

A Guide To
**BIOTECHNOLOGY
FINANCE**

2009 Supplement

A Collaborative Effort

Minnesota Department
of Employment and
Economic Development

LINDQUIST&VENNUM^{LLP}

A Guide To BIOTECHNOLOGY FINANCE –2009 Supplement is available without charge from the Minnesota Small Business Assistance Office, 1st National Bank Building, 332 Minnesota Street, Suite E200, St. Paul, MN 55101-1351; (651) 556-8425 or 1-800-310-8323 toll free, Email: deed.mnsbao@state.mn.us; or from Lindquist & Vennum, 4200 IDS Center, 80 South 8th Street, Minneapolis, MN 55402, telephone 612-371-3211.

**A Guide To
BIOTECHNOLOGY
FINANCE**

2009 Supplement

A Collaborative Effort

**Minnesota Department of Employment and Economic Development
Lindquist & Vennum P.L.L.P.**

Copyright © 2009 Minnesota Department of Employment and Economic
Development and Lindquist & Vennum P.L.L.P.

ISBN 1-888404-40-X

TABLE OF CONTENTS

I. Introduction.....	1
How to Use This <i>Supplement</i>	1
What is “Biotechnology”?	1
A Word About Terminology	2
Footnotes and Endnotes.....	2
Contributors	2
Legal Advice.....	3
II. Overview of Biotechnology Finance	4
A Shift in Financing Options.....	4
Changes in the Law and Their Effect on Biotechnology Finance.....	5
Looking Ahead	5
III. Biotechnology Finance Options.....	7
A. Strategic Alliances	7
Reducing Risk.....	7
Collaborations Between “Big Pharma” and Start-Up Biotechs	9
Global Opportunities	9
Collaborations with Academic Institutions.....	10
B. Mergers and Acquisitions	11
Motives for Mergers and Acquisitions.....	12
Structuring the M&A Transaction	15
Professionals in the M&A Process	23
Confidentiality Agreements, Term Sheets, and Letters of Intent.....	24
Due Diligence	26
Timing of Closing and Pre-Closing Considerations	29
Integration and Planning for Success	31
C. Private Capital Formation.....	31
Improving Corporate Governance	34
Protection of Intellectual Property.....	36
D. Public Capital Formation.....	38
Introduction	38
Recent Trends in Biotechnology Public Offerings	38
Should the Biotechnology Company Go Public?.....	38
Advantages to the Biotechnology Firm in Becoming a Public Company	39
Disadvantages to the Biotechnology Firm in Becoming a Public Company	41

Preparing the Biotechnology Firm for an Initial Public Offering.....	42
Underwriters	44
Offering Publicity	46
The Registration Statement Process and the Offering	46
Listing Requirements.....	48
Closing the Offering	49
Periodic Reporting Requirements.....	49
Sarbanes-Oxley.....	52
Timely and Adequate Disclosure of Corporate News	52
Requirements of Officers, Directors and 10% Shareholders	53
Individual Sales of Shares	53
Other Public Financing Alternatives and Transactions.....	54
PIPES.....	55
E. Debt	57
Introduction	57
Cost of Credit.....	57
Corporation Formation Documentation.....	58
Note	58
Security Agreement	58
Subordination Agreement	59
F. Federal Grants Through SBIR/STTR Programs.....	59
IV. Business Factors That Influence Biotechnology Finance	61
A. Management Equity Incentive Compensation.....	61
Background of Internal Revenue Code Section 409A.....	61
What Section 409A Requires	61
Effect of Section 409A on Equity Grants.....	63
Valuation Methods to Exempt Options from Section 409A	64
Effect of Section 409A on Bonus Plans	65
Effect of Section 409A on Severance and Change in Control Payments	66
Outstanding Equity Grants in a Down Round of Financing or a Down Market.....	67
Exchanging Options for Options	70
Exchanging Options for Restricted Stock	70
Exchanging Options for Cash.....	70
Incentive Bonus Plans in a Down Market.....	72
B. Intellectual Property Rights	73

Patents.....	76
Copyrights	95
Trademarks	97
Trade Secrets	99
C. Distress Stage	101
Recapitalization	101
Forced Foreclosure	102
Friendly Foreclosure.....	102
Bankruptcy Section 363 Sale.....	103
Benefits of Section 363 Sale.....	103
Disadvantages of Section 363 Sale.....	104
Summary of Section 363 Sale Process	104
Winners and Losers	105
Licenses of Intellectual Property in Bankruptcy	106
D. Tax and Tax Credits	106
Tax Rates	107
Federal Tax Incentives for Research and Development Expenditures.....	108
Research Credit Under Section 41 of the Code.....	108
Regular Research Credit.....	110
Alternative Simplified Research Credit	110
Energy Research Credit	111
Alternative Incremental Research Credit.....	111
IRS Enforcement Efforts Relating to the Research Credit.....	111
Proposed 2009 Legislation Regarding the Research Credit.....	112
American Recovery and Reinvestment Act of 2009.....	114
Proposed “Carried Interest” Legislation.....	115
E. U.S. Import/Export Considerations	117
Imports into the U.S.....	118
Exports from the U.S.....	119
F. International Regulation and Barriers.....	121
Background.....	121
International Structures for Legal Control or Standardization.....	123
European Directive 2001/18	123
The Cartagena Protocol	124
The Codex Guidelines	126
Conclusion	126

V. Regulatory Factors That Influence Biotechnology Finance..	127
A. The Impact of the FDA:	
The Passage of the FDAAA.....	127
Post-Approval Drug and Biologics Safety Studies.....	127
Risk Evaluation and Mitigation Strategies (REMS).....	127
Labeling Changes Based on New Safety Information....	128
Public Posting of Results of All Clinical Trials Involving Approved Drugs, Biologics or Medical Devices	128
Risk Identification Network.....	130
Incentives for Development of Pediatric Devices and Requirement for Pediatric Testing of Drugs and Biologics	130
Implications of the FDAAA	131
Suggestions For Drug, Biologics, And Device Manufacturers	132
B. Regulatory and Law Enforcement Oversight of Biotechnology Firms	132
Off-Label Promotion	133
Kickbacks	135
Physician Self-Referrals	137
Bad Reimbursement Advice	138
Price Reporting Fraud.....	138
State Laws Relating to Sales and Marketing	139
C. Genetic Engineering	141
Laws and Regulations Affecting Finance	141
International Issues	142
D. Stem Cells.....	143
Federal Policy	143
Minnesota	144
Other States.....	144
Current Trends	147
E. Cloning	147
Cloning of Humans.....	148
Agricultural Cloning.....	148
Effects on Corporate Finance	149
Glossary of Defined Terms	150
Endnotes.....	152

I. INTRODUCTION

How to Use This Supplement

We are publishing this *Supplement* to bring up to date *A Guide to Biotechnology Finance* that we originally produced in 2005. This is neither a new edition of the 2005 *Guide* nor simply a recitation of recent developments. Our goal has been to provide a resource that describes in a concise and meaningful way the biotech business environment as it exists in 2009, which is decidedly different from the environment that prevailed in 2005. In preparing this *Supplement*, therefore, we chose to provide extensive discussions of Strategic Alliances, Mergers and Acquisitions and Public Capital Formation in our Biotechnology Finance Section and to also provide extensive discussion of Intellectual Property Rights, an area that has changed significantly, in our Business Factors that Influence Biotechnology Finance.

This *Supplement* is designed to be a stand-alone resource allowing users to obtain a basic understanding of the recent evolution and the current “state of play” in financing biotech companies, without need to refer extensively to the 2005 *Guide*. If, on the other hand, you are looking for a more detailed treatment of subjects covered in the 2005 *Guide* (including some not covered in this *Supplement* because they have not changed significantly in the past four years), we invite you to refer to the 2005 *Guide*, as well as to this *Supplement* as an update on recent changes.

What is “Biotechnology”?

We define “biotechnology” as we did in the 2005 *Guide*. That is, biotechnology is the science of discovering, developing and manufacturing new products derived from living organisms or parts of living organisms (e.g., cells, genes or proteins). It is applied molecular biology, encompassing industries as widely diverse as medical devices, small- and large-molecule pharmaceuticals, animal health, food, renewable energy and renewable materials.

A Word About Terminology

We often refer to the original 2005 edition of *A Guide to Biotechnology Finance* as the “2005 *Guide*,” or simply the “*Guide*.” We use the terms “supplement” and “update” interchangeably (with or without initial capitalization) to refer to this 2009 *Supplement to A Guide to Biotechnology Finance*.

Footnotes and Endnotes

Our 2005 *Guide* included close to 700 footnotes that were placed at the end of the *Guide*. These “endnotes” provided additional background information and sources. In this supplement, we have not republished those endnotes, but refer the reader to the 2005 *Guide*. Where there have been significant developments in the law, for example in the Intellectual Property Rights section, or in sections where we believe citations or additional background is helpful, we have added endnotes.

Contributors

The following Lindquist & Vennum lawyers contributed their expertise as editors or authors of the sections of this *Supplement*, as listed below:

Thomas G. Lovett, IV, and

Robert L. Thompson—Co-Editors

Barbara Lano Rummel—Strategic Alliances

Joseph J. Humke—Mergers & Acquisitions

April Hamlin and

Jennifer L. Wuollet—Private Capital Formation

Jonathan B. Levy—Public Capital Formation

Roderick I. Mackenzie—Debt

Robert E. Tunheim—Federal Grants Through SBIR/STTR Programs

Edward J. Wegerson—Management Equity Incentive Compensation

Mark R. Privratsky,

David A. Allgeyer,

Bruce H. Little,

Garrett M. Weber,

Christopher R. Smith and

Christopher R. Sullivan—Intellectual Property Rights

James A. Lodoen and

George H. Singer—Distress Stage

Mark D. Salsbury—Tax and Tax Credits

Mark S. McNeil—U.S. Import/Export Considerations and
International Regulation and Barriers

Barbara J. Wood and

Karen E. Westwood—The Impact of the FDA: The Passage of the
FDAAA

Sheva J. Sanders and

Ryan McGary—Regulatory and Law Enforcement Oversight of
Biotechnology Firms

Daniel J. Schwartz—Genetic Engineering

David J. Snider—Stem Cells

Mark F. Trocinski—Cloning

We also thank other contributing staff at Lindquist & Vennum including 2009 Summer Associates Benjamin J. Skoglund and Carol R. Washington, as well as Christopher P. Barton, Christopher R. Bechtold, Sandra J. Danover, Suzanne D. DeGroot, Jane L. Nett, Vicki L. Henderson, Kathleen M. Nydegger, and Martha E. McNey.

Legal Advice

Although we discuss many legal issues in this *Supplement*, it is only intended as a general summary and does not constitute legal advice. Appropriate legal advice can be rendered only on consideration of a specific set of facts. Lindquist & Vennum P.L.L.P. and the State of Minnesota cannot and do not assume responsibility for decisions based on the information provided in this *Supplement*. *You should consult with legal counsel for specific advice regarding your situation before acting on any matter.*

To ensure compliance with requirements imposed by the U.S. Treasury, we inform you that any U.S. federal tax advice contained in this *Supplement* is not intended or written to be used, and cannot be used, for the purpose of (i) avoiding penalties under the Internal Revenue Code of 1986, as amended, or (ii) promoting, marketing or recommending to another party any transaction or matter that is addressed in this *Supplement*.

II. OVERVIEW OF BIOTECHNOLOGY FINANCE

The financing of biotechnology enterprises, indeed the whole field of biotech, has changed significantly since we published *A Guide to Biotechnology Finance* in 2005. Some of that change is due to the natural dynamism of science-based industries and to evolving views of investors concerning risk associated with biotech.

Some is due to changes in the law. But in large measure, the difference between financing biotechnology in 2005 and financing biotechnology in 2009 is rooted in the dramatic deterioration of the economy and the financial markets that began in a pronounced way in the summer of 2007.

A Shift in Financing Options

Raising equity capital, whether in public or private markets, is a much greater challenge today. Biotech IPOs simply went missing in 2008 and early 2009. Debt financing is also far harder to obtain. In the absence of these traditional and fundamental sources of financing, strategic alliances between firms active in biotech industries have taken on greater significance as a means of acquiring necessary resources. These alliances range from simple licensing of intellectual property, to complex research collaborations with equity options, to full mergers or acquisitions. Although the parties often vary significantly in size, as in the case of large pharmaceutical companies doing deals with smaller biologics firms, with greater frequency firms at the smaller end of the spectrum are coming together to collaborate in creative ways.

In this *Supplement* we have tried to place these changes in perspective. We first discuss in some detail strategic alliances and mergers and acquisitions, not because the mechanics of these transactions have changed dramatically in four years but because that is where much of the action is today. But we also discuss traditional sources of equity and debt financing because they will again become more viable options as the economy and financial markets improve in the months and years ahead.

Changes in the Law and Their Effect on Biotechnology Finance

The ability to finance biotech companies depends on more than the mechanics of specific financing options. Since we published the 2005 *Guide* there have been numerous developments in the laws that affect the way biotech companies operate and their potential for success. These factors in turn affect investor risk and ultimately the availability and cost of financing the biotech enterprise.

New law concerning deferred compensation changed the rules for issuance of equity compensation to company executives, a form of compensation that has been heavily relied on by biotech start-ups, making compliance in this area much more complex today. Several recent court decisions have fundamentally altered the complexion of intellectual property rights, a matter of critical importance to biotechs. In addition, challenges to IP rights continue in the U.S. and globally. Regulatory changes at the Food and Drug Administration (“FDA”) and other agencies that oversee biotechnology industries, as well as new policies adopted or advocated by the Obama administration, have also altered the biotech landscape. We highlight these developments and others in this *Supplement*.

Some topics that we covered in the 2005 *Guide* are not included in this *Supplement*, despite their importance for biotechnology firms. Our discussions in the 2005 *Guide* of Choice of Entity, Corporate Life Cycles, and Reimbursement remain of fundamental importance, but there have not been material changes since 2005. We refer you to the 2005 *Guide* for analysis of these topics.

Looking Ahead

We can expect that biotechnology, in all its forms, will continue to evolve at a rapid pace. Biotechnology is at the heart of some of the most significant and pressing issues of the day, including healthcare, affordable food supplies, alternative energy sources, and renewable materials.

Many states in the U.S., and many other countries around the world, are aggressively courting biotechnology industries

and proposing incentives too diverse (and in many cases too preliminary) to cover in this general *Supplement*. Minnesota is taking a long-range strategic approach to the promotion of biotechnology in the state. In January 2009, The BioBusiness Alliance of Minnesota released its “Destination 2025” report analyzing the state’s biobusiness resources and providing recommendations for promoting biotechnology in Minnesota. As biotechnology industries evolve to address society’s challenges, they will do so in a bright spotlight.

The laws and policies that govern biotechnology industries will also evolve. These laws and policies will affect what biotech can accomplish and the investor risk associated with biotechnology activities. Comparative-effectiveness research on medical treatments (funded with more than \$1 billion in the 2009 federal economic stimulus legislation and coordinated under the U.S. Department of Health and Human Services) and proposals for regulatory approval of “biosimilars” (follow-on large-molecule drug products roughly analogous to generic versions of small-molecule drugs) are just two current examples of the enormous potential impact law and policy can have on the business prospects of biotechnology industries.

We prepared this *Supplement* to help explain where we are today in terms of biotechnology finance and how we got here. That is important to understand because it is fundamental to the immediate challenges facing biotechnology enterprises and their advisors. But the biotechnology industries of the future, and the way they are financed, will undoubtedly be different from those of today. To position companies for success in that future will require sensitivity to broad trends and creativity. It is our hope that the following discussion will contribute to both.

III. BIOTECHNOLOGY FINANCE OPTIONS

A. Strategic Alliances

Generally, as the U.S. equity markets tightened and initial public offerings became less of a realistic option, strategic alliances (joint ventures, R&D funding arrangements, support agreements, license agreements, and M&A transactions) have become a more prevalent finance option for companies in the biotechnology industry. The traditional model of independently growing a fully integrated pharmaceutical company from drug discovery through commercialization has become more difficult and less common.

A key to success for an early-stage biotechnology company is finding a partner to provide cash and expertise needed to navigate expensive clinical testing and market launch. Licensing has historically been the prevalent form of partnering in the biopharma industry and will likely remain so in the long term. With public company stock values fluctuating to historical lows, parties are carefully evaluating acquisitions of whole companies where, given a higher stock value, a license or other contractual arrangement for specific technology may have otherwise been the transaction of choice. Some commentators have suggested that contractual joint ventures may gain popularity as a mechanism to develop virtual companies capable of reducing expenses. Regardless of the form, partnering arrangements will likely continue to play a major role in the financing of biotech companies.

Reducing Risk

In recent challenging economic times, parties in strategic alliances have attempted to develop structures to minimize risk and maximize value if the product is successful. One mechanism that financial investors have used to reduce risk in biopharma has been to move away from early-stage drug compounds and technologies to those that are at a later stage of development. Pre-clinical-stage drug candidates are technologically risky and costly. Venture capital firms and other investors need to see a reasonable

path to recognizing a return on their investments. This involves minimizing technology, regulatory, and reimbursement risks in order to attract financial investors.

In the licensing context, the pharmaceutical industry has attempted to reduce risk by reducing the upfront payment and tightening milestones more so than in the recent past. This suggests that the parties must carefully negotiate meaningful milestone events that generate value points for the parties. Otherwise, the licensee may be confronted with an obligation to make a milestone payment at a time when there has been no commensurate increase in the value of the transaction. Some licensees have recently elected to forego the initial equity investment to instead receive an option to take equity at a later date when product development is more certain.

The current climate has forced development-stage companies to reduce burn rates and focus development efforts on projects that show the greatest promise with foreseeable routes to commercialization, regulatory approval, reimbursement, and revenue streams. This requires discipline in a company with multiple product candidates.

Parties entering into licensing and other collaboration agreements should pay particular attention to the terms of the agreements that are affected by the economic uncertainties of the world economy. For example, the parties should carefully consider cure periods and termination provisions for nonpayment of milestones or royalties. Both parties to the license agreement should anticipate their remedies in the event of bankruptcy of the other party. (See Section V.L. “Distress Stage—Intellectual Property Licenses in Bankruptcy” in the 2005 *Guide*.) Generally, a U.S. bankruptcy proceeding will prevent termination of a licensee’s benefits under an existing license agreement for intellectual property during bankruptcy without bankruptcy court approval. Because bankruptcy has no effect on a license agreement terminated in advance of the bankruptcy filing, a party should be diligent to establish provisions that may serve as cause for legitimate termination prior to the point at which the other party initiates a Chapter 11 or Chapter 7 bankruptcy proceeding. The licensor should carefully define in the license or supply agreement what

constitutes “adequate assurance of future performance” (such as minimum net worth or performance benchmarks) that may provide the licensor or supplier a basis for demanding cash or other security for payment or a basis for termination pre-bankruptcy.

Collaborations Between “Big Pharma” and Start-Up Biotechs

Large pharmaceutical companies continue to collaborate with early-stage drug development companies to obtain new technologies to fill their pipelines of drugs facing patent expirations and generic competition. These collaborations often, but not exclusively, take the form of M&A transactions. Licensing is also a common mechanism. Large pharmaceutical companies can offer the financial backing, as well as significant regulatory, reimbursement, and marketing expertise and distribution systems. In addition to all of the technology and financial factors to be evaluated in a relationship between “big pharma” and an early stage biotech, the parties should consider the management and operational challenges that result when combining the entrepreneurial environment of the small start-up and the active, more formalized management of a large pharmaceutical company. Careful consideration should be given to the composition and authority of the operating committee (in the case of a joint venture or license arrangement) or integration (in the case of an acquisition).

Global Opportunities

Whether the result of current market conditions in the United States or the global nature of biotechnology, transactions involving purchasers and business partners from outside U.S. borders have increased dramatically. In some cases, a partner in another market may make more strategic sense because some technologies may have greater value in emerging markets than in the more mature U.S. market.

The negotiation of a licensing transaction with a foreign entity requires the United States entity to carefully consider provisions that may be considered standard boilerplate in transactions involving similarly situated U.S. entities. The governing law and venue provisions are obvious terms that take on new importance

in international transactions due to the expense and potential complexities of enforcing judgments in multiple jurisdictions. An international relationship also requires increased focus on currency issues, trademark and patent protection, and international regulatory obligations. Parties in a multi-jurisdiction arrangement should carefully consider the milestones for funding typically found in a license agreement. Those milestones may need to be jurisdictionally sensitive in order to tie them to events that create value for the licensee. Otherwise, the licensee may be paying without achieving value, or the licensor may not get the return it is expecting.

The parties should also carefully consider clinical trial requirements in multi-jurisdiction license agreements. For example, in designing a clinical study, the sponsor will need to be aware of, and comply with, the specific regulatory requirements of each jurisdiction. In designing a clinical trial in Europe, the sponsor will need to be aware of regulations limiting the sharing of patient-specific data.

Although global business is becoming far more efficient and commonplace than in the past, U.S. companies should not assume that their U.S. forms of agreements will adequately protect them in international transactions.

Collaborations with Academic Institutions

The frequency and importance of direct collaborations between big pharma and academic institutions has increased. Traditionally, biotech start-ups have played an intermediary role between the academic institution and big pharma. Academic institutions are under increased pressure to generate funds from their research and to out-license technology. There are, however, significant legal, and cultural differences between academic institutions and publicly traded pharmaceutical companies.

The primary objective of academic institutions is to advance science for the public good. They are nonprofit entities. On the other hand, publicly traded pharmaceutical companies have duties to enhance shareholder value. As a licensor under an exclusive license, an academic institution typically reserves the

right to continue to evaluate and use the licensed technology for educational, research, and clinical programs. Conflicts may arise out of the academic institution's desire to publish its findings and the commercial party's need to avoid publication that might limit the ability to patent the invention and obtain commercial value from excluding others from practicing it. Other intellectual property concerns may arise out of academic research that is performed by graduate students and other non-employees who are somewhat mobile and may not necessarily be bound by confidentiality and obligations to assign inventions. Further, academic institutions rarely give representations and warranties about non-infringement, or commit themselves to indemnification.

As in the case of international licensing, parties should not assume that their forms of commercial license or other collaboration agreements will automatically translate to work with academic institutions.

B. Mergers and Acquisitions

The term mergers and acquisitions ("M&A") refers to a variety of transactions involving the acquisition by one party - the acquirer - of one or more business entities or lines of business of another party - the target. The term also includes the combination of two companies into a single company. M&A transactions are considered the ultimate strategic alliance because a change in ownership of a business, whether in whole or in part, is the end result.

There has been a tremendous amount of domestic and international M&A activity in the past several years, both in the number of transactions completed and the value involved. Notwithstanding the global economic downturn in 2008 and 2009 and the general slowing of M&A activity in a number of industries, mergers and acquisitions continue to play a significant role in the biotechnology sector. This is attributable to a number of factors.

Historically, IPOs and M&A transactions have been the two primary exit strategies for corporate founders and venture capitalists. As financial markets have tightened and private

placement offerings and IPOs have become increasingly more difficult to complete, however, there has been a renewed emphasis on M&A as an exit strategy, especially in the biotechnology industry. Moreover, biotechnology companies are becoming more inclined to quickly replenish product pipelines through acquisitions rather than investing considerable capital, time, and resources to research and development efforts that may (or may not) prove worthwhile years out. Biotechnology acquisitions may also be more attractive to pharmaceutical companies than complex licensing deals, which can cost as much as gaining complete control of new treatments through acquisition.

The managed care revolution has also increased M&A activity among large pharmaceutical companies. Many of these organizations seem to believe that costs can be reduced or controlled by creating larger, more diversified and efficient business entities. The globalization of research, technology, and finance has fueled international M&A transactions.

In addition, the continuing convergence of medical devices with pharmaceuticals and diagnostics is driving M&A activity. Among other things, skyrocketing drug development costs and pressure from third-party payers to reduce costs are compelling many companies to direct their growth strategies toward convergence. Rapidly advancing technologies are resulting in a marked increase in convergent products, and industry participants have recognized that they may open up new markets by re-marketing existing medical device technologies with existing therapeutics and diagnostics. Furthermore, the FDA review process for medical devices tends to be less rigorous than that for pharmaceuticals, resulting in faster commercialization (although convergent technologies could take longer to get through the FDA than standard medical devices).

Motives for Mergers and Acquisitions

The rationale for entering into an M&A transaction will vary between a buyer and seller. A seller may be motivated to undertake an M&A transaction for any number, or a combination, of reasons, including the following:

- **Liquidity.** The seller's owners may want or need liquidity to fund other projects, or for personal reasons. This is becoming increasingly common as investors have seen the value of their personal portfolios significantly diminish in 2008 and 2009. Moreover, the business itself may be experiencing liquidity problems and, rather than engaging in prolonged restructurings with its lending institutions, the business may be sold or recapitalized.
- **Timing.** The seller's owners, if principally involved in the day-to-day operations of the business, may be ready to retire, but not have a succession plan. Some owners who purchased a company for investment purposes (see the discussion below regarding financial buyers) may have a set time within which they must exit the investment.
- **Lack of Resources.** The seller may not have the resources to take itself to the "next level" operationally, to deploy a new product, or to undertake a new project.
- **Transaction Pricing.** During the period from 2005 through late 2008, buyers were increasingly willing to pay more and more for companies. Sellers that would otherwise not have considered selling have, in fact, sold their businesses because they have "received an offer they couldn't refuse."
- **Hostile Takeovers.** In some cases, even if a company is not for sale, a potential acquirer may put the target "in play" and complete an acquisition through a tender offer or other mechanism.
- **Contractual Obligations.** It is fairly common for owners of private companies, and especially those with owners who are actively involved in the business, to enter into so-called "buy-sell agreements" that obligate one or more owners to buy out one or more other owners upon the occurrence of a specified event such as termination of employment, death, or disability.

A buyer's motivation for completing an M&A transaction is, in part, a function of whether the buyer is a "strategic buyer" or a "financial buyer." "Strategic buyers" are most often established operating companies that may be attempting to expand their footprint, access new technologies, complement an existing line of business, or vertically integrate their supply chain. Many large pharmaceutical companies complete strategic acquisitions because they have extensive production, distribution, marketing, and financial resources, but may lack particular scientific platforms or technologies needed to enter into new fields in order to expand and complement their existing product lines. In the biotechnology industry, large pharmaceutical companies routinely acquire small developing organizations to jump-start new, innovative products to replace mature ones that are facing patent expirations. There are also "financial buyers," so called because they acquire a target for investment purposes—that is, they intend to grow the value of the target and later sell the target for a profit but they may not have an existing business that is in a related or complementary field.

Strategic buyers may be willing to pay a premium for a given target relative to the value that a financial buyer might pay because strategic buyers are more likely to realize immediate synergies from the acquisition. Given the overwhelming cost of R&D, clinical trials, and regulatory compliance, biotechnology-related acquisitions often occur at stages earlier than originally envisioned by biotechnology company founders and venture capitalists. Financial buyers are generally more inclined to be interested in the target's cash flow and their own ability to exit the investment at some point in the future. Financial buyers look for well-managed companies that have a track record of consistent earnings, prospects for growth, and leverageable assets and cash flows. Because financial buyers typically do not manage the day-to-day affairs of their investments, they frequently rely on the managerial expertise of the target following the acquisition.

Structuring the M&A Transaction

Regardless of the parties' reasons for undertaking an M&A transaction, they will generally use one of the following structures (or a combination of them) to complete the deal:

- a purchase and sale of assets;
- a purchase and sale of stock (while this section refers to a purchase and sale of stock, the principles discussed likewise apply to the sale of any ownership interest in a business organization); or
- a statutory merger (conducted according to statutory requirements) of the entity to be acquired with and into a newly formed subsidiary of the acquiring entity (or a merger directly with and into the acquiring entity).

These three structural alternatives are discussed in greater detail below, and the exact structure ultimately used will depend on a number of factors. The tax treatment for any gain realized by the acquired entity and its owners will likely be one of, if not the most, important factor to consider in structuring a transaction. The critical inquiry, from a seller's perspective, is not what the gross purchase price is, but rather what the seller's after-tax net proceeds will be from the transaction. As a general rule, a deal structure that favors the buyer from a tax perspective normally is detrimental to the seller's tax situation, and vice versa. Use of net operating loss ("NOL") carry forwards is yet another factor, but recent limitations on the use of NOLs under Section 382 of the Code have somewhat lessened the significance of this issue.

Many parties mistakenly believe that "tax free" treatment is readily available in M&A transactions. Section 368 of the Code provides for three primary types of reorganizations to qualify for what is commonly referred to as tax free treatment—when in fact it is tax deferred treatment. If the requirements of the Code are met, the sellers are not required to pay tax at the time of the transaction. Instead, the tax basis of any new stock received will be the tax basis of stock

relinquished by the taxpayer in the merger. Gain would then be deferred until such time as the new stock is sold. The provisions of Code section 368 are very restrictive and require that stock be the primary consideration and that the payment of cash or other property, referred to as “boot,” be limited.

Other key considerations in structuring an M&A transaction include, but are not limited to:

- successor liability issues;
- whether the acquired entity is a privately held or a public company;
- whether the acquiring entity is seeking to purchase all or only part of a business;
- the extent to which the acquired entity operates in a regulated industry; and
- contract assignment limitations and the necessity of obtaining third-party consents.

Asset Purchase

In an asset purchase transaction, the buyer purchases all or substantially all of the assets of the target or purchases a line of business of the target, and the buyer generally assumes only those liabilities of the target that the buyer specifically agrees to assume. Unlike a stock purchase or merger transaction, the buyer in an asset transaction has the opportunity to pick and choose which of the target’s liabilities it will assume. In fact, one of the most important reasons for structuring an acquisition as an asset purchase transaction is the desire of the buyer to limit or avoid responsibility for liabilities of the target. That having been said, so-called “successor liability” doctrines may require a buyer to be responsible for certain liabilities of the target even if the asset purchase agreement provides otherwise. In addition, there are federal and state environmental laws that impose strict liability for environmental problems on successor owners.

The asset purchase agreement will contain numerous representations, warranties, and covenants addressing, among

other things, the business and operations of the target. The agreement will also contain indemnification provisions that require the target or its shareholders to indemnify the buyer for any breach of a representation, warranty, or covenant. The scope and duration of the indemnity can vary significantly depending on the perceived risks involved in the transaction. Approval of the boards of directors of both the buyer and target will generally be required to consummate an asset purchase transaction. Approval of the target's shareholders is also generally required under state law when all or substantially all of the target's assets are being sold. State law typically does not require the approval of the buyer's shareholders to consummate an asset purchase transaction.

From a tax perspective, a buyer will generally prefer to purchase assets rather than stock, and a target will prefer to sell stock rather than assets. For tax purposes, the buyer records the purchased assets at the fair value assigned to them as part of the transaction. This allows the buyer to "step up" its basis in the assets and take a larger depreciation expense on those assets going forward. The selling entity recognizes a gain or loss based on the difference between the sale price (including liabilities assumed) and the tax book value of the assets.

