEGY

The development pathway and initial target provide the three key parameters that drive financing: (1) the anticipated development costs, (2) the anticipated revenues, and (3) the timing of developmental milestones. The first two, anticipated revenues and market share, together with the estimated per unit price and rough cost, give an annual figure for gross profits that is the key variable in determining the rate of return on varying levels of prior investment. Thus, the business plan should demonstrate to the venture capitalist providing early funding and the investment bankers providing later-stage financing, that the well-thought-out first indication will translate into an adequate return on the investments required to pay the development costs.

For the third variable, the timing of development milestones, the criteria for initial public offerings or major corporate partnerships change over time (from early phase development on the one extreme to positive Phase II data with Phase III commenced on the other extreme). Even so, the milestones that are penciled in for the first indication can be prospectively equated with financing benchmarks. A plan that involves commencing Phase II trials within 24 months allows the inference that a major venture round or financing commitment from a corporate partner could be closed prior to Phase II trials if no adverse results are produced in Phase I or a Phase I/II. Similarly, positive Phase II data should certainly be enough to bring a strong possibility of an IPO.

The corollary of all this is, of course, that given the estimated expense of development as it is projected forward in time, each preceding investment or investments must be sufficient to carry the company to the next development phase and its accompanying opportunity for new money. Thus, the lawyer who is assisting in the negotiation of a venture capital financing or a corporate partnering/licensing agreement for a biotechnology company will not only need to understand the milestones provided for in the particular agreement, but must also understand that round of financing's place in the overall structure of product development. Although plans are inevitably subject to change due to a variety of unpredictable circumstances, management, with the assistance of legal counsel, needs to develop and revise on an ongoing basis an overall plan for financing the company through to profitability. An example of such a plan as it might look at the very beginning of development appears in Figure 1.

One of the greatest challenges for the emerging biotechnology company and its legal counsel is to integrate its intellectual property and regulatory strategies with its financial plan. This effort at long-range planning is complicated by two keys facts. First, the actual marketability to pharmaceutical company partners of particular development milestones (such as

completing a Phase I study) will vary with the cycles of the pharmaceutical companies' need for products and the general stock market conditions for biotechnology. Second, however, the marketability will also need constant and sometimes major adjustments as product development provides new opportunities and disappointments.

For example, let us assume that CURALL Biotech, the company depicted in Figure 1, is developing a technology based on monoclonal antibodies. The competitive advantage of this technology is that it targets a proprietary antigen (antibody target) which is a variant cytokine (inter-cellular messenger, usually a growth factor) receptor found on the surface of cancer cells, but not normal cells. The antibody binding to the target prevents the regular messenger from binding to the receptor. It also stimulates the immune system's response to the target cells (a regular function of antibodies) because deprivation of the cytokine signal shuts down the cell's proliferative pathway and slows the growth of the cancer cells by an additional route.

Based upon this brief synopsis of the technology, proprietary rights might be sought for the purified and isolated receptor protein, assuming that the variant found on cancer cells was not previously known. Propriety rights would also be sought for the gene sequence encoding the variant receptor, methods of making the receptor protein, the use of the receptor as a screen for small molecules that might be effective anti-cancer agents, antibodies targeting the receptor and their use in cancer therapy, and particular antibodies that have been identified as particularly useful because of their affinity and specificity.

The strategic issues of relating these proprietary rights to regulatory strategy and financing goals can be appreciated after a brief look at the initial technology and its possible development paths. Assume that the first antibodies are chimeric antibodies. These antibodies are made by combining the genes for the antigen-binding (variable) regions of an original mouse antibody to the receptor with the genes for the constant regions of a human Ig G antibody in Chinese Hamster ovary cells. This then produces the mouse-human chimeric antibody. Possible results of CURALL's research and development may include a second-generation antibody that is fully human in its genes for both variable and constant regions.

FIGURE 1A

The initial business plan for financing a new biotechnology company (CURALL Biotech) to develop proprietary therapeutics for treating cancer.
Initial Product Target (CA122): Dukes' B colon cancer, adjuvant to surgery and standard chemotherapy.
Second Product Target (CA945): Advanced Ovarian Cancer (with second indication breast cancer).