Stock Purchase

In a stock purchase transaction, the buyer buys the stock or other outstanding ownership interests in the target from the holders of those interests. In a stock purchase of a closely held business, the buyer will enter into one or more purchase agreements directly with the shareholders, all or most of whom are generally involved in negotiating the transaction. The stock purchase agreement will typically contain numerous representations, warranties, and covenants, and the shareholders will be required to indemnify the buyer for any breach of those representations, warranties, and covenants. Again, the scope and duration of these indemnification obligations can vary depending on the perceived risks inherent

in the transaction. If the shares of capital stock of the target are held by a large number of shareholders, or if the target is a public company, the buyer may make a friendly “tender offer” (with the approval of the seller’s board of directors) to purchase all of the shares of the target. If not all shareholders respond favorably to the tender offer, the buyer may undertake a second-step “squeeze-out” merger of the non-tendering minority shareholders, usually at the same price the buyer paid for the shares in the tender offer. In the “squeeze-out” merger, the buyer would cause the target to merge into a newly formed, wholly owned subsidiary of the buyer. In exchange for the shares of the target, the minority shareholders would receive cash and the buyer would own all the outstanding shares of the subsidiary. The rules governing tender offers can be complex and often require significantly more documentation than a stock acquisition not involving a tender offer. If the target is publicly traded and declines to engage in negotiations with the buyer regarding a potential acquisition, the buyer may put pressure on the management of the target to consider the buyer’s proposal through the use of a “hostile” tender offer and proxy fight. The target’s board of directors has a fiduciary duty to consider all reasonable business offers and is, therefore, prevented from altogether ignoring proposals that have the potential of enhancing shareholder value.

When stock is acquired, the liabilities of the target remain with the target after the shares have been transferred. This is because the legal form of the target, its assets, and its liabilities have not changed; only the equity ownership of the target has changed. By virtue of purchasing the target’s capital stock, the buyer is effectively taking on the target’s liabilities.

As noted above, a seller will generally prefer to sell stock rather than assets due to the more favorable tax treatment of a stock sale. Although different rules may apply in the sale of partnership or limited liability company interests, the assets and liabilities of the acquired business are not adjusted incident to the transaction. Rather, they continue to be carried and

depreciated in the same manner as before the transaction. The sellers recognize a gain (or a loss) based on the difference between the sale price and their basis in the ownership interests being sold. The parties may make an election under Section 338(h)(10) of the Internal Revenue Code, which has the general effect of treating a stock purchase much the same as an asset purchase for tax purposes. As such, a 338(h)(10) election can benefit the buyer, to the detriment of the seller's tax position, although there may be some situations in which the impact to the seller is negligible.

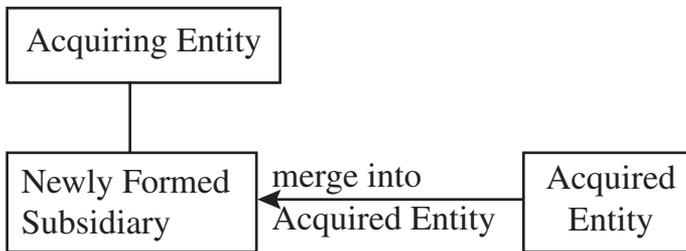
Merger

A statutory merger is the combination of two or more business entities into one of the entities that then becomes the “surviving entity.” Legally, there are “constituent entities” and a surviving entity in a merger. Practically, however, one of the parties is taking the role of the “acquiring entity” while the other party (or parties) is taking the role of the “acquired entity.” Under state law, the surviving entity automatically retains or acquires all the properties, rights and powers, as well as all the debts, liabilities and obligations of all the constituent entities. Upon effectiveness of the merger, the legal existence of the nonsurviving entity ceases and the shareholders of the nonsurviving entity receive consideration (typically, cash or shares of stock in the acquiring entity) in return for relinquishing their equity interests in the nonsurviving entity.

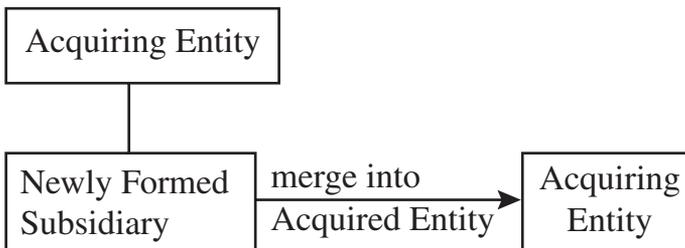
Generally, state law requires approval of the board of directors and the shareholders of each of the constituent corporations to a merger. To effectuate a merger, the acquiring entity typically forms a new wholly owned subsidiary to conduct the transaction, thereby only requiring the approval of the subsidiary's sole shareholder—the acquiring entity. Most state statutes allow for “appraisal” or “dissenters” rights that entitle shareholders of the acquired entity to vote against the merger and to receive a judicially determined “fair value” for their shares instead of the merger consideration. The

procedure is very detailed and must be strictly complied with in order for a shareholder to be entitled to this alternate consideration. Typically, the merger agreement will contain a termination provision allowing the acquiring entity to terminate or be released from the transaction if more than a specified percentage of shareholders of the acquired entity exercise appraisal rights.

There are two mechanical variations to a merger—the forward subsidiary merger and the reverse subsidiary merger (sometimes also referred to as forward and reverse triangular mergers). In a forward subsidiary merger, the acquired entity is merged with and into a newly formed subsidiary of the acquiring entity, and the newly formed subsidiary is the surviving corporation.



In a reverse subsidiary merger, the newly formed subsidiary of the acquiring entity merges with and into the acquired entity, with the acquired entity surviving as a wholly owned subsidiary of the acquiring entity.



The result after each merger is that the surviving entity will be wholly owned by the acquiring entity. The main benefit in consummating a reverse subsidiary merger instead of forward subsidiary merger is the manner in which the reverse subsidiary merger addresses the problem of contract assignments. More specifically, many supplier, vendor, consulting, lease and licensing agreements that the acquired entity has in place may contain clauses preventing their assignment without certain third party approvals. Because the form of the acquired entity does not change in a reverse subsidiary merger, the need for third party consents for assignment of agreements may be eliminated by conducting a reverse subsidiary merger.

Spin Out

When an acquiring entity does not wish to acquire all the lines of business of an acquired entity in a merger, or when an acquired entity desires to retain certain product lines, the seller may need to segregate certain assets of the acquired entity before conducting a merger. One possible mechanism to accomplish this is to “spin out” those assets into a separate legal entity prior to the merger. The acquired entity’s shareholders are then issued some form of security in the entity into which the assets are spun out.

Transaction Consideration

Generally, under any of these M&A transaction structures, the consideration paid by the acquiring entity will be cash, promissory notes or other debt instruments, stock of the acquiring entity, or some combination of the foregoing. In recent years, cash appears to have been the main form of consideration used in biotech M&A transactions. Any time securities are being issued as consideration in connection with an M&A transaction, the issuance will require registration under the Securities Act and applicable state laws or require an exemption from registration. Although registration can be costly and time-consuming for the acquiring entity, registered

securities that are given as consideration by a publicly traded acquiring entity provide the benefit of a liquid asset to the shareholders of the acquired entity and, except for registration-related costs, do not deplete the acquiring entity's cash. If the acquiring entity issues securities that exceed 20% of the acquiring entity's outstanding securities, NYSE and Nasdaq rules may require the acquiring entity to obtain shareholder approval for the issuance.

The amount of consideration in an M&A transaction may be fixed or it may vary based on events occurring after the closing. If the purchase price is based on the net asset value of the acquired entity, there may be an adjustment to the purchase price based on a closing date balance sheet that is prepared after closing of the transaction. The parties may also negotiate an "earn-out" as part of the total consideration in cases where:

- it is difficult to value the asset being acquired and more time will add clarity to the value;
- the buyer is willing to share with the seller a part of the upside that may result after the transaction; or
- the buyer cannot pay a lump-sum purchase price and the seller is willing to finance the transaction over some limited time period.

In an earn-out, the buyer pays the seller some amount over time based on some agreed-on operating results of the acquired business such as:

- a portion of the post-closing net sales of the product sold by the acquired business;
- a portion of post-closing net income of the acquired business; or
- a multiple of the post-closing net income achieved by the acquired business.

In acquisitions of early-stage biotech companies, earn-outs are sometimes structured around achievement of scientific

or clinical milestones. Earn-outs have become increasingly prevalent during the recent economic downturn, as sellers have seen their businesses struggle and, in turn, the values that buyers are willing to pay for those businesses has decreased. Because many sellers view their struggles as temporary, they often turn to earn-outs as a vehicle for bridging the value gap. The parties often agree to hold back a certain portion of the consideration in escrow for a period of time (typically 12 to 18 months) to satisfy any potential indemnification obligations of the acquired entity or its shareholders.

Professionals in the M&A Process

The process of completing an M&A transaction can be difficult, complicated, and time-consuming. It is critical for all parties to assemble an experienced team of professionals to develop strategy, locate the right partner, structure the transaction, negotiate the deal and facilitate the process. Depending on the nature and size of the transaction, the participants in the deal may include, among others:

- Acquirer (including owners, inside counsel and business team);
- Target (including inside counsel and deal team);
- Acquirer's outside counsel;
- Target's outside counsel;
- Acquirer's lender;
- Lender's outside counsel;
- Investment banker or business broker;
- Acquirer's independent accountants and tax advisors;
- Target's independent accountants and tax advisors;
- Acquirer's special consultants;
- Regulatory authorities (e.g., Securities and Exchange Commission, Department of Justice)

Investment bankers with expertise in the industry are considered essential to conducting a thorough analysis of the value of the

acquired entity. Investment bankers can also provide fairness opinions, which have become an increasingly important component of larger M&A transactions. A fairness opinion may be prepared at the request of the board of directors of the acquiring or acquired entity and used as an independent evaluation to determine whether a given transaction is “fair from a financial standpoint” to either the shareholders of the acquiring or acquired entity, or both. A board of directors may then use the fairness opinion as support for its decision to approve or reject a transaction in the event a shareholder suit challenges that decision.

Each of the parties will engage its own team of counsel experienced in the industry and with corporate, securities, intellectual property, regulatory, tax, antitrust, employment, environmental, real estate and other matters legally necessitated by the transaction. Industry-experienced accountants can also provide critical assistance with structuring the transaction in a tax efficient manner, assisting with the preparation of pro forma financial models and with completing the financial due diligence.

Confidentiality Agreements, Term Sheets, and Letters of Intent

Before parties to a potential M&A transaction begin meeting and exchanging confidential and proprietary information about their technology and business, they should enter into a confidentiality or nondisclosure agreement (“NDA”). NDAs in M&A transactions need to carefully and broadly describe the type of information that will be exchanged. The acquiring entity will want to review any and all public and nonpublic information about the acquired entity, including information related to items such as technology, employment, litigation, environmental, tax, intellectual property, finance, accounting, research, regulatory, marketing, production, and distribution. In acquisitions involving biotech companies, disclosure of sensitive scientific information, such as chemical structures, requires thoughtful analysis and careful treatment in NDAs. The fact that the parties are in discussions about a potential transaction, and the terms of those discussions, should also be treated as “confidential information” subject to the agreement. Entities that may be acquired should also demand a nonsolicitation

clause as part of their NDAs, prohibiting the prospective acquiring entity from soliciting or hiring the other entity's employees for a period of one to two years after the date of the NDA (other than in connection with closing the subject transaction).

After initial investigation of the acquired entity, the acquiring entity will typically generate a term sheet or letter of intent covering the principal business points of the deal so that the parties can develop a mutual understanding of the primary elements of the transaction. Letters of intent are used less frequently in transactions involving public companies because they may raise disclosure issues under SEC and stock exchange rules. To avoid any SEC and stock exchange requirements regarding the making of a public announcement about a transaction that is still preliminary and nonbinding, public companies may prefer to use preliminary term sheets to identify the key elements of the deal and then move straight to drafting definitive documents.

Whether using a letter of intent or a term sheet, the document is generally nonbinding, except for any obligations to:

- negotiate in good faith;
- maintain confidentiality of the terms of the transaction and the information disclosed between the parties; and
- comply with any nonsolicitation or no-shop provisions.

Parties should be especially careful when drafting the nonbinding provisions of the document, since there have been cases reported in which the would-be buyer and seller have bound themselves to complete a transaction by what was intended to be a nonbinding expression of interest. In the nonbinding sections of the letter of intent or term sheet, use words like “would” rather than “will” or “shall” when describing terms (e.g., “the closing would take place on or about July 31,” instead of “the closing shall take place on July 31”).

The term sheet or letter of intent will serve as the road map for negotiating and drafting the more detailed definitive agreements. Because pricing might very well be the most important factor in determining whether or not the parties agree to consummate an

M&A transaction, the question of when the parties fix a purchase price becomes a matter of strategy. As noted above, structure directly affects the net value of the transaction to the acquired entity, the acquiring entity and their respective shareholders. Acquired entities may choose to defer negotiating a purchase price until after the acquiring entity has completed its preliminary due diligence investigation (the due diligence process is described in greater detail below). Entities that may be acquired should realize that once they have tentatively agreed to a price, the likelihood of the acquiring entity negotiating a lower price if any issues are discovered during the due diligence process is far greater than the acquired entity being able to obtain a higher price if the due diligence is clean. This is largely attributable to the fact that acquiring entities begin the M&A process with the assumption that any due diligence investigation will not reveal anything sufficiently material to justify a change in price.

The acquiring entity will often demand an exclusivity period of at least 60 to 90 days in order to commit to spending the resources to undertake its due diligence investigation, which can be time-consuming and expensive. Acquired entities may be compensated by the acquiring entity for providing exclusivity, and for keeping the company off the market during the due diligence period.

Due Diligence

After a confidentiality agreement or letter of intent is signed, the acquiring entity will complete a detailed legal and financial investigation of the acquired entity to (i) determine (or confirm) the value of the entity, business, or product line being acquired, and (ii) analyze and allocate post-closing risks and responsibilities. While the nature and scope of the information sought will depend on the type of business being acquired and the industry in which it operates, the acquiring entity will typically request that the acquired entity provide access to, and copies of, all relevant information concerning:

- finance and tax, including financial statements, audit reports, supporting schedules, inventory and cost information, debt instruments and tax returns;

- corporate organization such as articles and bylaws, capitalization information, shareholder lists, minutes of all shareholder and board of directors meetings;
- intellectual property such as registered patents, applications and invention disclosures, trademarks and copyrights, technology licenses, and assignments from employees and consultants;
- R&D initiatives;
- products, sales and marketing, including customer lists, manufacturing and supply contracts, distribution agreements, marketing plans and programs;
- material contracts such as those with suppliers, customers and consultants;
- employment, contractor and labor matters such as employment or consulting contracts, employee benefits and ERISA plans, payroll information and benefits claims history;
- facilities, including real estate title or lease documentation;
- environmental items such as Phase I and Phase II environmental assessment reports and claims history, depending on the nature of the business activity;
- manufacturing and operations, including regulatory compliance, production processes, quality assurance procedures and files, including device or drug history files;
- regulatory and clinical information, including all approvals and applications, correspondence with the FDA and foreign authorities, third-party audit information and reports, adverse event reporting, insurance coverage; and
- litigation, including pending and threatened litigation.

Gathering this data can be very intrusive on the acquired entity, especially when it is attempting to keep its operations running smoothly and keep the potential transaction confidential from employees, customers, and vendors. Often a data room will be compiled offsite, such as at counsel's office, to avoid disruption of

the acquired entity's business activities. Increasingly parties may assemble "electronic data rooms" that facilitate review by multiple parties, or by parties that are geographically distant, with minimal disruption to the business.

Intellectual property is the key asset for most companies in the biotechnology industry. Significant time and resources should be spent assessing the status of the acquired entity's intellectual property including its patents, formulations, processes, and other trade secrets. This may include analysis of the validity of patents and noninfringement of third-party rights (including the potential blocking effect of third-party rights on activities of the acquired company), as well as assurance that title to all inventions has been properly assigned to the acquired entity from all employees, consultants, or inventors. The buyer should review any prior research agreements with consultants and universities to ensure that the acquired entity owns all rights to the property and to determine whether any future royalties may be owed post-closing.

A regulatory due diligence review is also critical. The acquiring entity will need to conduct adequate due diligence to satisfy concerns such as whether the acquired entity's clinical trials have been conducted in accordance with applicable requirements, and whether the acquired entity has adequate compliance procedures in place. The scope of the due diligence should be suitably detailed to answer all of the acquiring entity's questions.

If the acquired entity is marketing products that are covered by Medicare, then an analysis of the marketing practices should be conducted to ensure compliance with and avoid successor liability under the fraud and abuse laws that generally include state and federal anti-kickback statutes, civil and criminal false claims acts, the Stark laws, and the federal Civil Money Penalties Act. In undertaking due diligence, particular attention should be given to (i) the acquired entity's internal compliance program and business conduct standards (or lack thereof), (ii) sales and marketing practices, particularly in the area of pricing terms, customer sales incentives, payments to physicians or physician organizations, and (iii) the advice given by reimbursement specialists to existing or potential customers. Additionally, any promotion of off-label uses

for the seller's products, i.e., those not covered in the product's FDA approval, deserve special scrutiny.

All material contracts of the acquired entity must be reviewed to determine whether there are pricing terms and performance obligations that may be unacceptable to the acquiring entity, or whether there are change-of-control or assignment limitations or termination rights that may deprive the acquiring entity of the ability to continue the contract after closing.

Depending on the nature of the transaction, a seller should also conduct its own diligence investigation of the buyer. For example, if part of the consideration payable to the seller is by means of a promissory note from the buyer, the seller will want to get comfortable with the credit-worthiness of the buyer. If there is an earn-out, the seller will want to understand how the buyer intends to operate the acquired business in order to assess the likelihood of receiving any earn-out payments. If the buyer intends to retain existing management to operate the business following closing (which is most often the case with financial buyers), the seller and its management will want to get a sense for the buyer's expectations and management style. This becomes even more relevant in cross-border transactions. Integrating companies with markedly different cultures can be difficult even when the buyer and seller are close neighbors, but the difficulties are amplified when the parties are from different countries. For example, leaders in a target with a highly consensual, collaborative, entrepreneurial culture may be at odds with counterparts in an organization with a "top down" or bureaucratic management style.

Timing of Closing and Pre-Closing Considerations

Acquisition agreements are structured to contemplate either a "simultaneous" sign-and-close or a "staggered" sign-and-close. An acquisition agreement that contemplates a simultaneous sign-and-close is one under which the parties close the transaction on the same date that they enter into the agreement. By contrast, an acquisition agreement that contemplates a staggered sign-and-close is one under which the parties close the transaction after the date on which they enter into the agreement. The reasons for taking

one approach over the other are varied, but the decision to use one approach versus the other holds significant implications for both the buyer and seller.

In strategic biotech acquisitions the parties often have competing or overlapping products or R&D activities. These competitive overlaps must be carefully analyzed under the competition laws of the countries in which they occur or have effects. In larger acquisitions, notice to and clearance by government competition law authorities may be required. For example, under the U.S. Hart-Scott-Rodino Act, transactions in 2009 involving \$65.2 million by parties of sufficient size require prior notice to federal antitrust authorities followed by a prescribed waiting period before closing. Because of the global nature of biotech industries, it is not uncommon for a transaction to be subject to the competition laws of several countries.

Because many M&A transactions require the seller to obtain the consent of third parties to assign contracts, the buyer may want to speak with the seller's most important customers and vendors before closing to ensure that they will remain customers and vendors following closing. In addition, in some cases, governmental regulatory approvals are necessary to complete the transaction. At the same time, the seller may not want to notify its customers, vendors, and governmental authorities that a deal is pending if the buyer is not contractually bound to complete the transaction. To obviate this problem, the parties may enter into a staggered sign-and-close acquisition agreement, thereby binding them to consummate the transaction (subject to certain agreed-on contingencies), after which the seller will seek the consents, notify customers and vendors, obtain any governmental approvals and take other required pre-closing actions. Once all of the conditions to closing are satisfied, the parties close the deal.

The principal risk to the seller in executing a staggered sign-and-close acquisition agreement is that one or more conditions to closing may go unsatisfied, leaving the would-be buyer free to walk away from the transaction. The seller may have notified customers, vendors, employees, regulatory authorities, and others about the deal. If the transaction does not close, it could disrupt important

relationships that the seller has with various constituencies. As such, under a staggered sign-and-close acquisition agreement, one of the critical considerations for the seller is the nature and scope of the conditions to closing—that is, those things that must occur to trigger the buyer’s obligation to close. Given the current economic climate, so-called “MAC” (material adverse change) clauses have taken on greater significance. The buyer will often insist on a MAC condition to close, which effectively provides that, in the event of a material adverse change in the seller’s business between signing and closing, the buyer has the right to not close. Courts have generally been reluctant to allow buyers to rely on MAC clauses in an effort to avoid closing. A buyer also may insist on a financing contingency that gives the would-be buyer the opportunity to walk from the transaction if it is unable to obtain the financing necessary to complete the deal. For obvious reasons, sellers are reluctant to agree to financing contingencies (since their satisfaction is largely within the buyer’s sole control), requiring instead that the buyer secure its financing (or get binding financing commitments) before signing the acquisition agreement.

Integration and Planning for Success

Two of the key reasons cited for failure of acquisitions to achieve the strategic goals envisioned are lack of integration planning and poor integration execution. Integration planning should begin early in the transaction. Parties should carefully consider the cultural fit of the organizations when locating potential suitors. Integrating the entrepreneurial spirit of a biotechnology start-up into a large, inflexible organization can present many challenges and needs to be considered carefully as the deal is consummated.

C. Private Capital Formation

Since we was originally published the *Guide* in 2005, there have not been significant changes in the law applicable to private capital formation. There has been a significant downturn in private financing activity, however, primarily beginning in the third and fourth quarter of 2008. For example, according to the 2008 MoneyTree Report by PricewaterhouseCoopers and the National Venture Capital Association, 2008 marked the first year since 2003

in which investments declined from the prior year.¹ In particular, the fourth quarter of 2008 showed a marked decline in both number and dollar amount of venture capital deals. This fourth quarter trend was similarly reflected in reduced number and size of mergers and acquisitions and IPO activity.

M&A transactions and public offerings have historically served both as exit strategies for investors and as sources of capital that investors can roll over into new investments. In addition, with the tightening credit markets, demands for liquidity from existing portfolio companies or their own businesses, losses in the stock market, and defaults by limited partners in fulfilling their capital calls, many large prospective investors have sharply curtailed investments. Of course, wealthy individuals and other prospective investors have been similarly hurt by the significant declines in the stock market, lack of or loss of credit financing, and other demands on their own capital. Not only are funding sources less interested in new private capital investments generally, but they also have a decreased financial ability to fund any investment, no matter how attractive.

On a positive note, some data suggest that biotech companies have not been hit quite as hard by this confluence of factors as other industries—life sciences was still the number one venture capital investment sector in 2008.² While the spigot may have been turned off completely for other companies in other industries, there seem to be a few precious drops of capital available to biotech companies. As one might expect, the scarcity of private capital has also made competition for that capital fierce.

To effectively compete for private capital, biotech companies must present an absolutely compelling business proposition. From inception, companies should focus on building value in the enterprise and using every dollar judiciously to enhance that value. Capital raising efforts will not be successful without a business plan that demonstrates a long-term vision for the device, drug, or product. Investors are invariably focused on the product, the markets addressed by the product and their size, and the regulatory path and data demonstrating that the product will be safe, efficacious and commercially viable. Similarly, these should be the touchstones of decision-making at any biotech finance company.

If a biotech company has a compelling business proposition, unnecessary complications in the legal organization, business, or capital structure can cool the interest of prospective investors. A thorough “spit shine” may eliminate distractions in the prospective investor’s due diligence, help avoid increased financing costs (through increased legal, accounting or consulting expertise) of both the prospective investor and the company, and allow the company to demonstrate good stewardship of the business and its resources. In the private capital market, these efforts may set a biotech company apart from competitors for funds who may also have stellar business plans, talented management, and a great biotech idea. As biotech companies ready themselves to enter the private capital markets, they may want to consider the areas discussed below.

Selection of Financing Targets

Many biotech companies take a gunshot approach to raising capital, hitting every possible source hoping to land an investor. Instead, a biotech company should focus on identifying and cultivating relationships with the best sources for financing. To determine the best source for each particular biotech company, management must understand its industry and the funding players. Some funders invest in companies only at certain stages of development, while some are focused on particular diseases, technologies or distribution channels. Many investors do not simultaneously fund competitive products or technologies. Therefore, biotech companies should not assume their competitors’ funding sources would be ideal investors (for the protection of proprietary intellectual property and confidential information, many biotech companies would be well-advised to steer clear of their competitors’ sources of financing). Not only does this require research on funding sources, but biotech companies should network at industry specific events or conferences. Board members, attorneys, and accountants also can be resources to help a biotech company identify possible funding sources. In addition to those funders who are purely financial investors, it is important to consider a strategic funder since many larger biotech companies have in-house business development groups or investment arms.

Improving Corporate Governance

Biotech companies should review their organizational records and confirm that these records are accurate and up-to-date. This includes ensuring that the board and officers have been properly elected, demonstrating that approvals relating to significant decisions made by the company have been properly documented, and maintaining ownership records that accurately reflect the actual equity ownership of the company. If there are any informal, unwritten or “handshake” deals relating to ownership, the company should properly document these arrangements so there are no surprises or differences in understanding later. In addition, any loans or related-party transactions should be properly documented to ensure that all parties agree on the terms and to give investors some comfort as to the liabilities actually outstanding.

Quality Financial Information

It is common for an investor to send in an accounting team to perform diligence on the financial aspects of a company. During the process, the diligence team often finds accounting adjustments and errors that may substantially change the prospective investor’s valuation of the biotech company. Before beginning financial diligence, a biotech company should review its financial statements and financial information to determine if there are any problem areas, including, without limitation, accounting for related-party transactions, equity accounting, reserves for obsolete inventory, and allowances for doubtful accounts.

If the company is not in compliance with generally accepted accounting principals (“GAAP”), the company should consider changing its accounting principals to comply with GAAP or at a minimum be able to point out the differences between the company’s accounting methods and GAAP and why the company uses these methods.

Prior to looking for private capital, a biotech company should prepare reasonable financial projections of the business and be able to justify why those projections are reasonable. If an investor is putting money into the company, the company also needs to be

able to explain how it plans to use the proceeds and why the use is beneficial to the growth of the company.

Appropriate Equity Detail

As mentioned in the 2005 *Guide*, the issuance of equity including options or warrants to service providers also involves identifying exemptions from registration under federal and state securities laws. Because of the potential liability associated with the issuance of a security that is neither exempt nor registered, this is an area of concern for new investors. Therefore, biotech companies would do well to document that an exemption for each stock option or other equity grant has been perfected at the state and federal level and that there are contemporaneous records identifying the exemption strategy that was followed. Companies should also maintain accurate and complete records relating to each option or other equity grant, at a minimum consisting of evidence of board (or committee) approval of the grant and signed agreements relating to the award. Maintaining a ledger of all awards can also be tremendously helpful; a ledger would typically include information regarding date of grant, name of recipient, number of shares, exercise price, termination date, and vesting information. While this may seem like a housekeeping matter, sloppy equity grants and granting processes can change the treatment of the award for the income tax purposes of the recipient and for the accounting purposes of the issuer. These changes can be an unpleasant surprise for both management and potential investors. See Section IV.C of the 2005 *Guide* entitled “Management Equity Incentive Compensation” for more information regarding the income tax and accounting treatment of equity awards.

Employment Arrangements

When an investor is seriously considering an investment in a company, that company may try to enter into employment arrangements designed to protect some of its key employees. This may include items such as “stay” pay agreements and agreements that provide for a large severance or bonus amount to be paid to these employees in the event they are terminated within a certain time period after the closing of the investment. Although investors

usually want a strong management team in place, when these arrangements are in place it is common for the investors to require the previous owners of the company to bear the costs related to these agreements. Further, the company and its current owners should also be aware that investors are not likely to permit exorbitant salaries or other perks that an individual owner or small group of owners may be accustomed to receiving from the company. As a general matter, these arrangements should be avoided because, in the minds of prospective investors, they ultimately detract from the development of the biotech company's business.

Protection of Intellectual Property

Intellectual property is often a biotech company's most important and valuable asset. A biotech company needs to take steps to ensure that ownership of the intellectual property being created is vested in the company and is protected. One way to protect the company is to have employees enter into agreements regarding the confidential information of the company and the ownership of any intellectual property developed in connection with employment, including, for example, nondisclosure agreements and assignments of inventions. The company should also consider requiring key employees to enter into noncompetition agreements. If the company uses independent contractors to develop intellectual property, the company needs to make sure that there is a written agreement between the company and each independent contractor that ensures all the intellectual property developed belongs to the company. Each of these different agreements have specific legal requirements to make it enforceable, and some of these requirements vary from state to state. Therefore, the company should consult an attorney prior to entering into these agreements with employees or independent contractors.

Disclosure of Information

Diligence, management interviews, and written disclosures are natural parts of the financing process and usually a sign of the prospective investors' serious interest. Management sometimes approaches diligence as a game of hide-and-seek, however, believing that if the prospective investors do not identify an issue

in the diligence process, the risk of that issue will be borne by the investors. This mistaken belief may result in unpleasant surprises in the due diligence process that jeopardize hard-won relationships with prospective investors. Additionally, biotech companies invest significant time and expense in due diligence, and when prospective investors walk away from the table because of an issue discovered in diligence, that time and expense is essentially wasted. Further, if a biotech company succeeds in moving beyond due diligence, the securities purchase agreement relating to the offering will contain representations and warranties relating to every aspect of the business, its capitalization, and financial condition. In order to avoid breaching these representations and warranties, biotech companies must invariably disclose exceptions to the representations and warranties on schedules. Even if not called for specifically by the representations and warranties, most agreements contain a covenant that (i) material information was not withheld from the investor and that (ii) the information provided did not contain any untrue statement of a material fact or omit any material fact necessary to make the statements made not misleading. Failing to disclose material information can be a basis for fraud liability under the securities laws despite the absence of a specific covenant to that effect. At a minimum, deliberate omission of information may affect the relationship with a valuable investor and hinder the possibility of future investments even if the omission does not breach a representation or warranty. Similarly, biotech companies using private placement memoranda in their offerings should ensure that the disclosure is accurate and complete, especially since the SEC and state securities commissions have stepped up enforcement against issuers and their directors and officers for inadequate disclosure. When selling securities, disclosure is truly the best defense against securities law liability.

In this tight financing market, biotech companies should also be open to considering alternatives to a single influx of significant funds as an equity investment. For example a biotech company may consider investments in multiple tranches (with or without conditions), selling debt convertible into equity as a bridge to a larger financing, using stock to pay vendors, or licensing earlier in its life cycle.

D. Public Capital Formation

Introduction

The principal public financing alternative is, of course, an IPO. This section explores a biotechnology firm's decision to become public, reviews the advantages and disadvantages of being public, summarizes the steps necessary to prepare a firm for an offering, explores the process involved, describes the ongoing duties once the firm is public, and discusses additional public financing alternatives that become available once the firm is public.

Recent Trends in Biotechnology Public Offerings

An IPO is a widely known financing alternative for a biotechnology firm. The public capital markets have been a great source of capital for the biotechnology industry with widespread investor interest in life science and health-related companies. From 2000 to 2002, over \$70 billion was raised in IPOs by biotechnology firms in the U.S. In 2002 alone, biotechnology firms raised over \$60 billion in IPOs. In the years 2000 to 2002, venture-backed IPOs of biotechnology firms represented between 25 and 30% of all venture backed IPOs. These figures suggest that seeking financing from the public capital markets has often been a viable alternative. The market for capital in the public sphere is often described as a window. The window can be open for some period of time for certain industries, but then can shut abruptly and remain shut for long periods of time. In 2003, the biotechnology window opened wide, with *The Wall Street Journal* describing the market for public offerings in biotechnology as a "booklet." Because the window can shut as quickly as it opens, a biotechnology company raising capital from the public needs to do so nimbly and expeditiously. By 2008, with the challenging economy, the window slammed shut, with only one U.S. biotechnology firm successfully completing an IPO, and most experts predicting a similarly challenging 2009.

Should the Biotechnology Company Go Public?

The difficult decision of whether to raise capital from the public and become subject to all the duties of a public company is

not unique to biotechnology firms. If the firm has a product, technology, or business plan that makes it a strong candidate for an IPO, the firm's board and senior management must also weigh the expense, risk, and managerial resources that must be devoted to completing a successful public offering. These are significant, and therefore, a public offering is practical only for a larger biotechnology firm. The decision to go public involves a thorough consideration of many factors including: (i) financing needs, (ii) covenants to existing investors that may mandate a public offering, (iii) status of products, (iv) state of preparedness, (v) risks, (vi) market opportunities and valuation, (vii) business, (viii) tax and estate planning, (ix) alternative sources of financing, and (x) the cost of going and being public.

Advantages to the Biotechnology Firm in Becoming a Public Company

There are many advantages for the biotechnology firm to go public. These include:

Access to Capital Markets. For the biotechnology firm, public capital may be the only source of capital at a reasonable price. Selling equity to the public may be available without giving up significant control or accepting burdensome financial and other covenants that venture capitalists or established companies might impose in exchange for financing. For many biotechnology companies, bank financing is simply not a practical option because the life cycle stage is not mature enough and the risk profile is too aggressive for most banks.

Use of Proceeds. Many biotechnology firms sell shares to the public to satisfy a variety of capital needs including: (i) financing product development expenses such as R&D, (ii) funding clinical trials, (iii) building out a sales force or engineering team to distribute or develop a product or technology, (iv) acquiring or modernizing production facilities, and (v) acquiring other businesses or assets including intellectual property or necessary licenses.

Satisfaction of Covenants or Investor Agreements. Many venture-backed biotechnology firms will seek a public offering

to eliminate venture capital investments that carry burdensome liquidation preferences or dividend obligations that might not be extinguished in an M&A transaction.

Future Financing. By going public, the biotechnology firm will be able to raise additional capital and to increase its ability to obtain other types of financing. Future investors can be offered new securities with liquidity, and the firm will have an ascertainable market value that may help support debt financing.

Mergers and Acquisitions. A public biotechnology firm can create a “war chest” to acquire other assets or businesses by using cash or its securities.

Corporate Reputation. A public offering can enhance a biotechnology firm’s name recognition and strengthen its competitive position in the industry. Media attention accompanies the mere announcement of a public offering. There is also a certain prominence or “halo effect” that accompanies a successful IPO.

Officer, Director, Employee, and Consultant Recruiting and Retention. Once public, it is often easier to attract and retain key officers, directors, advisors, and employees through stock options, restricted stock grants, stock purchase plans, and stock appreciation rights. This is an important advantage for biotechnology firms because they often need to attract highly sought-after scientists, government-funded researchers, or executives from larger established biotechnology firms. These professionals must often be convinced to give up the security provided by larger organizations for the promise of financial rewards that come from joining, and acquiring an equity interest in, a growing biotechnology firm.

Estate Planning. Going public can help diversify founders’ portfolios. In addition to a primary offering of shares by the issuer, an IPO may include a secondary offering of shares owned by existing shareholders such as founders or early backers of the firm.

Disadvantages to the Biotechnology Firm in Becoming a Public Company

The disadvantages to going public include:

Liability Risks and Regulatory Scrutiny. Becoming public brings the biotechnology firm wider public exposure and scrutiny by governmental authorities. The public biotechnology firm becomes subject to SEC and stock exchange oversight. The firm will have disclosure obligations to public shareholders. The obligation to disclose material developments in a timely manner create very difficult issues when combined with regulatory or product development issues. Product or technology development challenges such as FDA rejection or disappointing clinical trial results may compound into immediate securities law disclosure issues and risks. Disappointing or unexpected financial results often lead to lawsuits alleging securities law disclosure violations.

Potential for Loss of Control. Depending on the amount of shares sold to the public, controlling shareholders will often lose control of the company at the time of the IPO or in the near future. Going public can also lead to risks of an unfriendly takeover.

Loss of Confidentiality. The biotechnology firm's prospectus and ongoing periodic reporting to the public must disclose previously confidential information about the biotechnology company including, among other things, material agreements, intellectual property, financial data, competitive position, and officer and director compensation.

Reporting and Ongoing Compliance. The public biotechnology firm will be subject to the periodic reporting requirements of the SEC. These requirements include (i) quarterly reports, (ii) annual reports, (iii) current reports of material events, (iv) proxy statement disclosures related to the board and officers in connection with shareholder meetings, and (v) reports of ownership in and trading of shares by insiders. These public filings require complex information

technology and accounting systems, internal controls, more accounting staff, and increased use of lawyers, accountants, and other outside advisors. Securities analysts and the financial press will also require attention from executives.

Initial and Ongoing Expenses. Going public is a costly and time-consuming endeavor. Legal, accounting, and related investor relations expenses will obviously increase on an ongoing basis as a result of a public offering. There are also the costs related to the offering itself. The underwriter of a public offering will charge a commission that can range from 6% to 10% of the offering price. In addition, legal and accounting fees, printing costs, and underwriters' expenses and fees will generally add \$500,000 or more to the cost of an offering.

Pressure to Satisfy Shareholder Expectations. Investors will generally expect the biotechnology firm to maintain and continually improve performance with respect to measures such as revenues, earnings, growth, and market share. This can be a significant challenge for a pre-revenue biotechnology company whose fortunes cannot necessarily be measured by revenue or earnings growth, but rather through product or technology development milestones that may or may not pay off in terms of revenue or earnings sometime in the distant future. If investors become disillusioned with the firm's performance, the firm's share price will drop.

Restrictions on Selling Existing Shareholders' Shares. Controlling or major shareholders of a public company cannot freely sell their shares. Additionally, no one with inside information may trade in the company's stock before that information becomes public under penalty of civil and criminal law.

Preparing the Biotechnology Firm for an Initial Public Offering

There is no magic rule to determine whether a company is ready to become public. A variety of factors including market conditions,

the right product or technology, financial condition and results of the company, the management team and the business plan will generally determine whether a company and its advisors can successfully complete a public offering. Many biotechnology firms require a long gestation period before they are able to generate revenue or earnings. Consequently, with the exception of proven or established companies, underwriters will generally demand that a traditional start-up biotechnology company going public have a strategy that can be easily explained and understood by investors to support a public offering.

Board of Directors. Selecting a board of directors for the public biotechnology firm is not that different from selecting directors for a public company in any other industry. The biotechnology firm needs a board that is experienced in the firm's industry and has financial expertise. The expertise of the firm's board, in addition to the strength of the management team and business plan, is typically an important selling or marketing tool for the underwriters. Additionally, the firm should have a majority of independent directors who do not have a relationships with the biotechnology firm such as consultants, former employees, vendors or suppliers. The scientific and technical expertise of a biotech firm's board of directors may be supplemented by a separate scientific advisory board that is not part of the formal corporate governance structure of the firm.

Board Committees. The biotechnology firm contemplating an IPO must have independent directors willing to serve on one or more of the an audit, compensation, and governance committees. In response to corporate scandals, the roles of these committees with respect to corporate governance, oversight of management, and responsibility to the public shareholders have been magnified.

State of Incorporation; Minnesota vs. Delaware. An underwriter for a biotechnology firm contemplating a public offering may ask that the firm consider reincorporating in Delaware instead of Minnesota. Many national underwriters

or their counsel are unfamiliar with Minnesota law and often try to persuade a company to reincorporate in Delaware. There are advantages to incorporating in Delaware, but there are also advantages to incorporating in Minnesota. A significant number of the largest and most widely known public corporations in this country are incorporated in Delaware. There is, consequently, a widely followed core of Delaware corporate law that has been interpreted over the years. Many directors are also more comfortable serving on the board of a Delaware corporation because indemnification of directors under Delaware law is well developed and more certain compared to most other states, including Minnesota. Disadvantages to incorporating in Delaware include franchise taxes and less protection for minority shareholders. Advantages to incorporating in Minnesota include protections afforded by Minnesota's strong anti-takeover measures that are generally favorable to companies and incumbent boards of directors.

Underwriters

The underwriter is an investment banking firm or broker-dealer that purchases shares from the firm in the IPO and immediately resells these shares to the public. The selection of the underwriter is one of the key decision points in the biotechnology firm's undertaking a public offering. Often, this decision will be made with input from the venture capitalists, investors, or other significant shareholders who have financed the firm.

In selecting underwriters for a public offering, a biotechnology firm should consider whether the underwriter is national, regional or local; has experience in the biotechnology industry; is excited about the company's business plan; has been successful with biotechnology-related IPOs; and has research and brokerage experience in the biotechnology industry. The following is a summary of typical underwriting arrangements.

Letter of Intent. An underwriting agreement is signed only after the registration statement becomes effective. The formal underwriting relationship typically begins with a letter of intent.

Offering Size and Price. Underwriters will not guarantee an offering price or total proceeds in advance. In order to meet market conditions, the offering price is set when the registration statement becomes effective. Underwriters will generally estimate a range for the offering price based on market conditions, but these estimates are not binding.

Underwriting Commissions. The underwriting commission, or discount, is the single largest expense in a public offering. The rate has generally been in the range of 6% to 10%.

Underwriter Warrants. Many underwriters will request a warrant to purchase additional securities in addition to the commissions paid to the underwriter. The warrant will generally give the underwriter a five-year right to purchase shares at a price equal to 120% of the IPO price.

Reimbursement of Underwriters' Expenses. The managing underwriters will often request reimbursement for some or all of their expenses incurred in the offering, including legal fees. The issuer and underwriter will often agree to limits on reimbursable expenses.

Rights of Refusal. Underwriters also often request a right of first refusal on any future underwritings or other financings by the biotechnology firm. If a right of first refusal cannot be avoided, the issuer should (i) establish a time limit after which the right expires, (ii) restrict the right so that it expires any time it is available but not exercised, and (iii) restrict the right so that it applies only to equity public offerings.

Lock-Up Agreements. Underwriters will typically insist that all company shareholders agree to “lock up” or not sell or transfer their shares from the time of the IPO until six or twelve months from closing without the express written consent of the underwriters.

Over-allotment Option. The underwriters will also ask for the right to purchase additional shares in an amount up to 15% of the offering for a period of 30 to 40 days after the closing of the initial offering. Whether this option is exercised depends on the market acceptance of the company's securities.

Offering Publicity

One of the most important aspects of a biotechnology firm's public offering relates to the SEC's restrictions on publicity and communications before, during, and after a public offering. The SEC has strict rules on what kinds of communications can and cannot be made during the offering process and on the required filings and other warnings that must accompany or precede certain communications outside of the formal prospectus. The biotechnology company must be very careful to comply. Specific issues unique to a biotechnology firm may occur if during the course of an offering the firm must make disclosures concerning the status of regulatory filings or approvals. It is critical that the firm comply with the publicity prohibitions of the securities laws. If the SEC determines there is inappropriate publicity or activity in connection with the offering, then the SEC could delay the offering, which could harm the firm if market conditions deteriorate and cause a liquidity crisis. Inappropriate publicity can also subject companies and their officers and directors to securities law liability.

The Registration Statement Process and the Offering

The biotechnology company and its counsel, the underwriter and its counsel, the company's independent auditing firm, investor relations counsel, scientific consultants (including intellectual property or FDA counsel) and others will meet many times in drafting sessions to prepare the registration statement. The registration statement includes the prospectus that will be delivered to investors. The entire registration statement becomes part of the public record immediately on filing with the SEC, and is available for public inspection. The prospectus is both a disclosure document designed to inform investors and limit liability to the company and its officers and directors by describing risks to investors, and a marketing document telling investors about the exciting investment opportunity that the company represents. These objectives often create conflict among the various constituencies involved in drafting the document and the SEC, which is responsible for reviewing the disclosure and declaring the registration statement effective to permit sales of the relevant securities.

Due Diligence Investigation. “Due diligence” is a key aspect of the registration process. Due diligence is the responsibility of all those involved in the preparation of the registration statement to conduct all reasonable investigation to ensure the accuracy of the statements made in the registration statement and to ensure that no material information has been omitted. Of course, the exercise of due diligence with respect to any particular statement or disclosure will imply differing responsibilities depending on the position and role of the individual and the nature of the information.

The biotechnology firm itself is liable, regardless of due diligence, for any material misstatements or omissions in its registration statement. The directors, controlling shareholders, underwriters, experts, and corporate officers may, however, avoid liability if they can show that they exercised reasonable or due diligence in examining the facts or relying on the reports of experts. They cannot avoid liability if “red flags” exist that should have alerted them to investigate an issue further.

The underwriters will request a “comfort letter” from accountants. This letter details the specific procedures carried out by the company’s accountants with respect to the unaudited financial data contained in the registration statement, and provides the underwriters with “negative assurance,” a statement that nothing came to the accountants’ attention that indicated that the unaudited financial statements and other financial data were not prepared in accordance with generally accepted accounting principles applied on a consistent basis, and that there have been no material changes in the financial position or results of operations.

SEC Review. The SEC reviews all registration statements of IPOs for adequacy of disclosure in accordance with its regulations and other pronouncements. Any deficiencies noted by the SEC staff are generally communicated by a “comment letter.” In many cases, the staff focuses on management’s discussion and analysis of the issuer’s financial condition and

results of operations, transactions between the company and related parties, and areas of weakness in the company, or risks to the company or industry. The SEC may ask the company to support certain claims or statements made in the prospectus by sending the SEC “supplemental information” and to remove the claims or statements if the SEC considers the support inadequate. The SEC may also take issue with a particular choice of accounting policy, or may request additional disclosures in the financial statements.

Underwriters’ Syndication. As soon as the preliminary prospectus is filed with the SEC, the managing underwriters begin their efforts to assemble an underwriting syndicate to sell the company’s securities. A copy of the red herring is provided to each prospective investor, who may then “express interest” in the shares. No sales may be made, however, or offers to buy accepted, prior to the effective date of the offering. Allocation of the underwriting commission is first made to the managing underwriters as compensation for managing the offering, with the balance allocated to the underwriting syndicate in proportion to both shares subscribed and shares ultimately accepted for sale to investors.

The underwriters will likely take the biotechnology firm’s executives on a “road show” to sell the offering. These meetings are designed to give prospective members of the underwriting syndicate and institutional investors an opportunity to understand the biotechnology firm and hear the “story.”

Listing Requirements

In consultation with the lead underwriter, the biotechnology firm must decide where to list its securities. Historically, the New York Stock Exchange has been considered the most prestigious exchange on which to list securities. The Nasdaq Stock Market, however, is typically the choice of technology companies including most biotechnology companies undertaking their first offering. Each trading market has its own quantitative listing requirements, which include market capitalization, price, revenue history, and its

own qualitative listing requirements, which will include provisions related to independence of directors and members of the audit, compensation, governance, and nomination committees.

Closing the Offering

If all agree to proceed with the offering, the deficiencies noted by the SEC have been cleared to the SEC's satisfaction, and the final pricing details have been agreed on, then the registration statement is declared effective by the SEC, the underwriting agreement is signed and the final prospectus is printed. The closing generally occurs three business days after the effective date, and the proceeds are released to the company and any selling shareholder. If the over-allotment option is exercised, a second closing will be held following that transaction.

Periodic Reporting Requirements

Following the completion of a public offering, the biotechnology company is publicly held. This new status imposes its own significant expenses, burdens and responsibilities on the company and its officers and directors. The following is a summary of the principal reporting requirements of public companies.

Form 10-K. After the biotechnology firm goes public, it must file with the SEC an annual report on Form 10-K within 60, 75 or 90 days of the end of its fiscal year, depending on its market capitalization. Form 10-K must contain audited financial statements for the last three fiscal years, or such shorter period as the company has been in existence, in addition to substantial information regarding the company and its past year's operations. Form 10-K must be signed on behalf of the company by its principal executive officer, its principal financial officer, its principal accounting officer, and by at least a majority of the members of its board of directors. Smaller issuers may disclose less information if they qualify as a "smaller reporting company" which generally applies to companies whose "public float" held by non-insiders is less than \$75 million.

Form 10-Q. In addition to Form 10-K, the company is required to file a quarterly report on Form 10-Q with the SEC for the first three quarters of its fiscal year. A report on Form 10-Q must be filed within 45 days after the end of each quarter (30 or 40 days for large companies). Form 10-Q must include unaudited quarterly financial statements and must be signed by the appropriate officers, but not the directors, of the company.

Form 8-K. A Form 8-K report is required to be filed with the SEC within four business days following the occurrence of significant corporate events. Events that trigger the Form 8-K reporting requirement include:

- Entering, terminating or amending a material agreement;
- Release of financial information;
- Filing bankruptcy;
- Completing a material purchase or sale of assets;
- Incurring certain direct or off-balance-sheet financial obligations;
- Receiving notice of being delisted from a stock exchange;
- Unregistered sale of equity securities;
- Change in accountants;
- Appointment or departure of officers or directors;
- Amendments to articles of incorporation or bylaws; and amendment or waiver of company code of ethics.

Management Discussion and Analysis. Public companies must include the Management’s Discussion and Analysis of Financial Condition and Results of Operations (“MD&A”) in their Form 10-Q reports, Form 10-K, and annual report (which often include the Form 10-K) to shareholders, as well as in registration statements under the Securities Act. The MD&A is intended to “provide in one section of a filing, material historical and prospective textual disclosure enabling investors and other users to assess the financial condition and results of operations of the registrant, with particular emphasis on the

registrant's prospects for the future." The SEC has consistently focused on the importance of the MD&A section as a guide to interpretation of a company's financial statements. Failure to include adequate disclosure may result in enforcement actions and possible civil litigation. The SEC has emphasized that a company is required to disclose currently known trends, events, and uncertainties that are reasonably expected to have material unfavorable or favorable effects on a company, such as a reduction in the company's product prices; erosion in the company's market share; changes in insurance coverage; or the likely nonrenewal of a material contract. The MD&A rules also require a description of short-term liquidity and capital resource needs, covering cash needs up to twelve months in the future, and long-term liquidity and capital resource needs beyond the next twelve months, as well as the proposed sources of funding required to satisfy such requirements.

Exhibits. The exhibits that must be publicly filed include basic documents of the company, consisting of its articles, bylaws, and "material" contracts. Under new SEC rules effective in 2004, when a company enters into a contract or terminates or amends a contract, the company must determine whether the contract would come within the definition of a "material" contract as set forth in Item 601 of Regulation S-K. If so, the company must file a Form 8-K within four business days, describing the contract.

Proxy Regulation. Public companies are required to comply with the proxy requirements of the Securities Exchange Act of 1934, as amended ("Exchange Act") and file proxy materials with the SEC in connection with any matter brought to a vote of their shareholders. Most public company proxy solicitations are on behalf of the board of directors and relate to an annual meeting at which directors are to be elected. This proxy statement must be accompanied or preceded by an annual report to security holders containing audited financial statements for the last three fiscal years and other information required by the Exchange Act.

Of particular interest to officers and directors is the requirement that the proxy statement must disclose the cash compensation, bonus arrangements, and stock option information relating to the company's CEO and four most highly compensated executive officers other than the CEO whose total cash and cash equivalent remuneration, during the preceding fiscal year, exceeded \$100,000. Larger companies must include a "Compensation Discussion and Analysis," or "CD&A" that describes each element of executive compensation and explains why each element was awarded. Material relationships and transactions between the company and directors, director nominees, or executive officers must be disclosed.

Sarbanes-Oxley

In response to widely reported corporate fraud and accounting lapses, in July 2002, Congress enacted a series of corporate governance and accounting reforms under The Sarbanes-Oxley Act of 2002³. This statute, along with rules and regulations promulgated by the SEC, contain the most significant changes affecting public companies since the passage of the Securities Act and Exchange Act in 1933 and 1934, respectively. Among other things, Sarbanes-Oxley contains important new reforms in accounting, disclosure practices, corporate governance and responsibility, insider trading, audit committees, and attorney conduct. In addition to expanding the SEC's regulatory powers, Sarbanes-Oxley reflects an aggressive and active regulatory philosophy toward publicly held corporations in which conservative accounting and transparent disclosure are the guiding principles. One of the important changes brought about by Sarbanes-Oxley is the explicit subjection of a public company's senior officers, including the CEO and CFO, to potential criminal responsibility for the company's failure to complete accurate and truthful disclosure documents, including financial statements and other information contained in SEC reports.

Timely and Adequate Disclosure of Corporate News

Publicly held companies are generally expected to release quickly to the public any news or information that might reasonably be

expected to materially affect the market in their stock. As with most “general rules” there are exceptions. If there are legitimate business reasons for withholding the public disclosure of material corporate information, many corporations (on advice of counsel) will defer disclosure. If the information leaks into the marketplace or if significant trading activity occurs in the shares of the nondisclosing company, disclosure is often required. The biotechnology company should act promptly to dispel unfounded rumors that result in unusual market activity or price variations. Disclosures must be widely and fairly disseminated and may not be given selectively to favored individuals or organizations.

Requirements of Officers, Directors and 10% Shareholders

There are three specific requirements of Section 16 of the Exchange Act dealing with “insiders” (executive officers, directors and shareholders with 10% or greater beneficial ownership in the common stock of the company). They are as follows:

- New insiders of the company must disclose their direct and beneficial ownership of the company’s equity securities on Form 3 within ten calendar days of becoming an insider;
- Insiders of the company must report all of their transactions in the company’s securities within two business days on Form 4 and, in some circumstances, must file an annual report on Form 5 to report certain exempt transactions; and
- Insiders of the company may not profit from the purchase and sale or sale and purchase of the company’s securities if both transactions occur within a six-month period.

Individual Sales of Shares

There are restrictions on resales by the biotechnology firm’s executives or directors who wish to sell some shares to diversify their portfolio or raise cash. First, the underwriters will generally insist that insiders not sell any shares for six or twelve months after the offering without the consent of the underwriters. Once this “lock-up” period expires, insiders must generally sell in compliance with Rule 144 of the Securities Act. In order for a sale to be effected in compliance with Rule 144, the following conditions must be met:

Holding Period. The insider must have held restricted securities for at least six months prior to the sale. Shares that were purchased in the market or acquired in a restricted issuance, e.g., shares issued pursuant to a registered stock option plan, are not restricted.

Limitation on Amount of Securities Sold. Rule 144 limits the amount of securities that may be sold by affiliates during any three-month period to the greater of 1% of the securities outstanding or the average weekly volume of trading during the four calendar weeks preceding the filing of the notice of the proposed sale on Form 144.

Manner of Sale. Securities sold by affiliates pursuant to Rule 144 must be sold by brokers acting as agents in unsolicited transactions or in transactions directly with a market maker of the securities.

Current Public Information. At the time of sale, there must be available adequate current public information with respect to the issuer, which means the issuer must be current in its SEC reporting.

Notice of Proposed Sale. If the proposed sale is more than 5000 shares or for more than a \$50,000 aggregate sale price, the seller must file a notice on Form 144 to be sent to the SEC on the same day the order for sale is placed with a broker.

Other Public Financing Alternatives and Transactions

Once the biotechnology company is public and has been reporting, it can access the public capital markets. The company may, depending on market demand and success of the company's product, service or technology, undertake a secondary offering in which the company, insiders or other selling shareholders participate. The firm may wish to acquire other companies or assets using its stock as currency. One common transaction that many biotechnology companies rely on as a public financing vehicle is the PIPE transaction.

PIPES

PIPE is an acronym for private investment in public equity (“PIPE”). This transaction is attractive for many new public companies including biotechnology companies because a PIPE offers relatively fast access to capital. Fast access may be necessary for biotechnology companies that need capital quickly to acquire assets, fund a clinical trial, or for some other corporate purpose when traditional bank financing is unavailable, and undertaking a follow-on public offering would take too much time. A PIPE transaction can be closed and funding provided to the public biotechnology company generally within ten to thirty days. Consequently, a PIPE transaction can be advantageous because it offers flexibility and speed to issuers and investors. It also is generally less expensive to consummate than a traditional public offering.

Essentially a PIPE involves a private placement of securities by an issuer to a relatively small number of investors. In connection with the PIPE, the issuer commits to file a registration statement to permit the investors to resell the privately placed security (or securities that are converted from the originally issued securities) into the trading market prior to the expiration of the six-month holding period that would be applicable under Rule 144.

Securities Issuable in PIPE Transactions. Many kinds of securities can be sold through a PIPE including common stock, convertible preferred stock, convertible warrants, or other equity security. Typically, the security sold in the private placement, or the security into which the privately placed security is convertible, has an existing trading market. That permits relatively expeditious resales by PIPE investors when they choose.

Typical PIPE Terms. The conventional PIPE transaction consists of a private placement to institutions or to a small number of accredited investors through a stock purchase agreement. The investors purchase a fixed number of shares of securities at a fixed price at some discount to the market. The stock purchase agreement contains typical representations and warranties but relies extensively on the adequacy of the disclosure contained in the biotechnology company’s existing

SEC reports. Immediately or shortly following the funding of the private placement, the biotechnology company files a resale registration naming the private placement purchasers as selling shareholders in the prospectus. Sometimes, the investors will receive interest on the privately placed security. Often the biotechnology company must pay the investors a penalty interest rate if the resale registration statement is not declared effective by the SEC within a certain time period.

Company Requirements. Typically, a biotechnology firm proposing a PIPE transaction is Form S-3 eligible. Form S-3 is a short-form registration statement that permits established companies to provide less disclosure to investors, and refers investors to publicly available information that becomes a part of the selling document. To be Form S-3 eligible, the biotechnology company must have been public for one year and have filed all required SEC reports in a timely manner and cannot have defaulted on any debt or failed to pay dividends on preferred stock in the past year. A PIPE can be accomplished with companies that are not S-3 eligible, but some of the advantages of speed and cost are lessened because of the time and expense required to comply with longer-form registration statements for the resale by investors.

Unorthodox PIPES, Toxic Conversions and Death Spirals. One PIPE transaction that desperate issuers sometimes succumb to is the “death spiral” or “toxic conversion” PIPE. In this transaction, the privately placed security converts into a variable number of shares of common equity that often is linked to the underlying trading price without a floor or bottom. If the market for the common equity declines, the private purchaser receives more shares. This type of transaction is commonly referred to as a “death spiral” because it is often associated with large declines in stock price and has been linked to price manipulation by short-sellers and others.

Regulatory Approvals. Depending on the terms, a PIPE transaction may require approval of the exchange on which the

company is listed. Also, listing rules of the American Stock Exchange, Nasdaq, and NYSE generally require shareholder approval for issuances of securities, including convertible securities, equal to 20% or more of the voting power of the company, subject to certain exceptions and qualifications. In circumstances where shareholder approval is required, the company may close on a portion of the offering and then seek shareholder approval or close into escrow.

E. Debt

Introduction

It has generally been true that as the biotechnology company matures, traditional debt from commercial lending institutions will become available as a financing alternative. The ability to obtain debt is a function of the borrower's cash flow, the value of the collateral that the borrower can post, and specific requirements unique to various lenders in the marketplace. Because of the serious recession in the United States that began in 2008, and the resultant freezing of credit, it is now extremely difficult for a new company to obtain loans from commercial lenders. Some sources of credit do remain, however. Biotechnology companies located in the trade areas of community banks may have a better opportunity of obtaining loans and credit from those banks. In addition, credit may be available from asset-based lenders if the biotechnology company has sufficient receivables and inventory to serve as collateral. This credit is more expensive than commercial bank credit because interest and fees charged by asset-based lenders are significantly higher than those charged by commercial banks. Finally, companies that "factor" (or purchase) receivables may be another source of financing for the biotechnology company that is willing to sell its receivables at a heavy discount in order to obtain immediate cash.

Cost of Credit

In Minnesota, as in most states, interest rates and fees charged by commercial lenders to borrowers in commercial transactions are less regulated under state law than those in consumer loans.

Most companies are aware that complex, expensive offering documents that are required when raising equity are not required in commercial loans, but the biotechnology company should bear in mind that there are also costs associated with debt financing, including front-end fees charged by commercial lenders, the payment of attorneys fees, and other transactional costs for both the lender and the company itself.

Corporation Formation Documentation

Lenders will analyze the company's formation, including documentation regarding the nature of the entity's operation and its owners. Lenders must review these documents in order to verify the company's legitimacy and understand who really owns the business. Beyond these formation documents, the lender will also want to examine corporate or limited liability company authorizations that identify those persons who have the authority to obtain credit on behalf of the company, and have authority to legally bind the company.

Note

A note is a negotiable instrument that specifically sets forth the borrower's promise to repay all credit advanced. It also indicates the type of credit being extended (e.g., term loan, revolver, line of credit), the dollar amount of the loan, and the company's promise as to how and when it will repay all related principal, interest and fees. Although detailed "events of default" are generally contained in the credit agreement, the note may also contain a list of "events of default" that, if they occur, would trigger the lender's right to accelerate the loan and demand immediate payment. Default provisions cover a wide range of situations from a failure to pay interest or principal when due, to the lender's belief that the company may be in financial trouble, which is commonly referred to as the "general insecurity clause."

Security Agreement

A security agreement grants the lender a security interest in specified personal property assets of the company such as receivables and inventory to secure the loan. The security agreement creates the lender's rights to foreclose on the collateral

in the event of nonpayment of the note or other default. The document will also contain restrictions on what the company may or may not do with the collateral while it is subject to the lender's security interest. The lender will take steps to perfect its interest in the collateral. "Perfection" is a Uniform Commercial Code ("UCC") term referring to the process whereby a secured party protects its lien interest in the collateral against all other lien holders—including a trustee in bankruptcy. Lenders will do this in a variety of ways depending on the nature of the collateral and the requirements of the UCC.

Subordination Agreement

Lenders will require a subordination agreement when the borrower already has existing debt payable to another creditor, including debt to a shareholder or member of the biotechnology company. The subordination agreement is a three-party agreement among the borrower, the bank as a senior creditor, and the other creditor as the subordinated or junior creditor. The document provides for the junior creditor to subordinate all its rights and remedies against the borrower to the interests of the senior creditor in right of payment and in the collateral.

F. Federal Grants Through SBIR/STTR Programs

Although federal grants for small businesses through the Small Business Innovation Research Program ("SBIR") and the Small Business Technology Transfer Program ("STTR") remained available as this edition went to press, funding for the SBIR and STTR programs is currently under a continuing Congressional funding resolution that expires on July 31, 2009. For the status of the programs, please check any one of the websites listed below, or contact the Minnesota Department of Employment and Economic Development ("DEED"), which has established, within its Office of Science and Technology, an SBIR/STTR assistance program to coordinate funding opportunities between Minnesota companies and participating federal agencies with respect to the SBIR/STTR programs. DEED's website can be found at <http://www.deed.state.mn.us/SciTech/index.htm> and the SBIR/STTR representative can be contacted at 651-259-7441. Other helpful websites include:

<http://inknovation.com/> or the United States Small Business Administration, Office of Technology, at **<http://www.sba.gov/sbir/>**. For more information, visit the websites of the SBA at **<http://www.sba.gov/aboutsba/sbaprograms/sbir/index.html>**, National Institutes of Health, Office of Extramural Research at **<http://grants.nih.gov/grants/funding/sbir.htm>**, the National Institute of Standards and Technology at **<http://tsapps.nist.gov/tsbir/default.asp>** and the Department of Defense at **<http://www.acq.osd.mil/osbp/sbir/solicitations/>**. The website **www.zyn.com/sbir** provides tools for easily searching open SBIR/STTR solicitation topics.

IV. BUSINESS FACTORS THAT INFLUENCE BIOTECHNOLOGY FINANCE

A. Management Equity Incentive Compensation

Background of Internal Revenue Code Section 409A

In the original publication of this *Guide*, we mentioned that Section 409A of the Internal Revenue Service (“Section 409A”), which was passed in October 2004 in response to the collapse of Enron and WorldCom, would have an effect on some equity grants such as stock options and stock appreciation rights. Since that time, the IRS has issued final regulations under Section 409A, and issuers that have equity plans and other executive compensation arrangements have had to consider, and in many cases comply with, the restrictions under Section 409A.