ANTICIPATED DEVELOPMENT COSTS AND TIMES:

Years	Costs	Milestones
1-3	$4 million	Identification of First Lead Compound (CA122), initial screening, preliminary work on identification of second lead:
2-5	Additional $15 million for years 4 and 5	CA122 completion of Phase I/II and Phase II(a) on CA122 CA945 complete toxicology and Phase I
6-8	Additional $40 million (Year 9 product launch and profit)	CA122 Complete Phase III and file NDA ($20 million) CA945 Complete Phase II and initiate Phase III $10 million Other Projects at that point: $10 million

TOTAL CASH THROUGH YEAR 8: MINIMUM OF $60 MILLION

FIGURE 1B

ANTICIPATED FUNDING AND TIMING

Funding	Year	Milestones
$4 million (venture capital)	1 (initial funding)	Identification of lead compound; successful completion of animal model, initial non-GLP toxicology
Second Round	Beginning of Year 3	$4 million venture capital. Milestones: Completion of Phase I/II
Third Financing	End of Year 3	Corporate Partnership: European and North American Rights to first compound in all cancers. Licensing Fee, Equity, Milestones. Full Directs Cost of Further Toxicology, Clinical Trials and Regulatory Submissions. Cash over costs (from partner): $4 million in first two years, ($15 million additional by year 5)
Fourth Financing	End of Year 4	$25 million IPO
Fifth Financing	End of Year 6	$25 million secondary offering

TOTAL FINANCING ANTICIPATED THROUGH YEAR 8: $77 MILLION (Hurray!)

Efforts might also be directed to the development of a cancer "vaccine" that uses the receptor protein with a vaccine "adjuvant" (or some other method that stimulates a strong immune response to the variant receptor) and thus, theoretically, to cancer cells which display the variant receptor protein. Still other research efforts might be directed to synthesizing or screening for small molecules that also bind to and inhibit the receptor. Other efforts may seek to make antibody fragments that bind to the receptor and inhibit the binding of the cytokine (but do not stimulate immune function), or antibody fragments that are linked to a toxin such as ricin. Such fragments would replace the antibody's immune system response potential with a cytotoxic chemical function.

All of these possibilities are being considered and juggled with some development opportunities selected for initial exploration. We will also eventually learn much about the particular cancer targets, the responsiveness of each cancer type at different stages, and the effect of using the antibody, its second or third generation alternatives (fully human, small molecules, antibody fragments, and so on), or the receptor-based vaccine, in conjunction with traditional therapies and surgery. As the second or third generation compounds are developed, they will generate additional proprietary rights that will need to be pursued. If the company is successful in generating sufficient venture capital to take the first-generation antibody through a relatively successful Phase I/II trial, the model in Figure 1 suggests that the time would be right for a corporate partnership, giving up the rights to the first-generation antibody in exchange for cash and development funding. It is, however, likely that the partner will want rights to some of the potential additional technology that can be developed as well.

It is at the stage of this initial corporate partner negotiation that the strategic issues of proprietary rights, financing, and regulatory strategy become urgent. At the same time, these issues reveal their complexity. How can the (hopefully ever-) increasing bundle of proprietary rights be allocated between CURALL and its first partner? What can CURALL keep for itself and what should its own development priority be? What problems might arise if the line between meum and teum (CURALL and partner) is not sharp enough to avoid conflicts of interest and ultimately competition?[15] There are no hard and fast rules that can guide the strategy and the negotiation; but it is clearly essential to have a good grasp of the technology, its development costs for different kinds of compounds and different indications (particularly with respect to obtaining FDA approval), and the scope of available intellectual property protection.

15. For the classic example of litigation arising out of a biotech pie too finely cut, see Ortho Pharm. Corp. v. Amgen, Inc., 887 F.2d 460 (3d Cir. 1989).

IV. CONCLUSION: CURRENT ISSUES IN THE LIFE CYCLE OF BIOTECHNOLOGY

This brief look at the lawyer's perspective on biotechnology business planning underscores the importance of patent predictability, as well as FDA predictability, in any biotechnology business strategy. The past 18 months have been exceptionally noteworthy for the biotechnology industry generally and for developments in biotechnology law. The transition to a world-wide intellectual property regime within the framework of GATT, the resolution of the controversy over the utility requirement in biotechnology patent applications for potential therapeutics, and a major effort at changing or reforming the FDA's regulatory process were just some of the major developments that led to the planning for the conference upon which this symposium is based. The debate between Dr. Edward Penhoet[16] and Commissioner Bruce Lehman[17] over the GATT-imposed changes in the duration of patent protection dramatically illustrates the importance of patent term protection for the biotechnology company. Eileen McMahon's symposium contribution[18] underscores the significance of the international dimensions of these intellectual property issues.

In terms of biopharmaceutical development strategy from the lawyer's perspective, it is clearly important to get into the marketplace sooner, with a greater patent term remaining—even to the extent of influencing, if not dictating, the choice of initial target indication for a biotechnology company's lead compound.[19] At the same time, any examination of the issues in planning for a biotechnology company also reemphasizes not only how important it is for the FDA to act swiftly, but also how important it is for the FDA to provide companies with enough information about the requirements of prospective clinical trials to enable companies to make appropriate decisions about alternative development pathways.[20]

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16. Edward Penhoet, Ph.D., *Science & Technology Policy: A CEO's View*, 33 CAL. W. L. REV. 15 (1996) (this volume).