Top executives at Enron, WorldCom, and other entities were able to withdraw funds from their nonqualified deferred compensation accounts shortly before these entities collapsed, thereby allowing these executives to receive millions of dollars that would have otherwise benefited employees and creditors. In response, Congress enacted Section 409A to impose restrictions on the time and form of payment to recipients of any deferred compensation, other than qualified pension plans, certain short-term bonuses, and welfare benefits. Prior to the enactment of Section 409A, a 1978 Congress-imposed moratorium prevented IRS regulation of nonqualified deferred compensation. This moratorium allowed executives to either accelerate or defer payment from one tax year to another under existing laws.

What Section 409A Requires

While Section 409A on its face dealt with deferred compensation, the IRS regulations defined deferred compensation, with limited exceptions, as any payment to an executive that *vests in one year* and is *payable in a subsequent tax year*. While a detailed discussion of Section 409A is beyond the scope of this *Guide*,

here are the essential requirements of Section 409A applied to nonqualified deferred compensation:

- Section 409A applies to any deferred compensation that first accrues or becomes vested after December 31, 2004, but will also apply to so-called “grandfathered plans” (where benefits accrued and vested before January 1, 2005) in the event those plans are materially modified after December 31, 2004.
- The time and manner of the payment of deferred compensation must be selected (whether by the employer or the participant) at the time the grant is made, except that the election to defer “performance-based” compensation (such as annual or long term bonuses) may be made up to six months prior to the end of the performance period.
- The time for payment must be either a fixed date (or schedule) or one of the following events (as defined by Section 409A): “separation from service” (which means near total cessation of duties with all entities in a controlled group), death, disability, unforeseeable emergency, or a change in the actual or effective control of the employer or its parent entity. For “specified employees” of public companies, payment must be delayed for six months following “separation from service.”
- Once elected, the time and manner of payment cannot be accelerated (with a few exceptions, such as payment of taxes on the amount or in the event of a divorce) and cannot be deferred unless the election is made at least twelve months prior to the original date of payment and payment is deferred at least five years. A terminated plan must delay payments for twelve months from the date of termination, and no replacement plan can be established for three years after payment is made.
- Deferred compensation that fails to comply with these requirements is subject to a 20% excise tax payable by the recipient of the compensation, in addition to income taxes and interest for the tax that should have been paid at the time the compensation vested.

Effect of Section 409A on Equity Grants

Of particular importance to both start-up and development stage companies, the IRS regulations include certain grants of options, stock appreciation rights, or restricted stock units, as well as certain executive severance arrangements and change-in-control bonuses, within the definition of deferred compensation. With respect to stock options and stock appreciation rights, deferred compensation is created if (i) the exercise price is less than fair market value as of the date of grant or (ii) there would be other payments to the holder that did not reflect solely the pure appreciation in value of the stock underlying the grant. Because such a grant can typically be exercised over a number of years subsequent to its vesting, this discount creates deferred compensation that does not meet the requirement that the year of payment be fixed at the time of grant. This issue has caused companies to review and amend prior grants. In considering new grants, companies need to determine whether to comply with, or meet the requirement to be exempt from, Section 409A.

The following types of equity grants are generally exempt from Section 409A:

- Incentive stock options under Code Section 422 and options under an employee stock purchase plan governed by Code Section 423.
- Capital or profits interest in an LLC (until further IRS guidance); however, a grant of an option or other appreciation right in an LLC or partnership, or a change-in-control bonus based on the value of an LLC, will be subject to Section 409A.

A nonqualified stock option or stock appreciation right will also be exempt from Section 409A if the following conditions are met:

- The grant is based on a fixed number of common equity rights of an entity, including any joint venture where the ownership is 20% or greater;
- The exercise or grant price is at least 100% of fair market value on the date of grant based on the “reasonable application of a reasonable valuation method”;

- There are no dividend preferences or put or call rights at a price greater than fair market value; and
- There is no deferral of the spread beyond the exercise date.

Valuation Methods to Exempt Options from Section 409A

By defining certain equity grants as subject to the definition of deferred compensation, the IRS regulations now require companies to meet new standards in determining “fair market value” in order to avoid being required to comply with the restrictions under Section 409A. Generally, the “reasonable valuation method” must consider the following five factors: (1) value of tangible and intangible assets; (2) present value of anticipated future cash flows; (3) readily determinable market value of similar entities; (4) recent arms-length transactions involving the entity’s equity; and (5) control premiums or discounts for lack of marketability, if applicable.

The IRS regulations put the burden of proving reasonable valuation on the company. The regulations also establish the safe harbor methods of determining fair market value. When one of these is used, the burden is placed on the IRS to prove that the valuation method was unreasonable. These safe harbor methods are:

- An independent appraisal within twelve months of valuation, if there is no change in control anticipated within 90 days or a public offering reasonably anticipated in 180 days; or
- For companies in operation for less than ten years, a written valuation by a person with at least five years experience in either: (i) business valuation, (ii) secured lending, (iii) investment banking, (iv) private equity, (v) financial accounting, or (vi) the business or industry in which the company operates; or
- If certain other conditions are met, the formula under a buy-sell or similar agreement that binds all equity holders and does not lapse.

These equity rights are exempt from Section 409A, even if a right is subject to a put or call, unless the price of the put or call is

greater than fair market value (as determined above). Generally, a right of first refusal will not cause the right to be subject to Section 409A.

Some modifications to an exempt option (or other equity right) will cause the right to become subject to Section 409A. These include extending or modifying an “in-the-money” equity right or allowing accumulated dividend (or dividend equivalents) on the optioned right to be paid at the time of exercise, which is deemed to be a discount on the exercise price.

The following other modifications of exempt options do not, however, trigger “deferred compensation” that would be subject to Section 409A:

- Substituting equity in connection with a corporate transaction or certain reorganizations of the company;
- Accelerating vesting;
- Using previously acquired shares to pay the exercise price or withholding shares to pay tax withholding; or
- Extending the expiration of equity rights to up to ten years from the date of grant with respect to “underwater options.”

Options or stock appreciation rights that fail to meet these definitions for exemption may nevertheless be granted if the period or periods during which the rights may be exercised (at which time the deferred compensation would be paid) are limited to the payment events set forth above for deferred compensation (that is, separation from service, death, disability, change in control, or a fixed date).

Effect of Section 409A on Bonus Plans

Companies that provide incentive bonuses based on performance, where the right to the payment “vests” if the performance goals are achieved at the end of the performance period, can generally be exempt from the requirements of Section 409A (and any penalties) if the amounts must be paid within 2 ½ months following the later of the end of (i) the participant’s or (ii) the paying entity’s tax year. Therefore, we recommend that any such bonus plans contain

a fixed date for payment that falls within this period. This “short term deferral” exemption does permit an accrual basis taxpayer to deduct bonus payments in one tax year even though the participant is taxed on bonus in the next tax year.

Effect of Section 409A on Severance and Change in Control Payments

As noted above, the IRS regulations define “deferred compensation” broadly. The IRS includes within that term certain severance payments to executives, unless the payments are limited to the following:

- The involuntary termination by the company or a constructive termination by the executive for “good reason” (as narrowly defined under Section 409A);
- All payments are made by the end of the second year following the date of termination; and
- The amount of the payment does not exceed two times the lesser of: (i) the executive’s regular compensation or (ii) the IRS limit on qualified plan compensation. (The IRS limit in 2009 is \$245,000; therefore the maximum severance allowed would be \$490,000).

As a result, a severance payment, whether made before or after a change in control, that is payable under any other circumstance, including death, disability, or constructive termination for a more liberal definition of “good reason” could result in the severance being subject to the requirements of Section 409A. The principal disadvantage of having a severance payment subject to Section 409A is the inability of the company and employee, at least until after the expiration of the stated term of the agreement, to modify the time and form of payment, such as an acceleration or further deferral of the severance payments.

Similarly, many employment agreements are triggered by a “change in control” in which the definition in the agreement is broader (that is, a change in control is triggered earlier) than that permitted as a payment event under Section 409A. Therefore, certain payments triggered solely on a change in control (rather

than on a separation from service after a change in control) may result in payment that would violate Section 409A.

Because of the potential for discovery of fraud by executives leaving public companies, Section 409A also requires that any “deferred compensation” paid to up to 50 employees of a public company may not be made earlier than six months after the date of termination.

Compliance with Section 409A for executive employment and severance agreements, change in control agreements, bonus plans, phantom stock, and stock appreciation or stock option plans has become a necessary and burdensome expense for both public and particularly private companies. The limitations under Section 409A often result in unintended consequences and less flexibility in the negotiation of a sale of, merger with or new investment in, technology entities. Additional drafting in purchase or merger agreements and additional due diligence regarding compliance has increased the time and cost for these transactions. Although the penalties are borne solely by the individual by payment of an excise tax and additional interest penalties, most companies intend to comply with Section 409A so that the full value of any incentives, stock options, or severance benefits are realized by the executives. For their part, executives are more sensitive to structuring transactions so that the requirements of Section 409A are met.

The transition period for bringing nonconforming plans into compliance with Section 409A ended December 31, 2008. The IRS is currently contemplating whether to provide a correction program to allow companies to now amend nonconforming plans to comply with Section 409A. The IRS has instituted a correction program for certain inadvertent operational errors under Section 409A. Nevertheless, there are likely many companies and executives that will be surprised when they discover that certain of the benefits to which executives are entitled may now be subject to an excise tax.

Outstanding Equity Grants in a Down Round of Financing or a Down Market

Prior to the economic meltdown in October 2008, most companies did not have to deal with employees whose equity grants had lost

value. As a result of the economic collapse in late 2008, however, many companies, both public and private, find that the equity compensation grants now provide little incentive to executive and technical employees. For example, the exercise price of many stock options or stock appreciation rights are now substantially above the current fair market value of the company's stock and the prospect of achieving any gain in those stock awards may be years away. Similarly, many performance awards that were based on achieving specific stock prices or specific financial or operational goals may not be achieved. Further, many executive employment agreements that once provided for reasonable severance now may provide little or none. Ironically this may help struggling companies looking to bring in additional rounds of financing.

The issue of whether to reprice prior equity grants, or to issue additional grants or retention bonuses to replace existing programs, creates a conundrum for a company's board and its executive team. While providing new grants or modifying existing incentives appears to reward poor performance by the company's executives or provide an opportunity to lower the bar for future gains on their stock holdings, this alternative is not available to the equity investors. On the other hand, failure to provide new incentives may result in the loss of key technical or executive personnel who may be receptive to offers of new compensation, incentives, and equities at another company—to, in effect, reprice their current incentives simply by changing jobs.

Many companies today are considering both the philosophical and economic issues involving “underwater options.” This term equally applies to stock appreciation rights (“SARs”) or unit participation plans where the value to the individual is based on appreciation in any form of equity that has actually substantially depreciated in value.

Setting aside the philosophical debate over whether or not to reprice, this action of repricing involves legal, tax, accounting, and securities issues that must be addressed. While private companies should have more flexibility and greater understanding from their shareholders, others, including public companies, may limit the right to exchange underwater options for lower-priced

options or equity grants to personnel other than management and directors. Other companies will only allow an option exchange if the current exercise price exceeds a threshold over the current fair market value (such as 150%). Some employees and officers may be willing to give up current options for no consideration or no promise of future consideration in order that those cancelled shares may be reissued to other management or technical employees at a more favorable price. It is important to review the terms of the option grant and the plan under which the options or SARs were granted because, due to the insistence of shareholder advocate groups, many plans today restrict or prohibit the ability of the Board of Directors to reprice options, at least without shareholder approval.

Most companies that undertake a program of this nature, however, provide for an exchange of underwater options for either a new grant of options at a lower strike price, or for a grant of restricted stock, restricted stock units or cash. Because employees are receiving a replacement grant that is now presumably worth more than the option that is relinquished, the number of shares awarded in a replacement grant, or the cash or restricted stock given in exchange is often less than the number of shares replaced. In some cases, companies will impose new performance requirements or other vesting conditions as an additional hurdle to employees to the replacement of underwater options.

Often, this consideration is based on the accounting treatment of the expense related to the cancelled options as compared to the accounting expense created by the grant of a new option or other replacement equity. An option or SAR exchange does not have the adverse accounting consequences under Financial Accounting Statement (FAS) 123(R), which became effective in 2006 for most companies. When companies consider a “value for value” repricing of options or the exchange for another form of equity or cash, they consider the difference in accounting value that would be expensed in future periods between the current grant and the replacement grant. There is also the “perceived” value among option holders as to the incentive value of the replacement options, restricted stock, or cash.

Exchanging Options for Options

The advantages of repricing an option or exchanging an underwater option for a new option at the current market are its ease of communication, a reduced burn rate and dilution (assuming fewer shares are issued in exchange), and its ability to provide for greater leverage over cash or restricted stock.

The disadvantages include investor resistance and the possibility that replacement options could lose value if price declines continue, which brings additional employee skepticism of the value of these replacement options.

Exchanging Options for Restricted Stock

Exchanging options for restricted stock or restricted stock units may be appropriate because restricted stock or restricted stock units are less volatile because they contain some value even as the share price declines. They also result in reduced burn rate and dilution, since fewer restricted stock shares are needed to provide the value of an option (based on the accounting value of whole share grants vs. options).

The disadvantage of issuing restricted stock or restricted stock units, however, is that the amounts are taxable to the employee when vesting occurs (vs. options where taxation occurs on exercise or disposition depending on the option type, rather than vesting), resulting in (i) a further reduction in the number of resulting shares (if shares are withheld equal to the necessary tax withholding) or (ii) a cash outlay by the employee to cover the tax on the income generated by the receipt of non-cash property. Restricted stock units are generally not taxed until the shares are issued, which is generally later than the vesting date. Restricted stock units, are, however, subject to Section 409A.

Exchanging Options for Cash

Exchanging an option for cash has many advantages, including reducing or eliminating the dilution of outstanding options, providing immediate value to the employee, and accelerating into the current accounting period the future accounting expense associated with the underwater options.

The obvious disadvantages are the use of company cash to replace the options, loss of the perceived retention value of options, and the employee's loss of the leverage if and when the value of the prior equity increases. It would also be difficult to determine the fair exchange rate for the number and exercise price of options outstanding and the cash price for each.

Because an option exchange involves the sale or purchase of a security (the option), the solicitation of a large number of employees to exchange their options for new options, restricted stock or cash must comply with both state and federal securities laws and, if the stock is publicly traded, NYSE and Nasdaq rules. This would increase the expense of the exchange of options. Federal securities laws require that, if more than a very limited number of employees are given the right to exchange options, a tender offer document explaining the exchange program and outlining the risks to the employees in exchanging their options for a new or different form of equity must be prepared and distributed to participants and the offer to exchange must remain open for at least 20 business days. There are exceptions for certain intrastate offerings or, as noted above, negotiated arrangements for a small group of employees.

If the underwater option is an incentive stock option, the repricing will constitute a new grant and will reset the two-year holding requirements before the subsequent sale of the underlying shares would qualify for long-term capital gains. The exercise and sale before the two-year holding period expires would result in a disqualifying disposition of the incentive option shares, and an immediate tax on the gain on the shares, similar to a nonqualified option. In accordance with Section 409A, an underwater option may be repriced and will continue to be exempt from the restriction under Section 409A, as long as the new exercise price is at or above fair market value on the date of regrant and the total term of the option is not more than ten years. Care should be taken before replacing an option exempt under Section 409A with restricted stock or restricted stock units or replacing an option that may be subject to Section 409A, because the vesting or payment of the replacement equity may cause either an acceleration or delay in the payment date in violation of Section 409A.

Incentive Bonus Plans in a Down Market

As mentioned above, the economic downturn has affected virtually every form of executive bonus, short and long-term incentive, and even severance and change-in-control agreements. Many commentators in fact blame stock option gains and other short term incentives in most executive compensation package as either a cause of the collapse or at least contributing to the severity of the collapse. No one has missed the outrage by Congress and the President over the size and purpose of the “retention bonuses” paid by AIG and other companies. Prior to that, there was equal outrage over severance, retirement benefits, and bonuses paid to executives by companies whose stock performance declined or that otherwise ended in bankruptcy.

Unfortunately, the same consultants who recommended the make-up of the compensation packages that the public now criticizes have now called for a paradigm shift in restructuring executive compensation and incentives to avoid a similar collapse in the future. Among the principles of this new paradigm with respect to short term incentive plans are the following:

- Base short-term incentive plans on performance criteria not on total shareholder return or stock price, but on internal or operational goals such as growth in sales, growth in profits, or reduction in operating expenses;
- Base performance goals not on absolute criteria, but on outperforming a peer group of competitors or related companies with similar market capitalization;
- Reduce the threshold for achieving the target from 80% to 70% to make earning a bonus more achievable.
- Set performance goals over shorter periods, such as six months, which would allow the Board to reset the goals during the second half of the fiscal year depending on the level of achievement and the payments received during the first performance period.

With respect to equity grants, as stock prices have declined, many companies have reduced the value of the awards by granting the same number of shares as in past years and more companies are

now providing a mix of options, restricted stock, performance stock, and cash as incentives rather than relying purely on options.

With respect to long term incentives, the new paradigm dictates that the achievement of an award or the vesting of an award be based on performance, but the payment of the award is thereafter extended over one or two years to provide both a retention and a right to forfeit future payments (or claw-back previous payments) if there are reversals of the achievement of the award's performance goals (whether as a result of accounting errors or subsequent events, including market conditions). Finally, many companies, especially public companies, are requiring that grants to executives, whether on vesting or on exercise, not be sold (other than to pay taxes) but must be retained until termination of employment or beyond. This prevents the executives from realizing a short-term gain on these incentives, but rather requires that any decisions they make that earned them the award are sustained throughout the holding period. In this regard, some plans even require that executives near retirement must retain a significant ownership in company shares even after retirement, so that even these executives have a long term view of the performance of the company at all times.

B. Intellectual Property Rights

Intellectual property is fundamental to the financing strategy of a biotechnology company. The right and ability to develop and exploit existing or new inventions, trade secrets, proprietary information, and know-how are the company's most valuable assets. To develop an effective financing strategy, a biotechnology company must consider the intellectual property it might develop, acquire, or license. It is equally important for that company to develop a thorough knowledge of the competing intellectual property that is or may be owned or under development by other companies or entrepreneurs in the same field.

Additionally, before venturing into a discrete area of biotechnology, a company must develop a thorough understanding of governmental regulations, scholastic research, and information in the worldwide public domain that may have an effect on

contemplated developments. The value of existing or proposed intellectual property is contingent both on the availability of legal protection and on the immediate and long-term demand for new developments in that area of biotechnology.

There are four broad categories of intellectual property: patents, copyrights, trademarks and service marks, and trade secrets. All intellectual property is international in scope, and no effective financing strategy can disregard international regulation and protection. Although a number of international treaties and conventions allow for some degree of international protection, there is no “worldwide patent” or “worldwide trademark” governed by a uniform, universal statute. For illustrative purposes, this section will primarily address U.S. intellectual property law.

In the U.S., patents and copyrights are authorized by the U.S. Constitution⁴ and are exclusively creatures of federal law.⁵ Although individual states do not issue patents or copyrights, trademarks are governed by an amalgam of state and federal laws as well as the common law.⁶ In about three-quarters of the states, trade secrets are governed by a version of the Uniform Trade Secrets Act.⁷ Those states that have not enacted trade secret statutes recognize other statutory or common law protection for proprietary confidential information.

There is an nexus between trade secrets and patents. While a new invention is under development, information about it is a trade secret and must be protected from public disclosure. In the U.S. and most other countries, patent applications are published by the reviewing agency 18 months after the filing date, unless the application has been abandoned or the applicant certifies that the application will not be filed in another country that requires publication. The U.S. Patent and Trademark Office (“USPTO”) publishes copies of issued and expired U.S. patents, and both the patents and the prosecution history of each patent are matters of public record.

Copyright registration certificates identifying a work by title, brief description, author, and owner are publicly available from the Register of Copyrights at the Library of Congress.

Registration is not mandatory, however, and many copyrighted works are not registered until they become the subject of a dispute or a transaction. The USPTO also publishes copies of issued and expired trademarks, as well as abandoned or rejected applications and marks.

Most states also publish lists of state-registered marks. Trade secrets are not published, although for obvious reasons references to their existence and general descriptions of their competitive impact may be found in the public record, such as published court decisions, filings with the SEC, public offerings, and financing materials.

The first step in evaluating intellectual property for financing purposes is to determine the demand for the invention or technology that a company seeks to protect or develop. This analysis requires an investigation not only of the availability of a patent or patents in the U.S., but also an understanding of international patents. The analysis also requires a review of the relevant worldwide literature, a survey of academic projects and activities, and full knowledge of information generally available to the industry. Products and processes that have been on the market for many years may not be subject to patent protection, but may be protected by trade secret law. A well-guarded trade secret may be protected by significant legal barriers that will endure well beyond the life of a patent in any country.⁸

In evaluating the commercial potential for new and existing intellectual property, it is also essential to determine what R&D is being performed by universities, colleges, and private research organizations by reviewing publications and presentations in the field. The unrestricted public dissemination of information may destroy the trade secret protection for which the information might otherwise qualify. Moreover, publication of patentable ideas becomes “prior art” and may negatively affect the availability of patent protection for even the most significant breakthroughs.

Thus, the first step in evaluating any new development is to determine if it is in fact new, and thus protectable, or if the idea has already made its way into the public domain. The “value” of an

idea in a scientific sense may far exceed its “value” as intellectual property, if the idea has been publicized in sufficient detail to commit it to the public domain before it can be legally protected. Conversely, the fact that an idea is not “new” does not mean that it is no longer valuable. Identification of a product with a famous trademark may allow that product to retain some of its value even after the patent expires.⁹ And as noted, a trade secret may outlast a patent by many years and provide its owner with a virtual monopoly.

Patents

There are three types of patents in the United States. Utility patents cover machines, articles of manufacture, compositions of matter, and processes.¹⁰ Plant patents cover asexually reproduced plants,¹¹ and design patents apply to the ornamental appearance of articles of manufacture or machines.¹² Ideas, products of nature, and laws or principles are not patentable.

For patent applications that were filed on or after June 8, 1995, the term of an issued U.S. plant or utility patent will be 20 years from the effective filing date of the application.¹³ For applications filed before June 8, 1995, the term is either 17 years from the date the patent was or is granted, or 20 years from the effective filing date, whichever is longer.¹⁴ Design patents have a term of 14 years from the date of issuance.¹⁵

As discussed below, since 2005 there has been a series of cases from the U.S. Supreme Court and the Federal Circuit Court of Appeals that have scaled back the power of patent holders. Although patents are still very enforceable and should not be taken lightly, through interpretation of various statutes and new holdings discussing long-standing doctrines, the courts have given competitors to patent holders more defenses if infringement suits are asserted. These developments affect the value of patents and related intellectual property, and therefore must be considered in the context of biotechnology finance.

Utility, Novelty, and Non-Obviousness

To be eligible for patent protection, an invention must be useful,¹⁶ “novel,”¹⁷ and “not obvious.”¹⁸ “Usefulness” may

be a difficult burden to meet for a biotechnology invention; a chemical formulation or process with no present practical application may be of scientific interest but cannot be protected by a U.S. patent. The USPTO does not formally handle biotechnology inventions any differently than inventions in other areas of technology, but as a practical matter the burden of disclosing specific utility or usefulness apparent to others in the field may be more difficult for a biotechnology invention. This statutory requirement also creates a risk for investors, in that it could result in disclosure of the idea to potential competitors, often before the patent has been issued and protection is in place.

An invention's utility "must be definite and in currently available form."¹⁹ Under the USPTO Guidelines for Examination, if an applicant asserts a credible utility for the claimed invention, or if utility is apparent to a person of ordinary skill in the art, then the patent examiner should not reject the claim based on a lack of utility. An applicant who fails to identify a specific useful application for an invention, or who fails to disclose adequate information about the invention by failing to make its usefulness immediately apparent to those familiar with the technological field of the invention, will not satisfy the statutory "usefulness" requirement. Under those circumstances, a patent would not issue.

In addition, the inventor is required to disclose the best mode for practicing the invention that is known to the inventor at the time the application is submitted.²⁰ Thus a patent applicant cannot disguise the true anticipated value of the invention by failing to disclose the preferred embodiment of the invention until after the patent has issued.

In patent parlance, "novel" means that, before invention by the applicant, the idea disclosed and claimed was not:

- i. known or used by others in the U.S.;
- ii. patented or described in a printed publication anywhere in the world;

- iii. invented by someone else in the U.S. who has not abandoned, suppressed, or concealed the invention; or
- iv. described in a patent application filed by a different person (if that application later issues as a U.S. patent).²¹

If the proposed invention was described in print in the U.S. or a foreign country at any time more than one year before a patent application has been filed, or if a version of the invention has been the subject of public use or sale in the U.S. for more than one year before filing, no patent may be issued.²² A trivial or “obvious” modification of an existing invention or state of the art (whether or not protected by a patent) will not be granted patent protection if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious to a person having ordinary skill in the art at the time the invention was made.²³

The “novelty” requirement presents special difficulties in biotechnology because inventions in the field often relate to discoveries of already existing natural biological compositions or mechanisms. Discovery of an existing natural biological composition or mechanism fails to meet the novelty requirement of Section 101 of the U.S. Patent Act. To obtain a patent for a biological composition that already exists in nature, the inventor must distinguish the claimed composition from the naturally occurring one by claiming that the composition has been isolated, or purified, or produced through recombinant DNA.

In making that distinction, the inventor must take into account the Doctrine of Inherent Anticipation, which can be fatal to a patent application, and its sibling, the Doctrine of Accidental Anticipation, which might in some cases rescue the same application. Under the Doctrine of Inherent Anticipation, even when a prior art reference fails to disclose explicitly the entire subject matter of a patent claim, the reference may inherently anticipate the claim if it is the “natural result flowing from” the disclosure of the prior art reference.²⁴ Under the judicially created Doctrine of Accidental Anticipation, however, inherent

anticipation does not apply if the prior art accidentally discloses the claimed subject matter.²⁵

The Doctrine of Inherent Anticipation prevents the removal from the public domain of features or properties that inherently exist, but are unknown and not taught in the prior art.²⁶ Discovery of a necessary and inevitable feature or characteristic that is inherent or otherwise implicit in a prior art reference, even if unrecognized or unappreciated, does not make it novel for the purposes of patentability.²⁷ Under the Doctrine of Accidental Anticipation, the Doctrine of Inherent Anticipation does not apply in cases of accidental or unwitting anticipation.²⁸ In *Tilghman v. Proctor*,²⁹ for example, the Supreme Court held that the previous unintended and unappreciated practice of a process to separate fats and oils was insufficient to anticipate a subsequent patent for that purpose. The contradictory and possibly overlapping meanings of these two doctrines have given rise to much litigation and to confusing judicial decisions.

In the 2003 case *Schering Corp. v. Geneva Pharmaceuticals, Inc.*, a group of generic drug companies challenged the validity of Schering's patent in descarboethoxy loratadine ("DCL"), a compound for non-drowsy antihistamines.³⁰ Schering previously had obtained a patent for loratadine, the active component in CLARITIN®, which is formed naturally in the human body upon ingestion.³¹ In its pre-clinical studies Schering determined that DCL was an active metabolite for loratadine. Although there was no prior art teaching concerning DCL, the Federal Circuit Court of Appeals³² held that Schering's prior art patent for loratadine inherently anticipated its later patent claims for DCL because DCL necessarily and inevitably forms when loratadine is administered to a patient.³³

The significance of the *Schering* decision was the Federal Circuit's rejection of the argument that inherent anticipation requires recognition of the inherent characteristic or result in the prior art.³⁴ Although DCL was not recognized in the prior art, it was a necessary and inevitable consequence. Elimination

of the recognition requirement makes sense. By their very nature, inherent properties or results are typically not disclosed or described in a patent. From a legal standpoint, however, *Schering* may have undermined the Doctrine of Accidental Anticipation.

The *Schering* court addressed the Doctrine of Accidental Anticipation and concluded that it survived elimination of the recognition element from the Doctrine of Inherent Anticipation.³⁵ In other decisions, the Federal Circuit has considered a number of factors to determine if Inherent Anticipation or Accidental Anticipation applies to a patent: Did the prior art intend the claimed composition or process? Did the prior art include knowledge of the claimed composition or process or of the newly discovered function of the composition or the newly discovered result of the process? Did the prior art include knowledge of a claimed component or function of the claimed process? Did the prior art perform the claimed process or make or use the claimed composition for a different purpose? Was the claimed composition useful in the prior art? Was the claimed process useful to achieve the claimed result in the prior art?³⁶

Obviousness has taken on more significance in recent years as well. In the 2007 case *KSR v. Teleflex*,³⁷ the U.S. Supreme Court issued the most sweeping decision on patent law since the 1960s, changing the scope of obviousness standards for patents and patent applications. Again, an invention must actually be new to be patentable. Therefore, patent law provides that although an invention may not be identical to a prior invention, if the new invention would be obvious to someone of ordinary skill in the technology or “art” involved, the new invention is not patentable. Before the *KSR* decision, fearing that courts and juries would use hindsight to determine what would be obvious to someone of ordinary skill in the art, the courts applied a rigid test in determining whether an invention was invalid as being obvious. The test allowed a party to combine prior inventions to render the invention at issue invalid for obviousness only if the party seeking to hold

the invention invalid could show a “teaching, suggestion or motivation” to combine the prior inventions. In *KSR*, the United States Supreme Court abandoned the rigid test in favor of a more common-sense approach, looking at all the relevant facts to determine whether or not the invention would have been obvious to someone skilled in the art.

Since the ruling in *KSR*, courts have been much more likely to find patents invalid as being obvious. The United States Patent Office has also become much more likely to refuse to grant patents on inventions it considers to be obvious. For example, in April 2009, in *In re Kubin*,³⁸ an attempt to patent a gene sequence failed because the Court of Appeals for the Federal Circuit concluded that well-known cloning techniques could derive the readily knowable and obtainable structure of an identified protein for that gene. After an examiner rejected as obvious, *inter alia*, certain claims of the patent application for polynucleotides-encoding-natural-killer-cell-activation-inducing-ligand-polypeptides, the inventor argued on appeal to the Board of Patent Appeals and Interferences (“BPAI”) that the decision was at odds with Federal Circuit precedent in *In re Deuel*.³⁹ The Federal Circuit in *Deuel* had decided in the biotechnology context that knowledge of a protein does not give a party a conception of a particular DNA encoding it, and “obvious to try” is not an appropriate test for obviousness. The BPAI in an unanimous decision affirmed the examiner’s rejection, concluding that at least one of the claimed polynucleotides would have been obvious to someone of ordinary skill in the art at the time the invention was made. The Federal Circuit subsequently affirmed the BPAI’s decision that the gene sequence was obvious to derive, but most importantly, concluded that *KSR*’s “obvious to try” applies to biotechnology.

Observed biological results and underlying mechanisms of biological actions often are not understood until after the publication of experimental findings. As a result, the early publication of an experimental finding may inherently anticipate, and therefore preclude, issuance of a patent based

on a subsequently achieved understanding of the earlier publication. For a biotechnology investor, a determination of whether the prior art necessarily and inevitably reveals a composition or process is essential to an evaluation of patentability or, conversely, of freedom to pursue use of a process or composition because the prior art has committed information, perhaps unintentionally, to the public domain.

Patent Infringement

In biotechnology finance, it is essential to analyze competing patents to protect against investing time and resources into development of a product or process that cannot be marketed legally because it infringes on an existing patent. A qualified patent attorney should provide an opinion regarding relevant patents in the field. That opinion should:

- i. meaningfully discuss the file history of each competitive patent;
- ii. present any legal and factual analysis for the basis for the opinions; and
- iii. specifically address all claims and interpret them.

Infringement analysis requires consideration of literal infringement and the “doctrine of equivalents.” A new device may literally infringe an existing patent if it follows the claims in the patent as written and interpreted by a court according to their meaning and scope.⁴⁰ Under the “doctrine of equivalents,” if a device performs the same overall function in substantially the same way to obtain substantially the same result as the claimed invention, then infringement may be found even if the device does not literally infringe each element of a patent claim.⁴¹ An opinion letter obtained should:

- i. discuss the limits of existing patents to assist an inventor of a new biotechnology product in designing around existing patents;
- ii. analyze information previously considered by the USPTO if the opinion relies on an obviousness or anticipation defense against infringement;

- iii. link prior disclosures to claim limitations if the opinion deals with obviousness or anticipation; assess secondary indications of non-obviousness if the opinion deals with obviousness; and
- iv. explain the burden of proof on accused infringers involving invalidity or unenforceability.

In addition to thinking through whether infringement in theory may exist, one must also consider the application of a handful of changes in patent law that have been articulated by the courts in the last few years. The matters raised by these cases shed additional light on the question of infringement and enforceability in general, and thus must be analyzed within the scope of financing decisions.

For example, in *eBay v. MercExchange, LLC*,⁴² the United States Supreme Court reined in lower courts after it had become a virtually automatic practice to issue a permanent injunction following a finding of patent infringement. Armed with the almost certain threat of permanent injunctive relief, patent owners enjoyed a powerful advantage in litigation and in settlement negotiations, because they were able to threaten to shut down entirely an infringer who refused to pay their royalty demand. Some courts found this practice particularly disturbing when the patent owners were “trolls” who did not actually practice the technology but made their money through licensing arrangements. This discomfort with “trolls” ultimately led to the *eBay* decision. The case came to the Supreme Court after MercExchange sued eBay for infringing online auction technology covering the “Buy It Now!” function that comprised more than 30 percent of eBay’s business. Following a jury determination that eBay had willfully infringed the patent, MercExchange moved for a permanent injunction. The District Court denied the request, finding that a patent owner like MercExchange that was not engaged in the commercial activity of practicing its own patents but instead licensed them to third parties could not show irreparable harm and thus was not entitled to an injunction.⁴³ The Federal Circuit reversed, applying the diametrically opposite

presumption that it is the “general rule that courts will issue permanent injunctions against patent infringement absent exceptional circumstances.”⁴⁴

The United States Supreme Court disagreed with both lower courts. The injunction was vacated because nothing in the Patent Act absolved the federal courts from applying to requests for a permanent injunction in patent cases the traditional four-factor test employed by courts of equity in other contexts. To obtain a permanent injunction, the patent owner “must demonstrate (1) that it has suffered an irreparable injury; (2) that remedies available at law are inadequate to compensate for that injury; (3) that considering the balance of hardships between the plaintiff and the defendant, a remedy in equity is warranted; and (4) that the public interest would not be disserved by a permanent injunction.”⁴⁵ Thus an injunction is not automatic following a determination of patent infringement. It also is not prohibited when the patent owner is a “troll” who may prefer to license “rather than undertake efforts to secure the financing necessary to bring [its] works to market. . . .”⁴⁶ The *eBay* decision did not in fact break new ground in the patent infringement arena. Rather, the Supreme Court sent a message to the lower courts and patent litigants that the traditional standard continues to apply. There is no automatic injunction for a successful patent owner, and there is no automatic denial just because that patent owner happens to be a “troll.”

In *MedImmune, Inc. v. Genentech, Inc.*,⁴⁷ the Supreme Court provided new direction for licensees or competitors of patents who must challenge a patent due to the patentee’s threats of suit for infringement. Prior to *MedImmune*, an accused patent infringer was required to show that it had a reasonable apprehension of being sued by a patentee in order to support the filing of a declaratory judgment action seeking an order that it did not infringe. Similarly, a licensee in good standing was not permitted to challenge the validity or enforceability of the licensed patent without first breaching the license and putting itself at risk of suit. The Supreme Court in *MedImmune* changed those rules, holding that a licensee may challenge a patent

without breaching the license under which it properly practices the patent. Moreover, the Court eliminated the safe harbor for accused infringers not already licensees. The Supreme Court removed the “reasonable-apprehension-of-being-sued” requirement for standing in such declaratory judgment actions. Instead, one must look at the entirety of the circumstances, including whether there exists a substantial controversy, whether adverse legal interests are present, and whether there is sufficient immediacy to the issues. After *MedImmune*, parties need to consider more than just the language of a cease-and-desist letter that the patentee may have sent.

As it had in *eBay v. MercExchange*, the Supreme Court in *Illinois Tool Works v. Independent Ink*⁴⁸ rejected a longstanding presumption that had been applied in error by the lower courts. Before *Illinois Tool Works*, a patent owner was presumed to have market power when accused of violating the Sherman Antitrust Act by allegedly tying the sale of patented products to unpatented products. The Supreme Court rejected that presumption, concluding that many “tying arrangements, even those involving patents and requirements ties, are fully consistent with a free competitive market.”⁴⁹ Although tying arrangements that are the product of a true monopoly remain illegal, ownership of a patent is not a *per se* demonstration of market power. Independent proof of power in the relevant market is required to transform the legitimate exercise of the monopoly power conferred by patent ownership into an antitrust violation.⁵⁰ For biotechnology companies, the *Illinois Tool Works* decision presents both an opportunity and an impediment. For patent owners, there is more leeway to link the licensing or sale of protected technology to other, unpatented products. For those who “license in,” however, there may be no recourse but to accept additional unpatented technology that is tied to the desired patented technology in order to avoid infringement.

Paving the way for broader worldwide distribution of computer software code, the Supreme Court issued a second important patent law decision on the same day as its *KSR* ruling. In

Microsoft Corp. v. AT&T Corp.,⁵¹ the Court limited the reach of U.S. patent laws overseas, ruling in favor of Microsoft in its dispute with AT&T over Microsoft's sale of Windows software outside the United States. The Court held that because software is not a component of an infringing device, exporting a copy of the software outside of the U.S. for copying onto devices is not an infringement of a U.S. patent. In addition, software is an idea without physical embodiment. The decision is likely to result in the reduction of damages awards in patent cases by excluding instances of patent infringement overseas from consideration.

Those defending against claims of patent infringement found themselves in a better position to defend those claims after the *en banc* decision of the United States Court of Appeals for the Federal Circuit in *In re Seagate Tech., LLC*.⁵² Before the Seagate decision, a plaintiff was entitled to up to three times the damages sustained as a result of the infringement if it could prove the infringement was willful. In order to avoid liability for willful infringement, the rule was basically that the defendant needed to have obtained an opinion of counsel that the defendant's device or method did not infringe the patent or that the patent was invalid. This was a problem for defendants because they would waive attorney-client privilege on those topics if they produced such an opinion. Defendants were spared this Hobson's choice by the *Seagate* decision. The Federal Circuit said that an opinion was not necessary to avoid liability for willful infringement, but instead a plaintiff would need to prove by clear and convincing evidence that the defendant acted with objective recklessness for the patent rights of the plaintiff.

In *In re Bilski*,⁵³ the U.S. Court of Appeals for Federal Circuit issued an *en banc* decision on the patenting of method claims, in particular business methods. Although the case related to the rejection of patent claims involving a method of hedging risks in commodities trading, *Bilski's* reach is significant. The court decided that patent law will protect only inventive processes that involve a "particular machine" or "transform

an article from one state to another.” Accordingly, the validity and viability of both existing and future process-type patent rights in software, finance, and life sciences are at risk. Because of its potential effects, a petition was filed with the U.S. Supreme Court for a writ of certiorari in January 2009, seeking to overturn the Federal Circuit decision. Adding to the mystery in the interim, however, is a Federal Circuit panel’s split in March 2009 over what *Bilski* had held.⁵⁴ In addition, in *In re Comiskey*,⁵⁵ an *en banc* court ordered a September 2007 opinion on business method patents withdrawn and to be issued in a revised form. Originally the opinion noted that the addition of a computer could make an otherwise unpatentable method patentable under section 101, but then subject to an obviousness defense under section 103. Although the panel had remanded for a consideration of obviousness, the *en banc* Court decided that the opinion should be revised for a remand to consider section 101. This may be seen as an attempt by the Court to find the boundaries of what business methods are patentable. Unfortunately, the Court left it for the USPTO to decide if merely adding a computer was enough to make an otherwise unpatentable invention patentable. Whether the U.S. Supreme Court will provide guidance on the issues related to method patents remains to be seen.

On June 9, 2008, the Supreme Court decided *Quanta Computer, Inc. v. LG Electronics, Inc.*,⁵⁶ regarding the doctrine of patent exhaustion, also known as the “first sale” doctrine. Under this doctrine, which serves as a default rule under both patent and copyright law, the rights holder controls only the first sale or use of a protected product, but not any subsequent sales or uses of that same product. In the context of intellectual property licenses, this doctrine means that license fees are therefore generally charged only once per product. At issue in *Quanta* was whether the doctrine of patent exhaustion applied to the sale of components of a patented system where those components, combined with additional components, infringed a method patent. In the case, LGE had granted Intel the right to manufacture and sell microprocessors and chipsets that

practiced LGE's method patents. Quanta purchased these products from Intel and then used them, in combination with non-Intel parts, to manufacture computers. LGE alleged that Quanta's computers infringed LGE's patents, and consequently, wanted Quanta to pay a licensing fee. Quanta refused. The Court unanimously held (1) that the patent exhaustion doctrine does apply to method patents and (2) that an authorized sale of an article that "substantially embodies" those patents does exhaust a patent owner's rights under the law. Specifically, the Court held that an "authorized sale of an article that substantially embodies a patent exhausts the patent holder's rights and prevents the patent holder from invoking patent law to control postsale use of the article."⁵⁷ It should be noted, however, that the Court expressly stated that its decision in no way limited the possibility that contract damages could be available even though exhaustion operates to eliminate patent damages. After *Quanta*, patent holders would be wise to carefully draft their conditions of sale to limit licensees' rights but not the rights of downstream third parties that flow from the licensee. Conversely, licensees should negotiate royalty fees that take into consideration the decreased value of these restricted patent rights. Finally, both patent holders and licensees should consider reevaluating what conduct actually is and is not "authorized" under their license agreements.

Pharmaceutical Patents

Pharmaceutical patents and patents in living matter are of special significance to biotechnology companies. Pharmaceutical patents are regulated in part by an addendum to the U.S. Patent Act, the Drug Price Competition, and Patent Term Restoration Act of 1984, known as "the Waxman-Hatch Act" after its respective chief sponsors in the U.S. House of Representatives and Senate. Waxman-Hatch creates a separate but related body of law that applies exclusively to pharmaceutical patents.

Waxman-Hatch was established to restore effective patent terms that had eroded substantially over the years. The FDA subjects new pharmaceuticals to a complicated and time-

consuming approval procedure, and one purpose of Waxman-Hatch was to permit the patent holder to enjoy the full term of the patent, or as much of the full term as possible, even if FDA approval were delayed beyond the issuance date. Thus, the term of patents on processes and composition of matter subject to FDA approval may be extended due to FDA-caused delays in distribution.

Waxman-Hatch provides for patent term extensions for pioneering drugs but also provides exemptions for generics that otherwise might infringe patents. Waxman-Hatch provides that it is not an act of infringement to make, use, offer to sell, or sell within or import into the U.S. a patented invention that is primarily manufactured using recombinant DNA, hybrid technology, or other processes involving site-specific genetic manipulation techniques solely for uses reasonably related to the development and submission of information under a federal law that regulates the manufacture, use, or sale of drugs or veterinary biological products. This “safe harbor” allows generic drug manufacturers to enter the marketplace as soon as the patent in a corresponding pharmaceutical product expires, thereby eliminating the unwarranted extension of the drug’s patent term.

As a result of a decision by the U.S. Supreme Court, a limited “research exemption” exists under Waxman-Hatch for drug manufacturers that later seek to obtain FDA approval. In *Merck KgaA v. Integra Lifesciences I Ltd.*,⁵⁸ a unanimous Court determined that a statutory exemption from patent infringement exists “for uses reasonably related to the development and submission of information” to federal regulatory agencies. In an opinion by Justice Scalia, the Court determined that Waxman-Hatch creates a broad safe harbor for the use of patented pharmaceuticals by those who may wish to develop medications that may be subject to regulation by the FDA or other regulatory approval processes.

The case arose from the efforts of scientists at the Scripps Research Institute, who discovered that blocking the receptor on certain cells inhibits new blood vessel generation, thereby showing

promise for a means to halt cancerous tumor growth and treat other diseases. Merck hired Scripps to identify potential drugs that would inhibit blood vessel generation. Scripps chose the cyclic RGD peptide EMD 121974, which had been patented by Integra, and tested it to assess the action of the peptides and the proper mode of administering them therapeutically.

Integra sued, claiming that use of the patented RGD peptide was patent infringement. In its defense, Merck relied on the “safe harbor” provision of Waxman-Hatch,⁵⁹ which states:

It shall not be an act of infringement to...use...a patented invention...solely for uses reasonably related to the development and submission of information under a federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products.

Merck argued that its research was intended to produce a drug that eventually would be submitted to the FDA for approval and that denying the exemption would delay the availability of the drug for medical treatment. The Supreme Court accepted that argument, eliminating the judge-made distinction between “clinical” and “pre-clinical” trials for the purposes of the Section 271(e)(1) safe harbor. The safe harbor “extends to all uses of patented inventions that are reasonably related to the development and submission of any information” to the FDA.

Although the scope of the *Merck* decision has yet to be determined, it is clear from the Supreme Court’s decision that the safe harbor extends even to the results of experiments that ultimately are not submitted to the FDA. The exemption is sufficiently broad to cover any research reasonably related to the process of developing information for submission under any federal law regulating the manufacture, use, or distribution of drugs. Basic research that is not conducted with the intent of identifying possible candidates for future FDA approval is not covered by the Waxman-Hatch safe harbor, however.

Moreover, although the Supreme Court provided that certain patents on substances used only as “research tools” would not

fall within the Section 271(e)(1) safe harbor, it was clear from the record in *Merck* that the RGD peptides patented by Integra were not so used only as research tools.

From the perspective of biotechnology finance, it is essential to determine the expiration date of any competitive patent, and when possible to exploit the broadened “safe harbor” provision of Waxman-Hatch as part of the process of developing generic pharmaceuticals. Generic equivalents may be submitted to the FDA approval process in advance in order to allow the generic manufacturer to enter the market with an equivalent product at the earliest possible time following expiration of the pharmaceutical patent. In addition, under the U.S. Supreme Court’s recent decision in *KSR v. Teleflex*, discussed above, one must also consider that some pharmaceutical patents and patent applications based on combinations, improvements, or optimizations may become more vulnerable to invalidation or rejection, meaning that at least in the short term, the value of pharmaceutical combination patents may also be decreased. Conversely, owners of patents in pharmaceuticals must monitor Abbreviated New Drug Applications filed with the FDA by generic manufacturers to ensure that generic pharmaceuticals that might otherwise infringe the owners’ patents will not be introduced into the market prior to expiration of the patents.

Patents In Living Matter

Patents in living matter have been available in the U.S. since 1980, when the U.S. Supreme Court decided in *Diamond v. Chakrabarty* that “a patent can be granted on anything under the sun which can be made by man.”⁶⁰ The inventor Chakrabarty genetically engineered a bacterium enabling it to break down crude oil. At first, the product was rejected because it was considered a “product of nature.” Because the enhanced bacterium was not naturally occurring, however, it was considered a “product of man,” and the Supreme Court ordered the USPTO to issue the patent.

Chakrabarty opened the portal for the issuance of numerous U.S. patents and genetically engineered life forms, including

transgenic animals and biological materials. The USPTO issued guidelines on how microorganisms produced by genetic engineering satisfy the conditions for patentable subject matter.⁶¹ For this purpose, the USPTO examines whether a proposed living-matter invention is the result of human intervention.⁶² Specifically excluded by this test are (1) laws of nature, physical phenomena, and abstract ideas; and (2) newly discovered plants found in the wild.⁶³ Human cells and tissues, including embryos and stem cells, remain unpatentable products of nature. These materials may be patentable subject matter, however, if they are modified in some way that transforms them into manmade material.

For much of the public, patents in living matter or modifications of embryos or stem cells raise moral and ethical questions. The courts have recognized these moral and ethical concerns in several older patent cases. The USPTO or the courts may deny patentability to inventions that are deemed to be “immoral, mischievous, contrary to public policy, or injurious to the well being of society.”⁶⁴ This so-called “moral utility doctrine,” first articulated in the nineteenth century, rests on the notion that, if an invention is evil, it cannot be useful, and if it is not useful, it cannot be patentable. Opponents of cloning and stem-cell research have argued that patentability for those practices could and should be denied based on the moral utility doctrine.

To date, neither the USPTO nor the courts have denied patentability to controversial inventions based on the “moral utility” doctrine. The USPTO has articulated a policy, however, that denies patentability to any claim that could encompass a human being. Of course, under *Chakrabarty*, unmodified human cells and tissues, including embryos and stem cells, are already considered unpatentable products of nature. As decisions in this area develop, however, they may have a significant impact on biotechnology development in controversial fields and will necessarily affect the financing strategy and decision-making of the biotechnology company.

European Patents

Patentability in the U.S. does not ensure patentability internationally. Under European rules, a patent must have industrial applicability, be novel, and involve an inventive step.⁶⁵ Unlike the USPTO, the European Patent Office (“EPO”) incorporates certain nontechnical concerns into its examination of biotechnological inventions. The EPO will not issue patents that violate public policy or morality when commercially exploited.⁶⁶ For example, the EPO has identified as unpatentable in Europe processes that include cloning of human beings and uses of human embryos for industrial or commercial purposes. In Europe, like the U.S., the human body at the various stages of its formation and development is unpatentable.

Differences in the patent laws in the U.S. and Europe were highlighted in the “Harvard Mouse” case.⁶⁷ A patent was issued to Harvard College for a mouse genetically engineered to make it more susceptible to cancer—it was useful for research purposes even if not useful to the mice involved. In Europe, the patent application for the same invention was initially rejected for failure to constitute patentable subject matter.

Following appeal, the invention was found not to violate the European morality provision, and a patent could be maintained in amended form directed to transgenic rodents.

Compulsory Licensing of Patents

Like other patents, biotechnology patents also may be subject to compulsory license in which the government removes some of the patentee’s control over the patent in exchange for compensation. A national government may force a patent holder to license the patented invention to other companies that may or may not be competitors, for a reasonable royalty or license fee. The U.S. government has the power to require compulsory licensing of patents obtained through federally funded research under certain circumstances.⁶⁸ Compulsory licensing is rarely done in the U.S., however, and licenses are normally only granted when a supplier of a critical patented product cannot meet the needs of the public.

On the international side, however, the international agreement on Trade-Related Aspects of Intellectual Property⁶⁹ (“TRIPS Agreement”), to which the U.S. is a signatory, provides for compulsory licensing or government appropriation under certain specified circumstances. The EU does not have general compulsory licensing provisions. Instead, compulsory licensing and other governmental intervention regarding inventions are typically handled on a national basis.

Governmental Appropriation of Patents

Outright appropriation is a more direct approach by which a national government may take control over patent rights. The U.S. government has the power to use, or commission another to use, any patented technology, but the government is then liable for reasonable and full compensation for the taking of these rights. Under U.S. law, whenever an invention described in or covered by a U.S. patent is used or manufactured by or for the U.S. without a license from the owner, the owner’s remedy is against the U.S. and is limited to “recovery of his reasonable and entire compensation for such use and manufacture.”⁷⁰ The patent owner may sue the federal government for a reasonable royalty but cannot obtain an injunction against infringement and cannot prevent its competitors from infringing the patent to the extent that the federal government directs the infringement.

The TRIPS Agreement also provides guidelines for government appropriation in member countries. Under British law, for example, the Crown may use, or authorize the use of, any patented invention if the patentee is compensated for lost profits due to appropriation.⁷¹

Research Exemption

Most international law recognizes a “research exemption” that allows use of a patented invention for experimentation with the intent to improve on the invention. The U.S. “research exemption” was recently defined by the Supreme Court in the *Merck* decision under Waxman-Hatch.

Even in those countries that do have a “research exemption,” it is generally only applicable to those who have no intent to use

or sell the improvement. In the U.S., an “experimental use” exemption applies for research done solely for amusement, to satisfy idle curiosity, or for strictly philosophical inquiry.⁷² Most academic research does not fall under the experimental use exemption, nor does most private research.

State universities are immune from federal patent infringement lawsuits under the sovereign immunity granted by the Eleventh Amendment to the Constitution. State universities therefore enjoy a sort of de facto research exemption not available to private colleges and universities.

The European Patent Convention does not contain rules regarding an experimental use or research exemption. General defenses exist, however, for acts done for experimental purposes related to the subject matter of the patented invention and for noncommercial private acts. International laws generally allow for more freedom for experimental research than U.S. law. As a result, experimental research will often be immune from patent infringement in Europe, even if done for commercial purposes.

Competitor Patents

It is essential for a biotechnology company to inventory and evaluate the patents in the portfolios of its competitors. An analysis of the scope of those patents and the technology they cover is essential, as well as of the territories and nations in which the patents apply. In evaluating competitor patents, investors in a biotechnology company must determine if it is financially worthwhile to design around existing patents, or to wait for the expiration date before introducing a competing product.

Licensing opportunities may be more attractive than designing around a patent, risking an infringement lawsuit, or challenging the validity of the patent.

Copyrights

Copyrights are of considerably less value than patents to biotechnology companies. Copyrights protect expression in

tangible form, but do not protect ideas.⁷³ The intellectual property most valuable to biotechnology is specifically excluded from copyright protection, which by statute does not “extend to any idea, procedure, process, system, method of operation, concept, principle, or discovery, regardless of the form in which it is described, explained, illustrated, or embodied.”⁷⁴ Copyright protection is not available for procedures for (i) doing, making, or building things, (ii) scientific or technical methods or discoveries, (iii) business operations or procedures, (iv) mathematical principles, or (v) formulas or algorithms.

A copyright is the exclusive right granted to the author of original literary or artistic works to reproduce, publish, or sell them for a limited period of time. In the U.S. and around the world, that “limited period of time,” is extremely long—the life of the creator plus 70 years,⁷⁵ and for works made for hire, anonymous, or pseudonymous works,⁷⁶ the shorter of 95 years from publication or 120 years from creation. The value of a copyright to a biotechnology company is in the protection of its marketing materials, manuals, or advertisements. Copyright protection extends to a description, explanation, or illustration of an idea or system, but only to the particular literary or pictorial expression chosen by the author. The copyright owner—which in the case of a work prepared by an employee would ordinarily be the biotechnology company—has no exclusive rights in the idea, method, or system described in the work.

Suppose, for example, that an author writes a paper explaining a new system for creating a transgenic mouse. The copyright in the book, which comes into existence at the moment the work is fixed in a tangible form, will prevent others from publishing the text and the illustrations describing the author’s ideas for creating and using the new creature. The copyright alone will not give the copyright owner any rights to prevent others from adopting the ideas for commercial purposes or from developing or using the machinery, processes, or methods described in the book. Copyright law, therefore, could be used to prevent, or obtain compensation for direct copying, but could not be used to protect against the use or dissemination of the ideas.

Although a copyright comes into existence as soon as a work is committed to a tangible medium of expression, federal registration is required to enforce copyright rights in the U.S.⁷⁷ Notice—the familiar ©—is no longer a statutory requirement but is permitted⁷⁸ and a recommended best practice.

International Copyright

There is no “international copyright” law that will automatically protect works in every country throughout the world. Protection against unauthorized use in a particular country depends on the national laws of that country. Most countries, however, offer protection to foreign works under conditions that have been greatly simplified by international copyright treaties and conventions. Two principal international copyright conventions exist, the Berne Union for the Protection of Literary and Artistic Property and the Universal Copyright Convention.

An author who seeks copyright protection for his or her work in a particular country should first determine the extent of the protection available to works of foreign authors in that country. If possible, this should be done before the work is published anywhere because protection may depend on the facts existing at the time of first publication.

In general terms, a work may be protected in a country in which protection is sought, if that country is a party to one of the international copyright conventions, by complying with that convention. Even if the work cannot be protected under an international convention, protection under the specific provisions of the country’s national laws still may be possible. Some countries, however, offer little or no copyright protection to any foreign works.

Trademarks

Trademarks and service marks compose the third category of intellectual property. Trademarks identify products and service marks identify services. A trademark can be commonly thought of as the name of a particular product, and a service marks as the

name of a service. It is important in the biotechnology field to obtain and maintain international trademark protection for valuable products. For example, the trademark “NUTRASWEET®” is associated throughout the industry, and among consumers worldwide, as an artificial sweetener for human consumption. Although the patent for the artificial sweetener has long expired, the product itself is well known by its trademark.

A trademark is a word, symbol, device or design, slogan, or any combination of those used by its owner to distinguish a good or service from those of another. A service mark is used in the sale or advertising of services. Trademarks are valuable to foster competition and prevent consumer confusion, identify and distinguish products, identify the source of goods, indicate the quality of goods, build consumer loyalty, and leverage advertising investment. The stated purpose of the Lanham Act, the federal trademark law in the U.S., is to regulate commerce by making actionable deceptive and misleading use of marks in commerce.⁷⁹

In the U.S., trademark rights are established by using the mark in commerce in connection with particular goods.⁸⁰ Although registration is not required to maintain trademark rights, registration is available by filing an application with the USPTO⁸¹ and provides substantial benefits. For example, a federal registration serves as constructive notice to all others that a mark is registered by its owner in connection with specified goods or services,⁸² and no subsequent user may in good faith use the same goods or services. The registration is prima facie evidence of the owner’s exclusive right to use the mark,⁸³ and after five years the registration may become incontestable.⁸⁴ Federal registration is required before the trademark owner is permitted to use the registration symbol ®.⁸⁵ By recording the registered trademark with the Department of Homeland Security, the trademark owner can exclude importation of goods bearing infringing marks.⁸⁶ If the company is involved in litigation, specific statutory remedies such as recovery of profits, attorney fees, and treble damages become available following registration.⁸⁷

In contrast to U.S. trademark law, in most other countries, trademark rights are established only through registration. Before

beginning to sell biotechnology products in foreign countries, it is important to first apply for and register the trademarks. It is essential to conduct a thorough national and international search in all countries where the biotechnology company might conceivably have a market to determine that the mark is available before adopting a product mark. Registration must be made in advance of entry in most countries. In many countries, a trademark may not be used without registration. Failing to register a trademark in a foreign country may require the trademark owner to re-brand or forego that market altogether.

Trademarks vary in their strength. The strongest trademarks or service marks are arbitrary or fanciful and have the least literal relationship to the product to which they are attached. For example, the coined term “PREMARIN®” is a very strong trademark for a hormone replacement drug.⁸⁸ Similarly, the arbitrary term “AMAZON®” is very strong for online book sales, because although it is an ordinary word, it appears out of its usual context. A suggestive term such as “NUTRASWEET” is also strong, but not as strong as an arbitrary or fanciful trademarks or service marks.

Descriptive terms, such as “NATIONAL CASH REGISTER™” for cash registers, are weak unless they have acquired “secondary meaning,” which means they have become recognized by consumers as associated with product or service. Generic terms such as “book,” “ice cream,” or “estrogen” are not trademarks and can never become trademarks.

Trade Secrets

In evaluating a biotechnology company’s intellectual property assets, or those of its competitors, it is also crucial, although sometimes difficult, to include an assessment of trade secrets. If properly protected, trade secrets can be more valuable than patents. The value of a trade secret derives in part from the fact that, unlike a patent, a properly protected trade secret will never enter the public domain.

Most states have adopted the Uniform Trade Secrets Act, which defines a trade secret as “information, including a formula, pattern, compilation, program, device, method, technique, or process that:

(1) derives independent economic value, actual or potential, from not being generally known to, and not being readily ascertainable by proper means by, other persons who can obtain economic value from its disclosure or use; and (2) is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.”⁸⁹ In the remaining states, the most common definition is that a “trade secret may consist of any formula, pattern, device, or compilation of information which is used in one’s business, and which gives him an opportunity to gain an advantage over competitors who do not know or use it.”⁹⁰ Both at common law and under the Uniform Trade Secrets Act, a trade secret may be a formula for a chemical compound, a process for manufacturing, treating, or preserving materials, a pattern for a machine or other device, or a list of customers.⁹¹ A trade secret can even be a practice of doing something “wrong”—not following generally accepted practices and procedures in the industry—if doing so provides a competitive advantage.⁹²

An example of the value of a trade secret as a sort of “super-patent” involved a lawsuit brought by Wyeth Laboratories.⁹³ Wyeth had acquired the rights to a secret chemical process used to extract estrogen from the urine of pregnant mares in order to make a hormone therapy replacement drug known as PREMARIN. The only “naturally” derived hormone therapy replacement drug, PREMARIN had been sold in the U.S. since 1942, when the FDA first approved it. Wyeth and its predecessors had obtained a number of patents, all of which had expired, in connection with estrogen extraction research. Because none of the patents covered the process actually used to create PREMARIN and because Wyeth and its predecessors had maintained that process as a trade secret, the Court prohibited a competitor from manufacturing a generic equivalent. The process had been in use for more than 60 years, and many competitors, including Wyeth, which purchased the process after failing to reverse engineer it, had tried unsuccessfully to duplicate it. The court concluded that the secret PREMARIN manufacturing process remained a valid trade secret and could not be used by a competitor that obtained it through improper means.

In order to protect trade secrets, a biotechnology company must take affirmative steps to identify those secrets and adopt procedures

to protect them. These procedures may include (i) adopting physical security procedures, such as locks and guarded entrances, visitor and employee badges, and limiting access to facilities where trade secrets might be kept, (ii) instituting a formal document handling policy, (iii) using confidentiality and noncompetition agreements with employees, (iv) using nondisclosure agreements with vendors, customers and prospects, (v) keeping track of copies of materials, (vi) limiting computer access to information, and (vii) observing the use of passwords to access computer data. It is also important that owners of trade secrets avoid inadvertent publication of these trade secrets in sales materials and at academic conferences.

C. Distress Stage

The “Distress Stage” of a biotechnology firm is likely much more relevant to those reading this update to the *Guide* than it was when the first edition was published in the summer of 2005. Financing, whether through equity or debt financing, is much more difficult to obtain today than it was at that time. In addition, the financial condition of many firms is weaker than it was. As a result, not only is it difficult to obtain additional sources of capital to pursue expansion or growth opportunities, but the survival of many biotech firms has been called into question, resulting in one or more of the following alternatives being considered.

Recapitalization

Investors in biotechnology start-up businesses will often anticipate that additional rounds of financing will be necessary in order to convert an idea with intellectual property into a profitable business. The current market conditions have made it much more difficult to raise new rounds of financing, particularly in a manner in which a significant number of initial investors continue to participate. As a result, next-round investors may require significant dilution of current equity holders in exchange for contribution of additional capital. Ongoing recapitalization, under which existing investors are diluted may or may not be possible, depending on the corporate governance documents and the company’s ability to obtain sufficient approval from boards of directors and, in some instances,

shareholders. Often an impasse develops, and the issuer may explore other alternatives, including foreclosure and bankruptcy.