17. *See* Bruce Lehman, *Major Biotechnology Issues for the U.S. Patent and Trademark Office*, 33 CAL. W. L. REV. 49 (1996) (this volume).

18. Eileen McMahon, *NAFTA and the Biotechnology Industry*, 33 CAL. W. L. REV. 31 (1996) (this volume).

19. The patent term extension provisions of 35 U.S.C. § 155(A) to § 156 partially mitigate the effect of the period of time necessary to test and obtain approval for new drugs, as only one-half of the testing time can be credited and the total credit (one-half testing time and all time from NDA filing to approval) is capped at a maximum of five years. Thus, every year of additional time in the clinic can extend a patent term a maximum of six months.

20. It is, of course, always possible that new information or understanding about a disease will necessitate changes in regulatory requirements for clinical trial data. For example, as continuing research into AIDS has increased our understanding of the dynamics of the disease, it is both natural and appropriate that the FDA require that clinical trials measure viral load as well as CD4 counts. However, absent such significant changes in the basic understanding of a disease, once the company and an appropriate FDA official have agreed that in a Parkinson's trial the principal measurement will be clinical measurements of muscle strength, flexibility, and function, it is simply devastating to have the NDA rejected because the reviewer felt that NMR

The symposium contributions by Dr. John Ashworth[21] and Dr. Martine Kraus[22] provide significant insight into the importance of regulatory speed and consistency. Dr. Ashworth's article looks at the role of regulation in an extraordinarily informative examination of the range of cultural and political variables that have contributed to the relative lag in biotechnology development in the countries of the European Union (EU). Dr. Kraus's article is based upon her detailed case studies of how the regulatory process in the EU and the U.S. affect the availability of pharmaceuticals and the cost of pharmaceutical development.

While Ashworth and Kraus provide an illuminating picture of the recent or current state of regulation and other factors in the EU and U.S., the articles by Lynne Lawrence[23] and Greg Simon[24] are significant contributions to the debate about the future of FDA regulation in the United States. Particularly noteworthy is the significant bipartisan effort that Ms. Lawrence describes, led by Senator Kassebaum for the Republicans and Senator Mikulski for the Democrats, to bring about significant changes in the FDA's statutory authority and requirements. It is equally noteworthy to observe the remaining fundamental differences between the Mikulski-Kassebaum approach to FDA reform and the Clinton Administration's response, as set forth in Greg Simon's article.

Since the symposium, Senator Kassebaum has retired, President Clinton has been reelected, and the 104th Congress has adjourned without addressing FDA reform. The issue is almost certain to arise in the next Congress however, and there can be no doubt of its significance for the biotechnology industry.

Finally, I would be remiss in this lawyer's perspective on biotechnology if I did not acknowledge that, despite the sound and fury over patents and FDA approval procedures, the most fundamental role that the federal government plays in the development of biotechnology is not at the point of commercial inception, through a sound system of intellectual property protection; neither is its most important role played during the long process of commercialization by laws and policies which promote a healthy investment climate; nor is it at the point of market entry, through approval by the FDA, or even after market entry, through the Health Care Financing Administration's reimbursement of Medicare and Medicaid expenses for patient's use of biotechnology products. Rather than all of these areas, in

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data on neuronal deterioration should have been supplied.

21. John Ashworth, Ph.D., *Development of the European Biotechnology Industry*, 33 CAL. W. L. REV. 83 (1996) (this volume).

22. Martine Kraus, Ph.D., *A Comparison of Drug Approval at the FDA and the CPMP*, 33 CAL. W. L. REV. 101 (1996) (this volume).

23. Lynne Lawrence, *Moving Science and Technology Policy Forward: The Role of Congress*, 33 CAL. W. L. REV. 73 (1996) (this volume).

24. Greg Simon, *FDA Reform: The White House View*, 33 CAL. W. L. REV. 109 (1996) (this volume).

which law and lawyers play a significant role, the greatest contribution of the federal government to the development of biotechnology is through the agency that is least staffed by lawyers and least bound up in administrative procedure: the National Institutes of Health (NIH).

Federal funding of research in molecular biology, biochemistry, and molecular genetics, primarily by the NIH, is unquestionably the driving force behind the growth of the biotechnology industry and United States' preeminence in biotechnology. As Dr. Floyd Bloom's symposium contribution on U.S. science policy[25] makes painfully clear, our commitment to basic science and a continuation of a science policy that supports basic research is of vital importance.

25. Floyd Bloom, M.D., *Science and Technology Policy: A Scientist's View*, 33 CAL. W. L. REV. 63 (1996) (this volume).