Forced Foreclosure

A secured lender who is not being paid as a result of a company's inability to generate cash flow or raise additional financing to make payments to its secured lender(s) may elect to "foreclose" on its collateral.⁹⁴ This results in the lender taking possession of the collateral with the ultimate goal of selling it to pay off some or all of the debt it is owed. This action will usually wipe out the value of existing equity and often limits the recovery of unsecured creditors as well. It may, however, create an opportunity for someone willing to invest additional funds to acquire the collateral from the secured lender. A forced foreclosure may cause disruption in the business, particularly when it is not done with the borrower and the secured lender working on a cooperative basis. The upside for a potential buyer, however, is that the assets are usually acquired at a distressed price and the buyer may find itself the beneficiary of the years of investment and development in the technology or goodwill of the business that has been previously funded by investors or lenders. A secured lender must dispose of the personal property assets in a commercially reasonable manner. This is done in the context of a "private sale" or a "public sale." Real estate foreclosed on by a secured lender is either purchased at a public auction by a potential buyer, or from the secured lender directly if it becomes the owner of the real estate by "credit bidding" its debt at the foreclosure sale.

Friendly Foreclosure

A friendly foreclosure is similar to a forced foreclosure in terms of the legal process and ultimate sale. In a friendly foreclosure, however, a company will coordinate the turnover of its collateral to the secured lender who in turn may be working with a third party to acquire the assets in what would ideally be a seamless transition. This works well in some circumstances if it is designed not to deprive existing creditors or shareholders of value. Board members of the distressed company must be mindful of their fiduciary obligations and not use this process to create a benefit

for themselves or others with whom they have a relationship. Any board member who may be interested in being part of a buyer group to acquire the assets from a secured lender once they have been foreclosed on would in most instances be well-served to resign from the board prior to the commencement of any actions or negotiations.

Bankruptcy Section 363 Sale

Bankruptcy filings of companies have increased substantially beginning in the second half of 2008 and may continue to increase during the months, if not years, ahead. A company in financial distress often looks to asset sales as part of a solution to its problems. While a strategic asset sale may provide the business with cash either to continue operations, restructure, or simply work through a liquidity crunch, a company may alternatively conclude that the best way to maximize value for its constituencies is the sale of substantially all of its assets. While a conventional asset sale outside of bankruptcy is often an option, businesses are, with increasing frequency, selecting bankruptcy as a preferred method of selling assets. Some buyers prefer acquiring their assets out of a bankruptcy proceeding because of the added protection provided by a bankruptcy court order approving the sale. Section 363 of the Bankruptcy Code allows a debtor in bankruptcy, after notice and hearing, to sell property as part of a Chapter 11 proceeding but prior to filing a plan of reorganization. These sales are referred to in bankruptcy parlance as “Section 363 Sales.”

Most of the companies that file Chapter 11 do not successfully reorganize in the sense of continuing as an ongoing entity. Rather, many of the companies filing Chapter 11 today do so with the expressed intent of using the bankruptcy as a process to conduct a “Section 363 Sale.” These are generally approved when justified by sound business purpose.

Benefits of Section 363 Sale

There are several advantages to a Section 363 Sale in bankruptcy. One advantage is that a buyer of assets in bankruptcy takes the assets free and clear of liens, claims and interest. To the extent various secured creditors have arguments over how the proceeds

should be distributed and allocated, these disputes typically get sorted out after a Section 363 Sale has occurred and do not become an issue for the buyer. Furthermore, a buyer of assets in a Section 363 Sale can determine which leases and other executory contracts it wishes to acquire, and leave the rest behind. The bankruptcy code allows many contracts to be assigned even if they have anti-assignment language contained in them. A bankruptcy sale also minimizes the liability to board members and officers with fiduciary obligations, and allows them to even be part of a buyer group if they so choose, because everything is done in the open as a matter of public record and the bankruptcy court approves the sale process. Finally, an advantage of a Section 363 Sale is that a bankruptcy court-sanctioned auction or sale process is often implemented, with extensive parameters and procedures in place, so that potential buyers understand exactly what the sale process will entail. This often maximizes the value of assets to the bankruptcy estate, which inures to the benefit of creditors of the company, and in some instances to the benefit of equity interests as well.

Disadvantages of Section 363 Sale

A disadvantage of a Section 363 Sale in bankruptcy is that it typically will not occur as quickly as a sale outside of bankruptcy. Furthermore, while a buyer obtains assurances of better title and other benefits by buying out of a bankruptcy process, it also creates a competitive environment and a buyer may end up paying more for the assets than would otherwise be the case. Finally, bankruptcy sales are public proceedings. A sale outside a bankruptcy avoids the stigma associated with a company having filed bankruptcy, which will be of a greater consequence in certain industries than others.

Summary of Section 363 Sale Process

A typical bankruptcy sale process involves a buyer entering into an asset purchase agreement. The initial buyer may be referred to as a “stalking horse.” This buyer may be identified by the debtor, or in larger cases is often identified as a result of the marketing efforts of an investment banker. The stalking horse has the benefit of

being able to negotiate the terms of an asset purchase agreement that often will become the standard agreement that other parties wishing to bid on the assets will be required to use. A stalking horse will typically negotiate a breakup fee in the event it is not the ultimate purchaser and may negotiate the various bid procedures designed by the stalking horse to try to obtain an advantage over other potential buyers. But the execution of an asset purchase agreement with a stalking horse is just the beginning of the process. Once this asset purchase agreement is signed, the debtor in possession in bankruptcy will usually file a motion with the bankruptcy court to approve the sale and bid procedures and to approve the stalking horse asset purchase agreement. An auction is usually scheduled for 30 to 60 days later, at which time other qualified bidders, as defined in the potential auction sale procedures, may come forward and bid on the assets. Typically, in order to be a qualified bidder at the auction, a new bidder is required to submit an asset purchase agreement conforming as much as possible to the stalking horse asset purchase agreement. A deposit is usually required prior to the time the bidder can be qualified.

The auction is usually held at a location designated by the company and conducted by the company's lawyers, investment bankers, or financial advisors. Once the auction is completed and the company declares who had the highest and best bid, the debtor in possession will promptly return to the bankruptcy court to seek court approval of the successful bidder. If the successful bidder does not close on the transaction, the backup bidder will usually be required to be in a position to close at the backup bid price.

Winners and Losers

Difficult economic times create challenges and adversity for some and opportunities for others. Sometimes, but not always, assets bought through a foreclosure or bankruptcy sale process are purchased at distressed levels, resulting in substantial upside for the buyer and lost hopes and dreams for investors and creditors. In many instances, especially through a bankruptcy sale process, value is maximized. At other times, the true value is lost because assets are sold at fire-sale prices. Often the business will continue in one form or another, under a new lender or investor mix.

Licenses of Intellectual Property in Bankruptcy

As noted in the Strategic Alliances section, above, and as discussed in detail in the Distress Stage section of the 2005 *Guide*, intellectual property licenses are treated, under sub-section 365(n) of the Bankruptcy Code, in a way that generally protects the licensee's access to the licensed IP.

D. Tax and Tax Credits

As discussed elsewhere in this *Supplement*, when the *Guide* was published in 2005, the economic climate was very different. One of the main tax priorities of the Republican Party, which controlled both the White House and Congress in 2005, was the permanent extension of the tax cuts made under the Economic Growth and Tax Relief Reconciliation Act of 2001 ("EGTRRA") that reduced the top marginal rate on ordinary income for individuals from 39.6% to 35%, reduced the maximum capital gains rates for individuals from 20% to 15%, and provided a 15% tax rate for certain qualifying dividends.

The tax cuts made under EGTRRA were not made permanent. Moreover, due to the deterioration in the economy that began in 2007, the legislative tax priorities changed dramatically. Many of the changes that were made to the Internal Revenue Code after 2007 were designed to address specific issues raised by the financial crisis and to stimulate the economy.

All levels of government are now facing significant reductions in tax revenue and increasing demands for services. This has resulted in state budget deficits and a dramatic increase in the size of the U.S. federal budget deficit. Based on the most recent budget projections by the Obama administration, the federal debt is projected to grow to a level where the ratio of the federal debt to gross domestic product (GDP) would increase from 40%, prior to the beginning of the financial crisis in 2007, to 70% in 2011, the highest level since the early 1950s immediately following World War II. In his recent address to Congress, Federal Reserve Chairman Ben Bernanke warned that steps must be taken to reduce the size of the federal budget deficit. According to Chairman Bernanke, "[a]ddressing the country's fiscal problems will require

a willingness to make difficult choices” and, in regards to taxes, “tax rates must ultimately be set at a level sufficient to achieve an appropriate balance of spending and revenues in the long run.”⁹⁵ It is very likely that the stimulus spending that occurred as a result of the recent financial crisis and the precipitous drop in tax revenue at the state and federal levels will require an increase in taxes in the coming years.

In addition to the economy, the political landscape has also changed dramatically since 2005 with the Democratic Party now in control of both the White House and Congress. As is evidenced by his initial tax proposals, particularly those relating to international tax reform, tax priorities have changed under the Obama administration.

Tax Rates

Federal

As of the date of this *Supplement*, the federal income tax rates that apply to biotechnology companies and investors in biotechnology companies are as follows:

	Ordinary Income	Capital Gain
Individuals	35%	15%
C Corporations	35%	35%

These are the same tax rates that were in effect when the *Guide* was published in 2005. These tax rates, however, are scheduled to expire for tax years beginning after December 31, 2010.

The Obama administration has proposed making the current tax rates that apply to individuals permanent for taxpayers with income of up to \$250,000 for joint returns (\$200,000 for single taxpayers). For individuals with income over \$250,000 for joint returns (\$200,000 for single taxpayers), however, the Obama administration has proposed reinstating the pre-EGTRRA tax rates, which for these taxpayers would have the effect of increasing the rates that apply to ordinary income to 36% and 39.6% and increasing the capital gains rate to 20%. The Obama administration proposes to make these changes effective in 2011.

Minnesota

Minnesota's income tax rates are the same as they were when the *Guide* was published in 2005. The maximum income tax rate for individuals is 7.85% and the maximum tax rate for corporations is 9.8%. The most recent tax bill passed by the Minnesota legislature contained a provision that would increase the maximum tax rate for individuals to 9% for taxpayers with taxable income of over \$250,000 for joint returns (\$141,250 for single filers). The 9% rate would expire in 2013 if, according to the February 2013 economic forecast, the unrestricted general fund balance at the end of fiscal year 2013 equaled or exceeded \$500 million. This bill was ultimately vetoed by Governor Tim Pawlenty on May 21, 2009.

Federal Tax Incentives for Research and Development Expenditures

Research and development activities are obviously vital to biotechnology companies. Congress has created several federal tax incentives that are intended to encourage research and development activities by reducing the after-tax cost of these activities. One incentive is the deduction for certain research or experimental expenditures under Section 174 of the Code. This provision allows companies to claim a current income tax deduction for qualifying research expenditures, notwithstanding the general rule that business expenses paid or incurred to develop or create an asset that has a useful life that extends beyond the current year are required to be capitalized.

Research Credit Under Section 41 of the Code

The other significant federal tax incentive for research and development activities is the research credit under Section 41 of the Code. The research credit was first introduced in 1981 as a temporary incentive to stimulate research and development activity. Since 1981, the research credit has been extended 13 times and, as of the date of this *Supplement*, has not become a permanent provision in the Code. The research credit has become part of the temporary tax provisions known as the "extenders" that due to budget constraints and other factors are typically extended for

relatively short periods of time. The most recent of these bills, the Emergency Economic Stabilization Act of 2008 (P.L. 110-343), extended the research credit through December 31, 2009. As of the date of this *Supplement*, the research credit is due to expire after December 31, 2009.

One of the major criticisms of the research credit is its lack of permanence. According to a Congressional research report, the fact that companies cannot count on receiving the research credit over the life of a multi-year R&D project may cause companies to discount the research credit for purposes of establishing their R&D budgets. In his 2010 budget proposal, President Obama has proposed a permanent extension of the research credit. President Obama proposes to pay for the projected \$74.5 billion cost of the permanent extension with offsets created by proposed international tax reforms.

Since the *Guide* was published in 2005, there have been several changes to the research credit, including the addition of a new simplified credit methodology, known as the alternative simplified credit (ASC), the addition of a credit for energy research, and the elimination of the alternative incremental research credit (ASIC) for the 2009 tax year.

Briefly, there are now five components to the research credit:

- The regular research credit;
- An alternative incremental research credit (AIRC);
- An alternative simplified credit (ASC);
- The basic research credit; and
- The energy research credit.

In any given tax year, a company may claim one of (i) the regular credit, (ii) the AIRC, or (iii) the ASC (but as discussed below, a company may not use the AIRC for the 2009 tax year). In addition to one of the foregoing alternative credits, a company may also claim the basic research credit and the energy research credit.

Regular Research Credit

As discussed in the *Guide*, the calculations involved in determining the research credit can be extremely complicated. The regular research credit is equal to 20% of the company's qualified research expenses ("QREs") above a base amount. The base amount is the product of the company's "fixed-base percentage" and average annual gross receipts for the previous four tax years. A company's base amount cannot be less than 50% of its QREs for the taxable year.

The "fixed-base percentage" depends on whether the company has gross receipts and QREs in three or more of the tax years from 1984 through 1988. For such a company, the fixed-base percentage is the ratio of its total QREs to total gross receipts in 1984 to 1988, with a maximum fixed-base percentage of 16%. For a company without gross receipts and QREs in three or more of the tax years from 1984 to 1988, the fixed-base percentage starts at 3% during the first five years of the company. After the first five years, the fixed-base percentage changes based on the company's actual experience.

Alternative Simplified Research Credit

Effective for tax years ending after 2006, the Tax Relief and Health Care Act of 2006 (P.L. 109-432) added a new alternative research credit methodology known as the alternative simplified research credit ("ASC"). The calculations under this methodology are much simpler than the other research credit methodologies. In addition, the ASC differs from the other methodologies in that it does not require calculation and documentation of gross receipts for prior years.

Under ASC, the research credit is equal to 14% (12% for 2007-08) of the QREs that exceed 50% of the average QREs for the three preceding taxable years. The credit is 6% of QREs if the company has no QREs in any one of the three preceding taxable years. The election to use the ASC applies to the taxable year for which the election is made and all subsequent years unless revoked with IRS consent.

Energy Research Credit

The Energy Policy Act of 2005 (P.L. 109-58) added a new component to the research credit. Effective August 8, 2005, companies are allowed a credit equal to 20% of amounts paid or incurred to an energy research consortium for energy research. An energy research consortium is an organization that is either exempt from taxation under Section 501(c)(3) of the Code or an organization that is organized and operated primarily to conduct energy research in the public interest. In addition, to qualify as an energy research consortium, the organization cannot be a private foundation, at least five unrelated persons must pay or incur amounts (including contributions) during the calendar year for energy research, and no more than 50% of these payments or contributions may be from a single person.

Unlike the other components of the research credit, the energy research credit applies to all qualifying expenditures, not just those in excess of a base amount.

Alternative Incremental Research Credit

The alternative incremental research credit (“AIRC”) was added to Section 41 of the Code in 1996 to simplify the calculation of the research credit for some taxpayers and to make the research credit available to some taxpayers who would not be able to claim the research credit under the regular credit methodology. Under the AIRC, a taxpayer is allowed a credit of 3% of the amount of QREs in excess of 1%, but not greater than 1.5%, of average annual gross receipts for the previous four tax years, plus 4% of QREs in excess of 1.5% but not greater than 2%, of average annual gross receipts for the previous four tax years, plus 5% of QREs greater than 2% of average annual gross receipts for the previous four tax years. The Emergency Economic Stabilization Act of 2008 (P.L. 110-343) repealed the AIRC for 2009.

IRS Enforcement Efforts Relating to the Research Credit

In addition to the complexity of the calculations required to claim and support the research credit, biotechnology companies should be aware that the IRS has a long history of opposition to

the research credit. The IRS has designated the research credit as a “Tier I” audit issue, which means that issues relating to the research credit may be subject to rigorous scrutiny on audit. In addition, guidance regarding the research credit, including the documentation requirements to support the credit, is uncertain.

Proposed 2009 Legislation Regarding the Research Credit

In June 2009, a bipartisan group of Senators, led by Senate Finance Committee Chairman Max Baucus (D-Montana) and Senator Orrin Hatch (R-Utah), introduced legislation (S. 1203) intended to improve and simplify the research credit. If enacted, this legislation would continue the trend of simplifying and expanding the research credit that began in 2006 with the introduction of the ASC.

The Baucus-Hatch bill would repeal the regular credit method effective after 2010. In addition, the bill would increase the credit available under the ASC method from 14% to 20%. For 2009 and 2010, companies would be given the choice of computing the research credit under the regular credit method or under the ASC method. The Baucus-Hatch bill would also extend the research credit, scheduled to expire after 2009, through December 31, 2010.

Minnesota Investment Tax Credit

One of the recommendations made in the Destination 2025 Report issued by the BioBusiness Alliance of Minnesota was the establishment of an angel investment tax credit in Minnesota to catalyze the formation of seed funds and to create an incentive for investment in early stage companies. According to the Destination 2025 Report, the establishment of an investment tax credit was among the most high priority actions items to stimulate job growth for the State of Minnesota.

The final tax bill that was passed by the Minnesota legislature on May 18, 2009 contained an investment tax credit provision intended to encourage investment in early stage companies. Although Governor Pawlenty supported the investment tax credit, he vetoed the tax bill due to his opposition to tax increases in other parts of the bill.

The tax bill would have created a 25% investment tax credit for qualified taxpayers who invest at least \$12,500 in qualified new business ventures. The credit was capped at \$50,000 for each investor and limited to \$10 million per year statewide.

Qualified taxpayers were defined as accredited investors under SEC Regulation D who did not own 20% or more of the outstanding securities of the qualified business or did not receive more than 50% of the gross annual income from the qualified business. Taxpayers seeking to claim the investment tax credit would need to obtain certification from the Department of Employment and Economic Development (DEED).

A qualified business was defined as a business that satisfied the following requirements:

- Its headquarters are in Minnesota.
- It has fewer than 25 employees and at least 51% of employees or payroll are located in Minnesota. If the business has more than five employees it must pay annual wages of at least 175% of the federal poverty guidelines for a family of four.
- The business must be engaged in a qualified high-technology, or qualified biotechnology or medical device field, or in green manufacturing, and must not be engaged in real estate development, insurance, banking, lobbying, political consulting, retail or wholesale trade, professional services, construction, transportation, producing ethanol from corn, healthcare, or similar ventures.
- It has not been in operation for more than 10 consecutive years.
- It has not received more than \$1 million in investments that qualify for the credit or more than \$2 million in private equity investment (regardless of whether they qualify for the credit).
- It does not have more than \$2 million in annual gross sales.
- It cannot be an affiliate or subsidiary of a business with more than 100 employees or gross annual sales of \$2 million or more.

American Recovery and Reinvestment Act of 2009

The American Recovery and Reinvestment Act of 2009 (“ARRA”) (P.L. 111-5) is a \$787 billion stimulus package that was signed into law by President Obama on February 17, 2009. While a detailed discussion of ARRA is beyond the scope of this *Supplement*, the following are a couple of changes made by ARRA that may affect biotechnology companies experiencing financial difficulties.

Increase in Carryback Period for 2008 Net Operating Losses (“NOLs”)

Under the ARRA, certain small businesses are permitted to “carry back” an NOL that arose in 2008 for three, four, or five years, instead of the normal two-year carryback period. To qualify as a small business for purposes of this provision, the average annual gross receipts for the business must not exceed \$15 million for the three-year period ending with the tax year in which the loss arose.

Deferral of Cancellation of Indebtedness Income

The ARRA creates an election under Section 108(i) of the Code that allows taxpayers to defer the recognition of cancellation of indebtedness income (“COD income”) in connection with the reacquisition of certain indebtedness occurring after December 31, 2008 and before January 1, 2011.

In general, when a taxpayer settles a debt for less than the amount owed, the taxpayer recognizes taxable COD income. There are several exceptions to the general rule regarding the taxability of COD income, such as exceptions for taxpayers in bankruptcy and taxpayers that are insolvent. Taxpayers that qualify for one of the exceptions (and thereby avoid paying current tax on COD income) are required to reduce certain tax attributes, such as NOL and capital loss carryforwards and the tax basis of its assets, to the extent of the excluded COD income.

New Section 108(i) allows taxpayers to elect to include COD income in gross income ratably over a five-year tax period. For reacquisitions of indebtedness that occur in 2009, the five-

year period begins with the fifth tax year following the tax year in which the reacquisition occurs. For reacquisitions of indebtedness that occur in 2010, the five-year period begins with the fourth tax year following the tax year in which the reacquisition occurs.

While deferral of income is generally beneficial, many taxpayers may not ultimately benefit from the election under Section 108(i) of the Code. For example, a C corporation that is “insolvent” at the time the reacquisition occurs may prefer to claim the insolvency exception under Section 108(a)(1)(B) and reduce its tax attributes accordingly. In fact, it is possible that the Section 108(i) election may be beneficial for only a small number of debtors, such as non-real-estate partnerships in which the partners are “solvent.”

Proposed “Carried Interest” Legislation

One of the changes proposed by the Obama administration that could have a significant impact on private equity and venture capital funds that invest in biotechnology companies is the proposal to tax income from carried interests at ordinary income rates. Carried interests (or “profits interests”) are equity interests in entities taxed as partnerships for federal tax purposes, including limited liability companies (LLCs), that are received in exchange for services. A significant portion of the income earned by fund managers and others who provide services to private equity and venture capital funds comes from “carried interests” or “profit interests.” Typically, 20% of the profit realized from a sale or other exit transaction is reserved for the fund managers and others who provide services to the fund. Under current tax law, the income attributable to carried interests is taxed at capital gains rates, which is currently 15%.

The Obama administration has proposed taxing income from carried interests as ordinary income subject to self-employment taxes. Taking into account the Obama administration’s proposed increase in tax rates for taxpayers with income of over \$250,000 (\$200,000 for single taxpayers), this would effectively cause income from carried interests to be subject to tax at a rate of 39.6% for most fund managers. In addition, by subjecting this income

to self-employment taxes, fund managers would also pay an additional 2.9% tax on this income.

In April 2009, Rep. Sander Levin introduced a bill (H.R. 1935) that would tax income from “investment services partnerships interests” as ordinary income. This bill is similar to bills that were introduced in 2007 during the Bush administration and were ultimately defeated.

One of the issues regarding the proposed legislation is the types of interests that would be subject to the rules. The legislation proposed by Representative Levin applies to “investment services partnership interests,” which appear to be limited to interests in partnerships received in exchange for providing investment management type services. The Levin bill would appear to apply to partners receiving carried interests in private equity funds, hedge funds, venture capital funds and certain real estate partnership.

In its general explanation of tax proposals, the Obama administration proposes to tax income from “services partnership interests” as ordinary income subject to self-employment tax. The Obama administration’s proposal would appear to apply to any partnership interest that is received in exchange for services and does not appear to be limited to interests received in exchange for performing investment management services.

Another significant issue raised by the proposed legislation is how to separate equity interests received in exchange for services from equity interests received for invested capital. Presumably, the carried interest rules should not apply to equity interests received in exchange for invested capital if the investor also acquires a carried interest in exchange for services. The bill introduced by Representative Levin attempts to create an exception for income attributable to qualified capital interests, which are equity interests received in exchange for invested capital. To qualify for the exception, however, allocations of income, gain, loss and deduction with respect to the qualified capital interest must be made “in the same manner” as allocations to qualified capital interests held by other investors who do not provide investment management services to the partnership. On the surface, it appears that this

exception may be fairly limited, and may not apply to many types of interests held by partners performing services for a partnership.

The Obama administration's proposal would apply beginning in 2011. Moreover, there is nothing in Representative Levin's proposed legislation or in the Obama administration's General Explanation that addresses grandfathering of existing carried interests. Thus, under the current proposals, it appears that the carried interest provision would apply to carried interests in existence prior to the date of enactment.

While the proposed carried interest legislation is controversial and would represent a significant change in the taxation of partnership income, as of the date of this *Supplement* the proposed legislation appears to be gaining momentum.

E. U.S. Import/Export Considerations

Global treaties, regional directives, country-specific regulations, and cultural biases all combine to make the international biotechnology landscape a complex one. While a number of countries seem to accept the idea of the creation of drugs and devices, they strongly resist the idea of creating or modifying organisms, and so at present the global regulatory arena is less concerned with pharmaceuticals than with genetically modified ("GM") crops. This increased concern about agricultural products makes global trade in biotechnology products increasingly complex.

From the U.S. perspective, import and export concerns are the responsibility of various agencies that regulate their respective areas of biotechnology. On the import side, emphasis is on protection of the U.S. population, and so all items are subject to the same certification and registration processes, regardless of whether they originate from friendly countries, biotechnology partners, or even foreign subsidiaries of the U.S. importer. On the export side, fewer agencies are involved, but concerns of national security add a different dimension to the task of compliance.

Imports into the U.S.

A U.S.-based company may import biotechnology products from foreign countries for purposes ranging from experimentation to further manufacture. In each case, Customs and Border Protection (“CBP,” formerly the U.S. Customs Service, and now an agency of the Department of Homeland Security), will examine products and documentation at the point of entry and apply the appropriate U.S. laws and regulations. CBP acts at the U.S. Border on behalf of other governmental agencies, including FDA, the United States Department of Agriculture (“USDA”), and the Environmental Protection Agency (“EPA”). Each agency has a different focus and different approval processes that may affect biotechnology imports, and sometimes their jurisdictions overlap to cover the same import.

Items such as food, medicine, and medical devices that interact with the human body are subject to regulation by the FDA, which requires them to be safe for use or consumption and, in the case of devices, to be both effective and properly labeled. FDA approval procedures, discussed in the 2005 *Guide*,⁹⁶ apply to imported as well as domestically produced items. For bioengineered plants, the FDA becomes involved when the plants are to be offered as foods or animal feeds, just as it would in the case of plants developed through more traditional means. FDA approval may take anywhere from a few months to several years to complete. In addition to the formal approval process, the FDA has a pre-market consultation procedure. The FDA involves itself in pre-market consultation and screening of a developer’s research information rather than conducting the research on its own.⁹⁷

Biotechnology plants and seeds are examined by the USDA, through extensive testing by its Animal and Plant Health Inspection Service (“APHIS”). APHIS offers both a formal method of inspection or permits and an alternative method of consultation, or “notification,” following certain guidelines that are available for imports as well as for domestically bioengineered plants. The importer (like the domestic producer) must meet the applicable safety requirements, which, though not numerous, may present difficulties for some newly developed organisms. Among other requirements, the importer must show that:

- the plants are not certain specified noxious weeds;
- the introduced genetic material is “stably integrated”;
- the function of any introduced material is “known”; and
- the material does not give rise to an infectious entity, encode substances “likely” to be toxic to non-target organisms associated with the plant, or encode products for pharmaceutical use.⁹⁸

The process of notification requires close consultation with APHIS applicable standards and any unsettled areas of regulation.⁹⁹ Pharmaceuticals and other products outside the standards of the notification method are dealt with through the more complex approval process of examination and permits.

Finally, the importing of pesticides and toxic chemicals will involve the EPA, which has identified a biotechnology element in each of these areas. Under the Federal Insecticide, Fungicide, and Rodenticide Act,¹⁰⁰ the EPA regulates not only manufactured chemical pesticides but also those produced by a designed organism. “Registration” to secure EPA approval for insecticides is complex, time-consuming, and strictly monitored, and permits for field-testing can be highly restricted. Similarly, in the EPA’s other area of biotechnology concern, toxic substances in the environment, the EPA considers its authority under the Toxic Substances Control Act (“TSCA”)¹⁰¹ to extend not just to chemicals, but also to organisms (all of which are at least to some extent chemical in nature or activity). Biotechnology regulation under the TSCA is primarily a matter of pre-release screening based on a detailed notice to the EPA.¹⁰²

In light of the above, the obvious word of caution for the U.S. importer is to be sure of clearance by all relevant agencies before assuming that an import program can be carried out.

Exports from the U.S.

U.S. export controls are administered by the Department of Commerce under its own regulation and those of the Departments of Treasury and Defense. Reflecting the self-protective approach of most countries, U.S. export controls of bio-engineered items

are not as detailed or restrictive as U.S. Import regulations. For example, the TSCA generally does not apply to substances being prepared in the U.S. for export.¹⁰³ In circumstances involving potential hazards, however, the U.S. government is required to notify the intended destination country.

In addition to the limited export issues specific to biotechnology, a U.S. exporter is subject to all of the ordinary rules of export control. These rules can be grouped into three categories:

- universal concerns;
- technology export concerns; and
- domestic “deemed” exports.

The universal concerns are the strict prohibitions against transacting business with, or exporting to, certain embargoed countries, listed individuals, or specified companies.¹⁰⁴ Technology concerns mean that each item proposed for export from the U.S. must be considered on a case-by-case basis with respect to product classification and proposed destination. If the U.S. prefers not to share the relevant product or technology with all or some other countries, an export license is required—and may be denied. Finally, the rules of “deemed exports” may apply to technical information. If an export license is required for a product destined for a particular country, export of the technology underlying the product is likely to require a license as well, and some technology exports are restricted even if export of the related products is not. Moreover, in the case of technology, an export is deemed to occur when the technology is presented (or simply made available) to a foreign citizen, even inside the U.S. In other words, a technical sales presentation to a foreign visitor, or more likely, the involvement of a foreign scientist in R&D within the U.S., or just the hiring of a foreign intern with access to computers housing restricted technical information, may require an export license. Conducting an unlicensed “export” of this sort within the U.S. is a serious violation of federal law. Because of changing prohibitions, classifications and licensing requirements, consultation with legal counsel is recommended with respect to all exports.

F. International Regulation and Barriers

In the biotechnology realm, moving beyond the U.S. borders increases the complexity of product development and distribution. As this section describes, international treaties between countries, directives of the EU, standards by the United Nations, country-specific regulations, trade policy, protectionism, and fear (rational or irrational) all come together to create a complex web of rules for the biotechnology exporter. In the case of drug and device biotechnology, country-by-country regulations create a patchwork of application and market entry regulations for biotech developers, and yet examination of the rules for each target country can allow a biotech exporter a considerable degree of certainty and reliability concerning the hurdles to be cleared and rules to be followed. Still, because of the proliferation of nation-specific policies, we do not here undertake any examination of this area. On the other hand, and somewhat ironically, the broad international agreement that has been reached on agricultural organisms and seeds may not actually permit the same degree of certainty and reliability as the drug and device regulation. We will look briefly at the legal structures involved, but we also present a cautionary recommendation that the prudent exporter of any GM products should have a thorough understanding of the product and the intended market in order to appropriately educate foreign government officials and citizens where needed to persuade them of the safety and efficacy of the products.

Background

Each country has different rules and regulations that apply to genetic engineering and other biotechnology initiatives, and these rules may be based purely on science or, more often, on personal, social, and religious beliefs of policy makers or the societies they represent. Consequently, success in the international market depends on favorable laws and regulations, as well as consumer and societal acceptance of new biotechnology.

As noted above, biotechnology regulation is a patchwork of national and quasi-national restrictions and requirements. In the case of drugs and devices, most countries have their own

equivalent of the FDA, but the agencies in the various countries apply vastly different standards and requirements. In some, little proof of efficacy or safety is needed. In others, years of time and millions of dollars are required for certification or approval. Standards other than national regulations may apply as well. For example, within the EU, the process of obtaining a CE mark (the manufacturer's declaration of compliance with the applicable regulations) can simplify or eliminate the country-by-country filings for devices. There is also an increasing willingness of national regulatory bodies to recognize, at least to some degree, the approval of a drug or device by another country.

In contrast, the field of agriculture, constantly in the public eye and mind, has shown at least formal progression and significant multinational cooperation. Formal acceptance of the concept of GM products does not mean, however, acceptance of GM food exports from the U.S. or other countries, as we will see. Often a nation's population, or large groups within it, will influence or alter the government's attitude or will render the final decision in the marketplace, and so a developer must recognize that a government's indication at any given time may well not be the long-term answer on imports. Rather, the successful exporter must focus sooner or later on changing or guiding foreign opinion.

A 2001 paper prepared by the USDA, and still resonating today with popular opinions, thoroughly examined consumer acceptance of GM foods.¹⁰⁵ That research indicated a public wariness for relatively new GM foods, or more simply stated, a concern for the unknown.¹⁰⁶ U.S. consumers reached a point of "indifference" toward GM foods in 2004, with half or more recognizing no difference between GM foods and others,¹⁰⁷ but the view is not reflected in all other countries, and even in the U.S. there remains skepticism by the public in some areas. In Japan, China, and the EU, citizens are concerned that foods should be proven safe rather than relying on the absence of proof that they are unsafe. They tend to follow the "precautionary principle" that if the potential harm caused by unsafe GM products is great, even a low percentage chance of that harm should be enough reason to bar the import or use of those products until their safety is adequately

demonstrated. In contrast, the view in the U.S. is more that GM products should be used unless there is substantial evidence that they are dangerous. In Europe, the precautionary principle permeates the laws and regulations with respect to genetically modified organisms (“GMOs”) and looks toward proof of the safety of all genetically engineered crops and foods.¹⁰⁸

International Structures for Legal Control or Standardization

International agreements, whether they concern GMOs or other matters, are usually in the form of conventions or treaties, signed by representatives of the countries involved, adopted by their legislatures in some cases, and implemented by their laws. The Cartagena Protocol on Biosafety (“Cartagena Protocol”) discussed below, is an adjunct to just such a treaty. In addition to treaties, economic trading areas such as the EU may issue directives that to a considerable degree bind their member states. Directive 2001/18/EC of the European Parliament and of the Council (“Directive 2001/18”) is an example of this directive in the area of biotechnology and GMOs. Finally, another international player, the United Nations, has entered the biotechnology discussion with its own standards, the Codex Guidelines on Food Derived From Biotechnology (“Codex Guidelines”). Each of these international accords has the potential to make foreign exports of biotechnology easier, but country-specific challenges remain.

European Directive 2001/18

The clearest example of regulation at the international level is that of the EU, where the main framework for the regulation of GMOs is contained in Directive 2001/18/EC and the Regulation (EC) No. 1831/2003 of the European Parliament and of the Council. Unless imports containing GMOs comply with Directive 2001/18, they will not be admitted into the EU. In accordance with the precautionary principle, Directive 2001/18 requires that the risk associated with each product be evaluated on a case-by-case basis prior to the product’s release or placement on the market.¹⁰⁹ For the importer to be in full compliance, certain disclosure requirements must be met, including the clear labeling of genetically engineered products.¹¹⁰ Labeling exports from the U.S. to comply with these

requirements is extremely costly and difficult because of the problems with identity preservation and traceability.¹¹¹ Directive 2001/18 is binding on all EU states with respect to the results to be achieved, but each EU member state enjoys considerable latitude in implementing the Directive. Historically, the country-by-country choices have involved considerable resistance to European imports of GMOs, but the adoption of Directive 2001/18 was to have greatly reduced or even eliminated most resistance and virtually all variations in favor of Europe-wide standards of GMO testing. In April 2005, to address the continuing reluctance of five member states to comply with the new directive and regulation, the EU had even gone so far as to warn them of legal action if they did not end their moratorium on certain GMO imports.¹¹² The U.S., early in 2005 and again in more recent years, has contributed to the problem of import clearance by “polluting” U.S. corn stock with Bt corn, causing another moratorium in 2005 and a rejection and return of corn shipments as recently as the first half of 2009.¹¹³

The Cartagena Protocol

In addition to Directive 2001/18, two international agreements respond to genetic engineering initiatives: the Cartagena Protocol¹¹⁴ and the Codex Guidelines, each of which is an emerging standard in its own way. The Cartagena Protocol has been adopted and ratified, or “assented” to, by 155 nations as of May 31, 2005, but not yet by the U.S.¹¹⁵ Like Directive 2001/18, the Cartagena Protocol employs the “precautionary principle,” which is invoked when a party makes a decision to import new GMOs, such as GM seeds, that are capable of reproduction. In this event, the Cartagena Protocol established an Advanced Informed Agreement procedure, under which an exporting nation must inform an importing nation in detail as to the facts of a new form of GMO before the first shipment of the organism.¹¹⁶ The importing nation must acknowledge receipt of the notice in writing and then decide to accept or reject the shipment.¹¹⁷ As with Directive 2001/18, each Cartagena Protocol signatory is free to decide for itself whether it will accept or reject a specific import. This freedom to decide creates additional work and uncertainty for U.S. biotechnology companies that are considering the export market, and it remains

in place even though it arguably conflicts with the “free trade” and “most favored nation” principles of the World Trade Organization (“WTO”). Under the WTO, the inquiry is whether the product is like other items that are being permitted entry into the country, and if the answer is affirmative, then the entry should be permitted. Under the Cartagena Protocol, in contrast, the receiving nation can rule out importation based on the science of environmental protection. Furthermore, if the science would tend to permit the product to pass, the Cartagena Protocol permits the nation involved to consider the human health risks and socioeconomic factors that may have an impact within the nation’s borders.

The Cartagena Protocol has no real enforcement mechanism for refusal to permit entry (though it does have penalties for unlawful entry), but there is one benefit of the Cartagena Protocol for exporters and importers alike that should not be overlooked. It introduces a common, international bank of knowledge on living modified organisms and establishes a system for sharing information. The Biosafety Clearing-House stores and provides information on laws, regulations, decisions, standards, illegal transboundary movements, international agreements, and contact details for national authorities. The related website¹¹⁸ can be expected to become a major reference tool for the importers and exporters of GM foods in the coming years.

As noted, variations in implementation of the Cartagena Protocol are permitted, but it has no direct influence at all on some major countries, because they have not signed it or have not ratified it, and they are therefore not subject to its provisions by any means greater than world political opinion. The United States has not yet signed the Protocol, and Canada, although it signed, has not yet ratified it. Mexico, China, the EU, and Japan, the major agricultural markets for the U.S., have ratified the Protocol but have implemented it differently, as permitted under its rules. Japan accepts GM products after careful study, whereas China, the EU, Mexico, and Canada utilize the cautionary principle more strongly and have rejected GM food products outright for varying periods in the past several years.¹¹⁹

The Codex Guidelines

The other major international effort for regulation of food products, known as the Codex Guidelines,¹²⁰ is a set of United Nations developed standards for food items, providing detailed specifications for foods possibly involved in international trade. In these guidelines, the United Nations has considered a position similar to that of the EU, that is, before any GM product is put on the market, it should be subject to a premarket safety assessment conducted on a case-by-case basis.¹²¹ Again, there would be some variation permitted for national adoption of the guidelines. So, depending on the manner in which various provisions of the Cartagena Protocol are implemented by each signatory, and if the Codex Guidelines are adopted and followed by each country, there could be a significant impact on U.S. exports.

Conclusion

Amidst controversy and resistance from consumer and industry groups, some countries are beginning to accept certain GM crops and even encourage this development. As nations continue to impose labeling requirements for products containing genetically engineered organisms or even outright bans on the importation of such products, U.S. producers will face difficult challenges to their continued profitability, potentially rendering considerable damage to the biotechnology industry and its beneficiaries.¹²² Because of the significance of current and potential foreign markets to GM crop producers, it is elementary that a ban or a significant reduction of imports could affect the producer's production, share price, and profitability. A company engaging in biotechnology R&D would be well advised to remain apprised of developing laws and regulations in potential markets around the world.

V. REGULATORY FACTORS THAT INFLUENCE BIOTECHNOLOGY FINANCE

A. The Impact of the FDA: The Passage of the FDAAA

Congress updated FDA laws in September 2007 with passage of the Food and Drug Administration Amendments Act (“FDAAA”).¹²³ These amendments directed the FDA to develop a systematic, scientifically sound approach to managing the risk-benefit ratio of a drug throughout its lifecycle, with an explicit focus on post-approval safety. Other provisions aim to increase drug, biologics, and medical device clinical trial transparency by requiring centralized reporting of clinical trial results. Although the FDAAA will be implemented over time, given the FDA’s substantial number of responsibilities, it is unclear how long the agency will take to implement some of the amendments.

Post-Approval Drug and Biologics Safety Studies

Under the FDAAA, if the FDA becomes aware of new safety information related to a drug or biologic, it has the authority to require the manufacturer to (i) perform a post-approval study or clinical trial to assess a known serious risk related to the use of the drug or biologic involved, (ii) gather more information on signals of serious risk, or (iii) conduct further research on an unexpectedly serious risk.

Risk Evaluation and Mitigation Strategies (REMS)

The FDAAA increases the ability of the FDA to require risk evaluation and mitigation strategies (“REMS”) both as part of the drug approval process and once a product is on the market. REMS are comprehensive studies aimed at ensuring that a drug’s benefits outweigh its risks. While the FDA has been using some form of REMS (formerly called RiskMAPs) for over 20 years, the FDAAA allows the FDA to expand their use to time periods throughout the drug’s life cycle and can take into account new safety information. The FDA may determine that REMS are necessary based on (i) the

estimated size of the population likely to use the drug involved, (ii) the seriousness of the disease or condition that the drug is designed to treat, (iii) the expected benefit of the drug, (iv) the expected or actual duration of treatment with the drug, (v) the seriousness of any known or potential adverse events related to the drug, and (vi) whether the drug is a new molecular entity. As of March 2008, the FDA had already identified 25 drugs and biologic products that will be required to submit REMS.

Labeling Changes Based on New Safety Information

The FDAAA now directs the FDA to require label changes based on new safety information. “New safety information” is (i) information regarding a serious risk or an unexpected risk associated with the drug since the drug was approved, or since the REMS was required or last assessed, or (ii) information regarding the efficacy of the approved REMS. This new safety information may come from a post-marketing study or clinical trial, an adverse event report, peer-reviewed literature, or “other scientific data.” These changes reflect the intent of Congress that the FDA be more responsible for initiating safety-related label changes. Perhaps the most notable exercise of this authority to date is the June 2008 announcement by the FDA requiring manufacturers of “conventional” anti-psychotic drugs to put warnings on their products telling physicians and consumers of the increased risk of death associated with the off-label use of these drugs to treat behavioral problems in older people with dementia. Manufacturers of both conventional and newer anti-psychotic drugs are being asked to change labeling so that all anti-psychotic drugs carry uniform warning language.

Public Posting of Results of All Clinical Trials Involving Approved Drugs, Biologics or Medical Devices

The FDAAA also makes significant changes to the FDA’s traditional post-market surveillance approach by authorizing the FDA to publish quarterly reports informing the public of drugs for which it has identified a potential risk of significant adverse events. Traditionally, the FDA has relied primarily on a voluntary reporting system under which manufacturers, healthcare providers,

and patients could submit adverse event reports regarding a particular pharmaceutical when they became aware that it might be linked to potential health risks. These reports were collected by the FDA and regularly examined to uncover potential risks and to determine whether further investigation was warranted. Critics claimed that under this system the FDA failed to communicate safety concerns to the public in a timely and effective manner. Significantly, this prior system of reporting was a passive system under which the FDA relied on patients, physicians, and manufacturers to report adverse events. Under the FDAAA, the FDA must set up an active risk identification network and then communicate its findings promptly to the public.

The FDAAA requires the Secretary of the Department of Health and Human Services (“HHS”), acting through the Director of the National Institutes of Health (“NIH”), to establish and administer through the Internet (i) a clinical trial registry database and (ii) a clinical trial results database for drugs, biologics, and devices. These databases apply to both privately and publicly funded clinical trials.

The registry database will include all except Phase 1 drug and biologics studies and all device trials that either compare a device against a control or involve pediatric postmarket surveillance-device studies. The FDAAA requires many more data elements for this registry than under previous law, including (i) study design, (ii) recruitment information, (iii) eligibility criteria, (iv) demographic information, (v) information on primary and secondary outcomes, (vi) contact information for details about the trial, (vii) start date, (viii) target number of enrollees, and (ix) for trials involving unapproved drugs, a determination of whether expanded access to the drug is available for subjects who do not qualify for the trial. In general, sponsors of trials will be required to submit data to the registry database for ongoing or new studies within 21 day after the first patient is enrolled.

The results database will include FDA assessments of the trial results, FDA advisories regarding the drug or device, citations to any publications focused on the study results, and other details from the study. The FDAAA requires HHS to determine how

to include detailed summaries of the results in language that the public can understand, along with the full protocol. For the results database, sponsors must provide the required information to NIH within a year of completing the study or 30 days after the FDA approves the product, whichever is earlier.

The FDAAA also requires HHS to issue a regulation mandating sponsors to submit adverse event information to the databases in a way that is not misleading to patients or doctors. If this regulation is not issued by September 27, 2009, the statute will still require sponsors to submit adverse event information to be included in the databases. The required information includes tables for all anticipated and unanticipated serious adverse events and tables for “frequent” adverse events that occurred at a rate of more than 5% within any arm of the trial. Interestingly, the adverse event requirements currently only apply to drug trials. An amendment or corrections bill will be needed to clarify that device trials are also subject to the requirements.

Risk Identification Network

To improve the FDA’s surveillance system and to foster greater communication with the public, the FDAAA also requires the FDA to launch an active risk identification network. This will comprise a master database with data from several sources, such as the Department of Veterans Affairs, the Centers for Medicare & Medicaid Services, and other administrative organizations’ databases. The FDA is required to actively monitor the database for new safety signals related to approved products. This distributed research system, which includes multiple electronic data sources that will be the cornerstone for building the active surveillance system, has been named Sentinel.

Incentives for Development of Pediatric Devices and Requirement for Pediatric Testing of Drugs and Biologics

There are several provisions in the FDAAA aimed at the development of drugs and devices for children. Particularly important are Title IV, which reauthorizes the Pediatric Research Equity Act of 2007, and Title V, which reauthorizes the Best Pharmaceuticals for Children Act of 2007. As of the date of this

publication, there has been limited guidance from the FDA with respect to these provisions.

Implications of the FDAAA

Manufacturers should be aware that new drug and biologics approvals and device registration may take more time, and advertising and labeling for new products may be more restricted. In addition, drug approvals may come with strings attached, in the form of post-approval study or REMS requirements. The FDAAA requirements will likely make drug lifecycle management more complex, more costly, and more resource-intensive for manufacturers.

In particular, the registry and results database requirements can affect proprietary information, inventions, publication, insurance coverage, and agreements with institutions. Sponsors reporting adverse events will need to revise their reporting mechanisms and policies to address what kind of adverse events they need to report. But they should also include language in their protocol and clinical trial agreements to ensure site compliance and minimize liability. Greater transparency in clinical research data and results may yield greater transparency in possible product liability. Patients (and their attorneys) will have access to almost every adverse event, which may facilitate more product liability claims related to listed adverse events.

Additionally, the FDAAA requirements may affect publication of research results. If a sponsor and the principal investigator have agreements that restrict the principal investigator from disclosing trial results, those agreements will have to be re-drafted in order to allow the reporting required under the FDAAA. Sponsors concerned about potential threats to intellectual property or the disclosure of proprietary information can take advantage of time extensions provided by the act to delay reporting until after publication of the research results.

Finally, if HHS expands the database to require submission of results for unapproved drugs and for devices not approved or cleared, there is a potential threat not only to intellectual property, but also the advancement of research in general. Most companies

protect their early-phase research to prevent their confidential information from reaching competitors. Disclosing early phase trial results could reveal analyses or end points derived from significant negotiation with FDA and international regulatory authorities.

Suggestions For Drug, Biologics, And Device Manufacturers

Noncompliance with the requirements of the FDAAA can have significant ramifications. For instance, violations of the new labeling provisions can result in civil penalties of not more than \$250,000 per violation, not to exceed \$1 million for all violations addressed in a single proceeding. If the violation continues despite written notice, the manufacturer can be subject to a penalty of \$250,000 for the first 20-day period, doubling every 30 days thereafter, subject to a \$10 million cap in any single proceeding. Additionally, the FDA can levy civil monetary penalties for noncompliance with post-approval study requirements as high as \$10 million.

Given all the changes and new requirements under the FDAAA, it is wise to begin discussions with the FDA early to appropriately plan for any additional study requirements or post-approval commitments. Also, manufacturers should be aware that as the number of ongoing studies rises, researchers may find it increasingly difficult to recruit participants for their studies, and that data standards allowing integration of data from electronic health records and other databases into observational studies will be critical.

B. Regulatory and Law Enforcement Oversight of Biotechnology Firms.

Biotechnology firms selling items that are ultimately used in the healthcare industry are subject to laws directed at preventing waste, fraud, and various other abuses. Any company that provides goods or services reimbursed under Medicare, Medicaid, or other federal healthcare programs may be subject to civil or criminal penalties under federal laws including the federal anti-kickback statute, the Stark law, the Federal False Claims Statute, and various FDA

laws. Companies that provide goods or services reimbursed by state healthcare programs, or even by individuals or private payors, may find themselves subject to similar, but usually not identical, state statutes. This chapter will introduce several key risk areas for pharmaceutical and device manufacturers, with the aim of identifying fact patterns that may, if not properly managed, lead to allegations of fraud, waste, or abuse.

While there are a multitude of scenarios under which a biotechnology company can find itself in trouble, the following are common enforcement targets.

Off-Label Promotion

The FDA seeks to ensure the safety and efficacy of most drugs and devices. This means that most drugs and devices must be approved by the FDA prior to promotion or marketing. As part of this process, the FDA approves certain uses or “indications.” The FDA generally prohibits manufacturers of new drugs or medical devices from promoting or marketing products for any use that the FDA has not approved.¹²⁴ According to the FDA, an approved new drug that is marketed for an unapproved use is an unapproved new drug with respect to that use.¹²⁵ Specifically, an approved drug or device that is marketed for an unapproved use is considered to be misbranded.¹²⁶ If a manufacturer promotes a drug or device for any unapproved indication, it is called “off-label promotion” and may violate FDA regulations.

The FDA recognizes that off-label use can be appropriate and valuable to patient care, and therefore the statutory scheme allows for off-label use by physicians. In fact, drugs and devices are commonly used for off-label indications with good results. The FDA also understands that there must be some room for free exchange of educational and scientific information in order to advance the cause of science and healthcare. Thus, it allows dissemination of certain scientific information by manufacturers, with constraints designed to ensure that these exchanges are not used as subterfuge for off-label promotion.¹²⁷ Most companies have special processes and procedures that must be followed when disseminating off-label information to ensure adherence to FDA guidance on this point.

The federal government takes an aggressive stance regarding the enforcement of off-label promotion and has obtained some significant judgments against manufacturers for off-label promotion. These cases tend to emanate from sales and marketing practices designed to sell products to healthcare providers for off-label uses. For example, in January of 2009, the DOJ accepted a guilty plea from Eli Lilly and Company (“Lilly”) and fined that company \$515 million.¹²⁸ This fine was in addition to a civil settlement of approximately \$800 million. These criminal and civil settlements resulted from a claim that Lilly was promoting its drug Zyprexa for the treatment of dementia, Alzheimer’s, depression, anxiety, sleep problems, and behavioral symptoms such as agitation, aggression, and hostility—despite the fact that the drug was approved only for the treatment of psychotic disorders and bipolar disorder.

Similarly, in April 2009, Nichols Institute Diagnostics (“Nichols”), a subsidiary of Quest Diagnostics, Inc., pled guilty to a felony misbranding charge in violation of the Food, Drug, and Cosmetic Act and agreed to pay a criminal fine of \$40 million as part of a \$302 million global settlement with the federal government.¹²⁹ In its guilty plea, Nichols admitted that, over approximately a six-year period beginning in May 2000, it marketed a misbranded test. The misbranding charge was premised on the allegation that Nichols distributed marketing materials regarding the Advantage Intact PTH Assay describing the product as having “excellent correlation” to another assay—despite the fact that Nichols was aware that the Advantage Intact PTH Assay was not consistently providing equivalent results.

In addition to monetary relief, the FDA may seek to obtain an injunction to prohibit companies from manufacturing and distributing unapproved drugs. For example, in April 2009, the FDA announced that it was barring Neilgen Pharmaceuticals Inc., its parent company Advent Pharmaceuticals, Inc., and two of their officers from manufacturing and distributing any unapproved, adulterated, or misbranded drugs.¹³⁰ According to the FDA, the unapproved drugs (primarily prescription cough and cold products) manufactured by Neilgen and Advent had not

undergone the FDA's drug approval process. Accordingly, the companies failed to establish the drugs' safety and effectiveness, and the FDA had not reviewed the adequacy and accuracy of the directions for use and related label warnings. As part of the consent decree with the FDA, Neilgen and Advent were ordered to destroy their existing drug supply and were expressly prohibited from commercially manufacturing and distributing any new drugs without the FDA's approval. The companies were also required to obtain written authorization from the FDA to resume operations and to consult with outside experts who could provide guidance regarding appropriate compliance standards. Neilgen and Advent now face the prospect of steep financial penalties for any future violations. While the failure to obtain any FDA approval makes this an extreme case, the enforcement action demonstrates the significant business disruption that can result from violations of FDA regulatory requirements.

It is also important to note that claims of off-label promotion are not levied exclusively against manufacturers. For example, in 2006, the DOJ charged a psychiatrist with conspiring with the manufacturer of a drug called Xyrem to promote the drug for off-label uses (the drug was approved for the treatment of two medical conditions: cataplexy, a condition characterized by weak or paralyzed muscles associated with narcolepsy, and excessive daytime sleepiness in narcolepsy patients).¹³¹ According to the indictment, the manufacturer of Xyrem, Orphan Medical, Inc., paid the psychiatrist thousands of dollars for promoting Xyrem for off-label uses at various speaking engagements. As a result, both the company and the physician were charged and in July 2007, Orphan Medical pled guilty and agreed to pay \$20.0 million in settlement of criminal and civil suits.¹³²

Kickbacks

Patients rely on their physicians to recommend the best treatments, drugs, and devices. Indeed, patients cannot obtain prescription medical products and services without a referral or order from a medical professional. Thus, the physician-patient relationship is regarded as a special, fiduciary relationship—one where the physician is obliged to act with the best interest of the patient

as the motivating concern. Remunerative relationships such as consulting arrangements between manufacturers and physicians who refer for the manufacturers' products can create an apparent or real conflict of interest, thereby potentially tainting referral decisions.

This concern underlies the federal anti-kickback law (the "AKL").¹³³ Very generally, the AKL prohibits soliciting, receiving, or offering any remuneration (including any kickback, bribe, or rebate) in return for referring an individual to a person for the furnishing of any item or service for which payment may be made under a federal or a federally funded state healthcare program. The mandatory penalties for violations of this statute are severe, and a party guilty of violating the AKL is guilty of a felony and subject to a prison term of up to five years. Moreover, a party who has violated the AKL is excluded from participation in Medicare, Medicaid, and other federal healthcare programs.

Application of the AKL is complex. Many common situations involving remuneration between manufacturers and referral sources can be structured to comply with the statute. Because there are many hurdles in order to ensure compliance, it is important that all "remunerative relationships" or transfers of value between manufacturers and their customers and others in a position to generate business for the manufacturer be properly vetted.

There have been many prosecutions under the AKL. These prosecutions typically arise from cases where a device or pharmaceutical manufacturer gives something such as money, a gift, or a meal to a physician or another person in a position to recommend its product, and the apparent motivation for the transfer was to induce the recipient to refer for or recommend the manufacturer's product. Notably, it is not unusual to see a prosecution involving allegations that a company made improper payments to a physician to induce the physician to prescribe products for off-label uses, thereby coupling a violation of the prohibition against off-label promotion with an AKL violation.

These prosecutions often involve payments to physicians, but they can also involve payments to other parties in a position to promote

the manufacturer's product. For example, one fairly recent prosecution involved the large pharmacy benefit manager Medco.¹³⁴ The government alleged that Medco violated the AKL by soliciting and accepting payments from pharmaceutical companies for favorable formulary placement, and by paying kickbacks to induce health plans to award Medco contracts to provide mail-order pharmacy benefits for the plans' beneficiaries.

Many states have adopted their own versions of the AKL.¹³⁵ These statutes may affect arrangements involving items or services that are not covered under one of the programs protected by the AKL. Also, these statutes may implicate slightly different behavior than is implicated by the federal AKL. Ultimately, the existence of these state AKLs means that remunerative relationships with referral sources must be scrutinized for compliance with both state and federal law.

Physician Self-Referrals

Historically, physicians have branched out from the practice of medicine to provide their patients with ancillary services such as laboratory tests, pharmaceuticals, digital imaging, and lithotripsy. Physicians may own interests in hospital or other facilities to which they refer patients, or in device companies producing items used by their patients. While this practice seems like a natural evolution—and is beneficial to the extent that it increases accessibility or quality or spurs innovation—it also has the potential for creating a conflict of interest. The financial interest provides the physician with an incentive to direct patients to purchase services or products from the physician's practice or from the entity in which the physician has an interest, despite the fact that these products or devices may not be the best or cheapest available to the patient. In addition, the conflict of interest may provide an incentive towards overutilization.

The Stark law, named after its primary sponsor Rep. Pete Stark, and its associated regulations address this concern by prohibiting physician self-referrals for certain "designated health services" reimbursed by Medicare or Medicaid, except in certain specified circumstances.¹³⁶ As with the AKL, many states have adopted their

own variant on the Stark law and prohibit self-referrals in the same or similar circumstances. Of course, not all of these arrangements will be problematic. Rather, they may fall under one of numerous statutory or regulatory exceptions. All of these arrangements do, however, require careful attention.

Of particular interest to device manufacturers is the question of whether the Stark law should apply to prohibit physician-owned companies that produce medical devices from selling those devices to hospitals and other facilities for ultimate use by the physician-owner's patients. The Centers for Medicare and Medicaid Services is currently considering how to properly regulate physician-owned companies, and has just recently solicited comments from the public and the industry on the proper approach to take.

Bad Reimbursement Advice

Manufacturers of complex or innovative products may provide reimbursement advice to their customers. Liability for manufacturers can arise from faulty advice or from advice that is perceived as promoting overutilization. For example, in *United States v. Augustine Medical Inc.*, the government alleged that a manufacturer directed its customers to a bill in a manner that obscured the true nature of their product because it believed that if Medicare knew exactly what product was being billed, Medicare would reimburse for the product at a less favorable rate.¹³⁷ Augustine Medical and various individuals associated with the company faced criminal and civil enforcement actions. The company eventually settled all claims against it. Several Augustine Medical executives pled guilty to criminal charges related to withholding facts used to determine rights to Medicare payments, and received probation and paid significant fines.

Price Reporting Fraud

Pharmaceutical manufacturers report drug prices under a number of different programs using several different methodologies (*e.g.*, average manufacturer price, best price, average sales price, average wholesale price, and wholesale acquisition cost). Additionally, sponsors of programs operating under Medicare Part D are required to report to the Center for Medicare and Medicaid Services all

price concessions obtained from manufacturers (*e.g.*, rebates or discounts).¹³⁸ Allegations that a pharmaceutical manufacturer defrauded Medicare or Medicaid (or other governmental program) are often premised on the alleged inaccuracy of the various pricing reports. Charges of misconduct can arise in connection with, for example, the inaccurate reporting or characterization of discounts or rebates. Allegations of “marketing the spread”—where manufacturers report their average wholesale price to Medicare as “x” but sell to physicians at “x minus y,” thereby granting a windfall gain to physicians—have been prosecuted aggressively. Similarly, causes of action based on concealment of best price (where manufactures do not report certain discounts to the states in connection with their best-price reporting obligations under Medicaid) have also been popular theories for prosecution.

Beyond ensuring the integrity of data generated and submitted for governmental reimbursement purposes, accurate compliance with the various programs requires attention to periodic filing and reporting requirements. Key federal programs that may require pharmaceutical manufacturers to submit price reporting data include the Medicaid Drug Program, Federal Upper Limit (applicable to multiple source drugs under Medicaid), Public Health Service Program, Federal Government Ceiling Price (applicable only to single source and innovator multiple source drugs), Medicare Part B, and Medicare Part D (outpatient drug program).

State Laws Relating to Sales and Marketing

A number of state legislatures have sought out new approaches to contain healthcare costs, track interactions between company employees and healthcare practitioners, and generally reduce healthcare fraud. It is estimated that, as of late 2008, at least 20 states had passed or were considering legislation affecting pharmaceutical or medical device company sales, marketing, and advertising activities. State-level efforts may require periodic disclosure of related payments to healthcare-provider customers or the adoption of compliance programs. Statutes adopted by California and Massachusetts offer two notable examples of schemes designed to both define the appropriate boundaries

and restrict the nature of industry relationships with healthcare-provider customers.

In California, a regulated company (which includes both pharmaceutical and medical device companies) must (i) adopt a “Comprehensive Compliance Program,” (ii) annually declare, in writing, that it is in compliance with both its “Comprehensive Compliance Program” and the statute, and (iii) make this declaration *and* its “Comprehensive Compliance Program” available to the public on the company’s website and via a toll-free telephone number.¹³⁹ The “Comprehensive Compliance Program” must be “in accordance with” the Office of the Inspector General’s “Compliance Program Guidance for Pharmaceutical Manufacturers.” Further, each company’s “Comprehensive Compliance Program” must establish policies designed to ensure compliance with the PhRMA Code. The California statute further requires that the “Comprehensive Compliance Program” include annual limits on the value of gifts or incentives that a regulated company may provide to a healthcare professional.

In March 2009, the Massachusetts Department of Public Health issued final regulations implementing its Pharmaceutical and Medical Device Manufacturer Conduct requirements.¹⁴⁰ These regulations make Massachusetts’ disclosure requirements the broadest and most stringent in the nation. The final regulations, among other things, require that regulated pharmaceutical and medical device manufacturers (i) establish a marketing code of conduct, (ii) set forth restrictions on the manufacturers’ ability to use non-patient-identified prescriber data, (iii) annually disclose compliance with the code of conduct, and (iv) annually disclose certain payments or other economic benefits provided to healthcare professionals and certain entities.

In addition to regulation at the state level, Congress is considering federal legislation that would establish a nationwide standard requiring pharmaceutical and medical device companies to publicly disclose information about their financial relationships with physicians. As currently drafted, the Physician Payment Sunshine Act of 2009 would apply to all manufacturers of drugs, devices, and biologicals for which payment may be made under Medicare,

Medicaid, or SCHIP, and would preempt some—but not all—state laws mandating reporting of financial relationships.¹⁴¹ If Congress enacts some version of the Sunshine Act, as many in the industry believe it will, the adopted legislation will potentially both simplify and complicate compliance efforts by affected companies. On one hand, the Sunshine Act offers the promise of a uniform national compliance standard. On the other hand, several features—such as the preemption provision, reporting thresholds and exclusions, and significant penalties for nondisclosure—may present considerable burdens for pharmaceutical and medical device companies.

C. Genetic Engineering

Laws and Regulations Affecting Finance

Regulation of Plant Pests and Noxious Weeds

The U.S. Department of Agriculture’s Animal and Plant Health Inspection Services (“APHIS”) is recommending changes to current biotechnology regulations.¹⁴² As it currently stands, APHIS regulates genetically engineered organisms and products that are (or are believed) to be plant pests.¹⁴³ The proposed regulatory changes would broaden the scope of APHIS’s regulatory reach to include (i) noxious weeds, (ii) non-plant, nonvertebrate organisms that pose a plant pest or noxious weed risk, and (iii) macroorganisms (e.g., insects) that are genetically engineered to control plant pests or noxious weeds.¹⁴⁴ The inclusion of noxious weeds into the scope of APHIS’s regulatory authority will include plants that pose risks similar to plant pests as well as plants that can cause harm to non-plant organisms, including humans.¹⁴⁵

Another important proposed change involves APHIS’s remedial and enforcement authority. Under the proposed rule change, those holding permits with respect to genetically engineered organisms would be required to maintain specific records relating to their permits and to allow APHIS to audit these records. Failure to abide by the new regulations could result in penalties ranging from the denial of future permits to the issuance of civil penalties.¹⁴⁶

The proposed regulations also include procedural measures, including revisions to the current permit and notification procedures, the permit procedures for environmental releases and the procedures to obtain nonregulated status and exemption from permit requirements.¹⁴⁷

Food Products Containing Genetically Engineered Animals

The FDA has recently made a series of proposals regarding the regulation of genetically engineered animals.¹⁴⁸ To begin, the FDA announced a proposal to regulate genetically engineered animals under the FDA's animal drug regulations.¹⁴⁹ The FDA also plans to regulate new animal drug applications under the Animal Drug User Fee Act ("ADUFA").¹⁵⁰ One goal of regulating animal drug applications under ADUFA is to increase revenue to the FDA with the hope of achieving more efficient regulatory reviews.¹⁵¹ Importantly, the FDA also made clear that it does not intend to require food products containing genetically engineered animals to be labeled as such.¹⁵²

Gene Therapy Products

In April 2008, the FDA published guidance setting standards for reviewers and sponsors of human gene therapy investigative new drug applications ("IND").¹⁵³ The new guidelines are only recommendations and are not legal enforceable obligations.¹⁵⁴ Nevertheless, the guidelines will assist sponsors of INDs to prepare a "submission that will be adequate to permit FDA reviewers to make an assessment of the safety, identity, purity, and potency of [the] investigational product."¹⁵⁵

International Issues

In response to the European Union's five-year moratorium on approving genetically engineered crops, the United States, among others, filed a complaint with the World Trade Organization ("WTO") against the EU in May 2003, alleging, generally, that the EU's ban was an improper barrier to trade.¹⁵⁶ More specifically, the U.S. maintained that the EU ban violated certain provisions of the Agreement on the Application of Sanitary and Phytosanitary

Measures (the “SPS Agreement”).¹⁵⁷ While setting forth basic rules for food safety and animal and plant health standards, the SPS Agreement allows countries to develop their own standards, so long as those standards are based on science.¹⁵⁸ In November 2006, the WTO issued its decision in respect to the complaint. While finding that the EU had caused “undue delay” in its approval procedures, the WTO dismissed the majority of the US’s allegations.¹⁵⁹

D. Stem Cells

Since 2005, there have been many changes in state and federal laws and policies regarding the extent of stem-cell research and public funding for this research. This debate rages on, particularly regarding the use of human embryos, resulting in a constantly shifting landscape of stem-cell policies, most notably at the state level. Certain states have aggressively encouraged research and public funding, while others have equally aggressively limited both. At the federal level, President Obama’s reversal of the Bush administration’s restrictions on federal funding of stem-cell research has received much recent attention.

Federal Policy

Federal stem-cell policy remains a politically divisive issue. The Obama administration moved quickly to reverse the previous restrictions on human stem-cell research and funding imposed by former President Bush’s administration, issuing Executive Order 13505 “*Removing Barriers to Responsible Scientific Research Involving Human Stem Cells*” on March 9, 2009. The executive order effectively permits federally funded researchers to work with human embryonic stem cells from a wide variety of sources, without the limitations imposed by former President Bush. As noted below, the National Institutes of Health issued final guidelines to implement the new executive order on July 7, 2009.

Additionally, with President Bush vetoing previous stem-cell research legislation, Congress is proposing corresponding legislation for President Obama’s executive order.¹⁶⁰

Minnesota

Stem cell research continues to be widely supported in Minnesota. While Minnesota law does not prohibit or restrict research on already existing stem cells, it does continue to prohibit the derivation of new stem cells from a living human embryo or fetus, and it imposes a criminal penalty for violations.¹⁶¹ This prohibition applies to research on any human organism conceived either in the human body or produced in an artificial environment other than the human body from fertilization through the first 265 days thereafter.¹⁶²

Legislation establishing a state policy for stem-cell research, authorizing the University of Minnesota to spend state appropriated funds on this research, and specifically permitting human embryonic cell research passed the Legislature in 2008, but was subsequently vetoed by Governor Pawlenty.¹⁶³ Minnesota continues to actively seek to provide a supportive environment for all types of biotechnology. Although there is no specific state funding for stem-cell research, the Minnesota Department of Employment and Economic Development can provide guidance on the resources, financial and otherwise, that are available to Minnesota businesses.

Other States

Since 2005, a number of states have implemented programs designed to fund and promote stem-cell research. Given the current worldwide economic climate and subsequent impact on state budgets, a number of these programs may be faced with less funding than originally anticipated or potential outright termination. In addition, several states have attempted to enact legislation to enhance the level of state promotion of stem-cell research, but have not yet been successful.

The following is a selection of state programs for stem-cell research and funding.

California. Despite the current budget hardships facing the state of California, the California Institute of Regenerative Medicine (“CIRM”), which administers the state stem-cell

research program, has approved 279 grants totaling more than \$693 million since CIRM's establishment in 2005 after the passage of Proposition 71. CIRM's stated goal of distributing \$3 billion by 2015 makes it the largest source of funding for embryonic and pluripotent stem-cell research in the world.¹⁶⁴

Connecticut. On June 15, 2005, the Governor of Connecticut signed legislation providing \$100 million over 10 years for human embryonic stem-cell research.¹⁶⁵ In 2006, the Stem Cell Research Advisory and Peer Review Committees awarded almost \$19.8 million for 21 stem-cell research proposals; 2007 resulted in \$9.84 million for 22 stem-cell research proposals; and in 2008, \$9.8 million was awarded for 24 stem-cell research proposals.¹⁶⁶

Illinois. Former Governor Blagojevich signed an executive order in 2005 creating the Illinois Regenerative Medicine Institute ("IRMI") and providing for grants to medical research facilities for adult and embryonic stem-cell research.¹⁶⁷ This included transferring \$10 million to this new program, the first grants from which were awarded in April 2006. An additional \$5 million was awarded in August 2006.¹⁶⁸ The Illinois legislature passed a bill in August 2007 permitting IRMI to conduct stem-cell research on cells from any source and authorizing public funding.¹⁶⁹

Maryland. In 2006, the Maryland legislature created the Maryland Stem Cell Research Fund, which provides grants for adult and embryonic stem-cell research. Over \$36 million and 82 research applications have been funded in the first two years, with a budget of \$18 million for the third year.¹⁷⁰

Massachusetts. The Massachusetts Life Science Center, a quasi-public agency of the state created by the legislature in 2006,¹⁷¹ has responsibility for implementing the Massachusetts Life Sciences Act, a ten-year, \$1 billion initiative signed by Governor Patrick in 2008. Of the total appropriation, \$500 million is earmarked for the Massachusetts Life Sciences Investment Fund, \$250 million for the award of grants, and \$250 million in tax credits.¹⁷² This funding may support stem-cell research.

Michigan. Proposal 2, a state constitutional amendment approved by Michigan voters in the November 4, 2008 general election, overturned a 1978 Michigan law that prohibited creation of new stem-cell lines from discarded embryos. The amendment took effect December 19, 2008. Prior to passage of Proposal 2, Michigan was one of the most restrictive states in the country with respect to embryonic stem-cell research.¹⁷³

New Jersey. New Jersey continued to advance its stem-cell research and funding initiatives, with the legislature's approval in 2006 of \$270 million to build research facilities for the Stem Cell Institute of New Jersey.¹⁷⁴ A \$450 million bond referendum to finance stem-cell research was rejected by voters in 2007, however, which resulted in placing plans to build the facilities for the Stem Cell Institute on hold.¹⁷⁵ The current economic conditions have also resulted in a reduction in available stem-cell research funding.¹⁷⁶

New York. The 2007 legislature created the Empire State Stem Cell Trust and Empire State Stem Cell Board to collect and distribute grants in support of stem-cell research. A total of \$100 million was earmarked for 2007, and \$500 million was earmarked at \$50 million per year for ten years beginning in 2008. The program specifically prohibits grants for research involving human reproductive cloning.¹⁷⁷

Washington. The Washington legislature created the Life Sciences Discovery Fund in 2005, which is authorized to distribute up to \$350 million over ten years for a wide range of "life sciences research," including embryonic stem-cell research.¹⁷⁸

Virginia. The Virginia legislature has created a fund to support adult stem-cell research only. In March 2009, Governor Kaine signed a bill containing language inserted by the General Assembly that would prevent a state fund from providing funds to organizations or businesses that undertake "research in Virginia on human cells or tissue derived from induced abortions or from stem cells obtained from human embryos."¹⁷⁹

While permitting stem cell research, several states place research restrictions on the use of aborted embryos and fetuses. For example, Minnesota law prohibits the use of any human organism,

conceived in the human body or produced in an artificial environment, for any type of scientific research or experimentation from the moment of fertilization through the following 265 days.¹⁸⁰ Violation of this statute is a gross misdemeanor.¹⁸¹ This provision of Minnesota law is significant because, as discussed above, Minnesota law does not otherwise expressly permit or prohibit embryonic stem cell research.

Similarly, while embryonic stem cell research is generally permitted in Illinois, Illinois law prohibits the use of any living or non-living human fetus or embryo resulting from an induced abortion.¹⁸² California has similar prohibitions.¹⁸³

Current Trends

Although President Obama's reversal of the Bush administration's restrictions has been widely applauded by the scientific community, the actual impact of this reversal has yet to be fully determined, as the NIH recently issued final regulations implementing federal funding. The final regulations, "The National Institutes of Health Guidelines For Human Stem Cell Research," were published in the Federal Register on July 7, 2009 and can be found in their entirety at 74 Fed. Reg. 32170 (July 7, 2009). Nevertheless, the availability of federal funds for an expanded level of stem-cell research activities should result in a significant increase in the overall level of stem-cell research funding.

Many states have leapt at the opportunity to fund stem-cell research in order to establish a national presence as a biotechnology industry leader. These programs have had varying degrees of success, and given the current economic conditions, many states are encountering difficulty in continuing to fund these programs. When combined with the change in federal policy regarding stem-cell research, it remains to be seen the extent to which state stem-cell research programs remain a focus for limited state budgets.

E. Cloning

Animal cloning does not involve genetic modification. In effect, it produces "twins" rather than altered or modified animals. So while it is clear that cloning is the result of advanced technology, because no genetic modification is involved, cloning is arguably not

“biotechnology.” Because it is often considered alongside many of the concepts covered by biotechnology, however, a brief discussion of it is warranted in this *Supplement*.

Cloning of Humans

Human cloning remains a highly controversial subject to many people in America. While many groups advocate a ban on reproductive cloning of human beings, others strongly advocate the potential of therapeutic cloning. To many, therapeutic cloning holds the promise of developing methods to produce genetically identical cells, tissues, and organs for regenerative therapies. Advocates believe that therapeutic cloning may lead to development of many regenerative therapies potentially including those for Alzheimer’s and Parkinson’s diseases.

The United States House of Representatives voted on bills to adopt a ban on all human cloning in 1998,¹⁸⁴ 2001,¹⁸⁵ 2003,¹⁸⁶ and 2007.¹⁸⁷ Each one of these bans would have covered both reproductive cloning and therapeutic cloning and, widespread support among a number of members of Congress for therapeutic cloning resulted in the eventual defeat of each of these efforts.

Agricultural Cloning

Cloning of plants and animals for agricultural use has faced very different receptions throughout the world. While cloning animals for agricultural use has faced multiple levels of opposition, plant cloning has been common for years. Vegetative propagation is used in the cultivation of many species of plants including grass, strawberries, and potatoes. This area is largely unregulated.

With respect to the cloning of animals for agricultural use, scientific developments in this area have outpaced social acceptance. In 2001, the FDA published a request that animal clones and their offspring be kept off of the market until that agency had a chance to evaluate whether cloning posed risks to the food supply. Although this moratorium was voluntary, it was widely accepted by the industry and most cloned animals and their offspring were kept away from the market.

In December 2006, the FDA published its preliminary findings that

cloned meat and dairy were safe for human consumption and posed no significant health risks.¹⁸⁸ The FDA statement was based on a review of more than 100 scientific studies conducted on the safety of cloned agricultural products. On January 15, 2008, the FDA published a final assessment stating that meat and milk from the clones of cattle, swine, and goats and their offspring were as safe to eat as meat and milk from conventionally bred animals.¹⁸⁹ On the same day, the USDA issued a statement supporting the findings of the FDA.¹⁹⁰

The voluntary moratorium that the FDA requested in 2001 was partially lifted following the publication of the risk assessment,¹⁹¹ and no longer applied to the progeny of cloned animals. Cloned animals, themselves, are generally expensive to produce. It is unlikely that they would be headed to market because of this fact. The sexually produced offspring of these cloned animals could now, however, legally and practically, be sent to the market.

The USDA has struggled with how and whether to label these meat and dairy products. The meat and dairy products of cloned animals and their offspring cannot be labeled as “organic,”¹⁹² regardless of whether they satisfy the other criteria required for that designation. There is a further movement, however, to require that all meat and dairy derived from cloned animals or their progeny be specifically labeled as derived from cloned animals. Although this question has not yet been resolved on the national level,¹⁹³ several states have proposed statutes and regulations regarding the labeling of meat and dairy from cloned animals and their offspring.¹⁹⁴

Effects on Corporate Finance

Regenerative therapies hold significant potential, but face obstacles in many states. It is also possible, based on previous efforts, that a movement at the federal level could impede the progress of their development. Each of these risks will have an effect and must be considered in the analysis of any related corporate finance project.

Proponents of cloned meat and dairy products have made progress, including obtaining endorsements by both the FDA and USDA. These products are still not widely accepted by the marketplace or the general public. Investors in this area must be sensitive to both the remaining legal hurdles and those hurdles associated with this public sentiment.

GLOSSARY OF DEFINED TERMS

AKL	The Federal Health Care Program Anti-Kickback Act
APHIS	Animal and Plant Health Inspection Service
ADUFA	Animal Drug User Fee Act
Cartagena Protocol	Cartagena Protocol on Biosafety
CBP	Customs and Border Protection (formerly U.S. Customs Service)
CEO	Chief Executive Officer of the company
CFO	Chief Financial Officer of the company
Code	Internal Revenue Code of 1986, as amended
Codex Guidelines	Codex Guidelines on Food Derived From Biotechnology
DCL	descarboethoxyloratadine
DEED	Department of Employment and Economic Development for the State of Minnesota
Directive 2001/18	Directive 2001 /18 /EC of the European Parliament and of the Council on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90 / 220 / EEC
DNA	deoxyribonucleic acid
DOJ	Department of Justice
DRG	Diagnostic Related Group
EGTRRA	Economic Growth and Tax Relief Reconciliation Act of 2001
EPA	Environmental Protection Agency
EPO	European Patent Office
ERISA	Employee Retirement Income and Security Act
EU	European Union
Exchange Act	Securities Exchange Act of 1934, as amended
FDAAA	Food and Drug Administration Amendments Act
FCPA	Foreign Corrupt Practices Act
FDA	Food and Drug Administration
GAAP	Generally accepted accounting principles
GM	genetically modified
GMO	genetically modified organisms
HHS	Department of Health and Human Services
IND	Investigational New Drug
IPO	initial public offering
IRS	Internal Revenue Service
LLC	limited liability company
M&A	mergers and acquisitions
MD&A	Management's Discussion and Analysis of Financial Condition and Results of Operations

NASDAQ	National Association of Securities Dealers Automated Quotations
NDA	Nondisclosure Agreement
NIH	National Institutes of Health
NOL	net operating loss
NYSE	New York Stock Exchange
PIPE	private investment in public equity
QLCC	Qualified Legal Compliance Committee
RAC	Recombinant DNA Advisory Committee
REMS	risk evaluation and mitigation strategies
R&D	research and development
Regulation 1830/2003	Regulation (EC) No. 1830 of the European Parliament and of the Council of the European Union, of 22 September 2003, concerning the traceability and labeling of genetically modified organisms and the traceability of food and feed products produced from genetically modified organisms and amending Directive 2001 /18/EC
Sarbanes-Oxley	Sarbanes-Oxley Act of 2002
SBA	U.S. Small Business Administration
SBIR	Small Business Innovation Research Program
SEC	Securities and Exchange Commission
Section 363	Section 363 of the Bankruptcy Code
Section 409A	Section 409A of the Internal Revenue Code
Securities Act	Securities Act of 1933, as amended
STTR	Small Business Technology Transfer Program
TRIPS Agreement	Trade-Related Aspects of Intellectual Property Agreement
TSCA	Toxic Substances Control Act
UCC	Uniform Commercial Code of any relevant state, as amended
U.S.	United States of America
USDA	U.S. Department of Agriculture
USPTO	U.S. Patent and Trademark Office
VC	venture capital
WTO	World Trade Organization

Endnotes

- ¹ 2008 MoneyTree Report, *available at* www.pwcmoneytree.com (last visited June 12, 2009).
- ² *Id.*
- ³ Pub. L. No. 107-204, 116 Stat. 745 (2006).
- ⁴ U.S. CONST. art. I, § 8, cl. 8 (“The Congress shall have the power...[t]o promote the progress of science and the useful arts, by securing for limited times to authors and inventors the exclusive right to their respective writings and discoveries[.]”).
- ⁵ The statutory patent system is set forth in the U.S. Patent Act, 35 U.S.C. § 101 (2006). Copyrights are governed by the Copyright Act of 1976, as amended, 17 U.S.C. § 101 (2006). Some states have “inventor” statutes to protect employees from unknowingly surrendering to their employer ownership rights to personal inventions. *See, e.g.*, MINN. STAT. § 181.78 (2006).
- ⁶ The federal trademark statute is the Trademark Act of 1946 (commonly referred to as “the Lanham Act”), as amended, 15 U.S.C. § 1051 (2006). This arises under the Commerce Clause of the U.S. CONST. art. I, § 8, cl. 3. All 50 states have adopted trademark registration statutes. Trademark rights also may be acquired and protected in the United States as a matter of common law.
- ⁷ Although 43 states, including Minnesota, have adopted the Uniform Trade Secrets Act, some have modified the statute with language that may be significant in individual cases.
- ⁸ *See* note 95 *infra* and accompanying text discussing Wyeth Laboratories secret process for manufacturing PREMARIN®.
- ⁹ A well-known example is NUTRASWEET® artificial sweetener, which remains a vital brand name nearly a decade after the patent in the chemical formulation went into the public domain.
- ¹⁰ 35 U.S.C. § 101 (2006).
- ¹¹ § 161.
- ¹² § 171.
- ¹³ § 154.
- ¹⁴ § 154(c)(1).
- ¹⁵ § 173.
- ¹⁶ § 101.
- ¹⁷ § 102.
- ¹⁸ *Id.*
- ¹⁹ § 101; *Brenner v. Manson*, 383 U.S. 519, 534-35 (1966).
- ²⁰ § 112.
- ²¹ § 102.
- ²² § 102(b).
- ²³ § 103.
- ²⁴ *Schering Corp. v. Geneva Pharm., Inc.*, 339 F.3d 1373, 1379 (Fed. Cir. 2003) (*quoting* *Eli Lilly & Co. v. Barr Labs.*, 251 F.3d 955, 970 (Fed. Cir. 2001)).
- ²⁵ *Id.* at 1378.
- ²⁶ HERBERT F. SCHWARTZ, *PATENT LAW AND PRACTICE* 68-69 (4th ed. 2003).

27 1 DONALD S. CHISUM, CHISUM ON PATENTS § 3.03 at 67 (2003).
28 *Id.*
29 102 U.S. 707 (1881).
30 339 F.3d 1373 (2003).
31 *Id.* at 1375.
32 The Federal Circuit has exclusive jurisdiction over patent appeals.
33 *Schering Corp.*, 339 F.3d at 1378-79.
34 *Id.* at 1377.
35 *Id.* at 1378.
36 Anne Brown & Mark Polyakov, Remarks at the Third Advanced Forum on
Biotech Patents: The Tactical and Practical Guide to Today's Most Complex
Issues, Boston, MA: The Accidental and Inherent Anticipation Doctrines:
Where Do We Stand and Where Are We Going? (Mar. 30, 2004).
37 550 U.S. 398 (2007).
38 561 F.3d 1351 (Fed. Cir. 2009).
39 51 F.3d 1552 (Fed. Cir. 1995).
40 *Elkay Mfg. v. Ebco Mfg.*, 192 F.3d 973 (Fed. Cir. 1999).
41 *Graver Tank & Mfg. v. Linde Air Products*, 339 U.S. 605 (1950).
42 547 U.S. 388 (2006).
43 275 F.Supp. 2d 695, 712 (E.D. Va. 2003).
44 401 F.3d 1323, 1339 (Fed. Cir. 2005).
45 547 U.S. at 391.
46 *Id.* at 393.
47 549 U.S. 437 (2007).
48 547 U.S. 28 (2006).
49 *Id.* at 45.
50 *Id.* at 43-44.
51 550 U.S. 437 (2007).
52 497 F.3d 1360 (Fed. Cir. 2007).
53 545 F.3d 943 (Fed. Cir. 2008).
54 *In re Ferguson*, 558 F.3d 1359 (2009).
55 499 F.3d 1365, *rev'd en banc*, 554 F.3d 967 (Fed. Cir., Jan. 13 2009).
56 *Quanta Computer, Inc. v. LG Elecs., Inc.*, 128 S.Ct. 2109 (2008).
57 *Id.* at 2122.
58 545 U.S. 193 (2005).
59 35 U.S.C. § 271(e)(1) (2006).
60 447 U.S. 303 (1980).
61 MANUAL OF PATENT EXAMINING PROCEDURE § 2105 (8th ed. 2008).
62 *Id.*
63 *Id.*
64 *Lowell v. Lewis*, 15 F.Cas. 1018, 1019 (C.C. Mass 1817).
65 Convention on the Grant of European Patents, Oct. 5, 1973, Munich, Article
52(1).
66 WTO Agreement on Trade-Related Aspects of Intellectual Property Rights.
67 *Ex parte Harvard*, Case V-6/92, 1992 O.J. E.P.O. 589 at Part 2 (Examining
Div. 1992).
68 35 U.S.C. §§ 200-212 (2006).
69 35 U.S.C. § 154 (2005).

70 28 U.S.C. § 1498(a) (2006).
71 Patents Act of 1977, §§ 55-59.
72 *Madey v. Duke Univ.*, 307 F.3d 1351 (Fed. Cir. 2002).
73 17 U.S.C. § 102(a) (2006).
74 § 102(b).
75 § 302(a).
76 § 302(c).
77 § 411(a).
78 § 401(a).
79 15 U.S.C. § 1127 (2006).
80 *Id.*
81 § 1051(a)(1).
82 § 1072.
83 § 1057(b).
84 § 1065.
85 § 1111.
86 § 1124.
87 § 1117.
88 As will be discussed in more detail *infra*, “PREMARIN®” may arguably be
characterized as “suggestive.”
89 *See, e.g.*, MINN. STAT. § 325C.01 (2004).
90 RESTATEMENT (FIRST) OF TORTS § 757 cmt. b (1939).
91 *Id.*
92 In *Mangren Research & Development Corp. v. National Chemical Co.*,
87 F.3d 937 (7th Cir. 1996), the valuable trade secret was routine use of a
chemical component widely regarded in the industry as unsuited for the
very application for which it was used.
93 No. Civ. 98-2469, 2003 WL 22282371 (D. Minn. Oct. 2, 2003)
(unpublished opinion), *aff’d* by 395 F.2d 897 (8th Cir. 2005).
94 Although, technically, “foreclosure” relates to real estate and “replevin” is
the term relating to recovery of personal property by a lender, “foreclosure”
is widely used to reference both scenarios.
95 Testimony of Ben S. Bernanke before the House Committee on the Budget,
June 3, 2009, *available at* [http://www.federalreserve.gov/newsevents/
testimony/bernanke20090603a.htm](http://www.federalreserve.gov/newsevents/testimony/bernanke20090603a.htm).
96 *See supra* Part V.B.
97 *See generally* U.S. Department of Agriculture, *Roles of U.S. Agencies: U.S.
Department of Agriculture (USDA) Animal and Plant Health Inspection
Services (APHIS)*, *available at* <http://usbiotechreg.nbio.gov/roles.asp>
(discussing U.S. agencies’ responsibility concerning bioengineered foods,
presented through a joint effort of the FDA, EPA, and USDA. *See a more
detailed discussion of the FDA examination and approval processes in infra*
Part V.B).
98 7 C.F.R. § 340.3 (2004) (discussing notification for the introduction of
certain regulated articles).

⁹⁹ For example, the term “stably integrated” is covered in the relevant regulation as a demonstrable standard, namely that “[t]he cloned genetic material is contiguous with elements of the recipient genome and is replicated exclusively by mechanisms used by recipient genomic DNA,” but many of the terms are yet to be standardized. § 340.1.

¹⁰⁰ FIFRA was essentially rewritten in 1972 when it was amended by the Federal Environmental Pesticide Control Act (FEPCA). The law has been amended numerous times since 1972, including some significant amendments in the form of the Food Quality Protection Act (FQPA) of 1996. In its current form, FIFRA mandates that EPA regulate the use and sale of pesticides to protect human health and preserve the environment. See EPA website for details at www.epa.gov.

¹⁰¹ 15 U.S.C. § 2601 (2008).

¹⁰² See the EPA website for details on regulations and practices at <http://www.epa.gov>.

¹⁰³ 15 U.S.C. § 2611 (2006).

¹⁰⁴ The several agencies and departments that list prohibited persons, companies and countries publish their respective lists, which unfortunately are not available in one place. Please check with your legal advisors regarding the current lists, but generally at least the following website should be consulted: http://www.customs.gov/xp/cgov/export/persons_list/. This website provides links to the appropriate lists from the Bureau of Industry and Security the Office of Foreign Assets Control, and the Office of Defense Trade Controls.

¹⁰⁵ Robbin Shoemaker et al., *Economic Issues in Agricultural Biotechnology*, ECON. RES. SERVICE AGRIC. INFO. BULL. No. AIB762 28-35 (2001) (available at <http://www.ers.usda.gov/publications/aib762>).

¹⁰⁶ *Id.*

¹⁰⁷ Curtis, K.R., McCluskey, J.J., & Wahl, T.I. (2004). Consumer acceptance of genetically modified food products in the developing world. *AgBioForum*, 7(1&2), 70-75. Available at: <http://www.agbioforum.org/v7n12/v7n12a13-mccluskey.htm> or <http://www.agbioforum.org/v7n12/v7n12a13-mccluskey.pdf>.

¹⁰⁸ Mystery Bridgers, *Genetically Modified Organisms and the Precautionary Principal: How the GMO Dispute Before the WTO Could Decide the Fate of International GMO Regulation*, 22 TEMP. ENVTL. L. & TECH. J. 171, 172 (2004).

¹⁰⁹ Parliament Directive 2001/18/EC, Official Journal L 106/1, 2, 4.

¹¹⁰ Bridgers, *supra* note 108 at 179.

¹¹¹ *Id.*; see also *Genetic Engineering; Traceability of Genetically Modified Organisms in the Food Chain Discussed*, GENOMICS & GENETICS WKLY, Aug. 20, 2004, at 73 (discussing a new package of legislation that would make the labeling requirement more cumbersome).

- ¹¹² See EurActiv.com, Commission Warns Five Member States to Lift GMO Bans or Face Legal Action (April 27, 2005), *available at* <http://www.euractiv.com/en/biotech/commission-warns-member-states-lift-gmo-bans-face-legal-action/article-138638> (including a note that the European Health and Consumer Commissioner suggested that the U.S. should adopt a system similar to that of the EU on labeling and traceability).
- ¹¹³ Press Release, European Union, *Commission Requires Certification of U.S. Exports to Stop Unauthorized GMO from Entering the EU* (April 15, 2005), *available at* <http://www.eurunion.org/News/press/2005/2005038.htm>; *see also: Germany Bans Genetically Modified Corn*, New York Times (April 14, 2009), *available at* <http://www.nytimes.com/2009/04/15/business/global/15gmo.html> : (providing a more recent example).
- ¹¹⁴ Cartagena Protocol on Biosafety to Convention on Biological Diversity, opened for signing, January 29, 2000, 39 I.L.M. 1027 (entered into force September 11, 2003).
- ¹¹⁵ See the website of Convention on Biological Diversity www.cbd.int.
- ¹¹⁶ *Id.* at art. 8, para.1; *Id.* at Annex I.
- ¹¹⁷ *Id.* at 7 art. 9; 8 art.10, para. 6; 10 art. 12 (noting that any rejection must be based on scientific findings).
- ¹¹⁸ *See* <http://bch.biodiv.org>.
- ¹¹⁹ *Id.*
- ¹²⁰ Issued by CODEX Alimentarius, which was created in 1963 under the auspices of the United Nations' World Health Organization and Food and Agriculture Organization. The official website of the CODEX is http://www.codexalimentarius.net/web/index_en.jsp.
- ¹²¹ Daniel M. Krainin, *Biotech Crops, Biosafety Protocol: Genetically Modified Sustainability?*, NAT. RESOURCES & ENV'T 63, 67 (2004).
- ¹²² John Charles Kunich, *Mother Frankenstein, Doctor Nature and the Environmental Law of Genetic Engineering*, 74 S. CAL. L. REV. 857-858 (Mar. 2001)
- ¹²³ Food & Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, 121 Stat. 823 (2007).
- ¹²⁴ Food, Drug & Cosmetic Act, 21 U.S.C. §§ 355, 505(a), 502(0), 501(f)(1)(B), 301(a),(d); 352(0), 351(f)(1)(B), 331(a),(d).
- ¹²⁵ §§ 505(a), 301(d), 355(a), 331(d).
- ¹²⁶ §§ 502(f), 352(f); 21 CFR § 201.100(c)(1) (2006).
- ¹²⁷ *See* FDA Guidance for Industry.
- ¹²⁸ Press Release, Department of Justice, Eli Lilly and Company Agrees to Pay \$1.415 Billion to Resolve Allegations of Off-label Promotion of Zyprexa (January 15, 2009), *available at* <http://www.usdoj.gov/opa/pr/2009/January/09-civ-038.html>.
- ¹²⁹ Press Release, United States Attorney's Office, Eastern District of New York, Quest Diagnostics Incorporated to Pay \$302 Million to Resolve Allegations That a Subsidiary Sold Misbranded Test Kits (Apr. 15, 2009), *available at* <http://www.usdoj.gov/usao/nye/pr/2009/2009apr15b.html>).

- 130 Press Release, U.S. Food and Drug Administration, FDA Obtains Permanent Injunction Barring Two Companies from Manufacturing and Distributing Unapproved Drugs, (Apr. 16, 2009), *available at* <http://www.fda.gov/bbs/topics/new01995.html>.
- 131 Press Release, U.S. Attorney’s Office, Eastern District of New York, Psychiatrist Charged with Conspiracy to Illegally Market the Prescription Medication Xyrem, Also Known as “GHB,” For Unapproved Medical Uses on Behalf of its Manufacturer (Apr. 5, 2006), *available at* <http://www.usdoj.gov/usao/nye/pr/2006/2006apr05.html>.
- 132 <http://www.usdoj.gov/usao/hye/2007/2007jul13a/html>
- 133 42 U.S.C. § 1320a-7b (2006).
- 134 Press Release, U.S. Department of Justice, Medco to Pay U.S. \$155 Million to Settle False Claims Act Cases (Oct. 23, 2006), *available at* http://www.usdoj.gov/opa/pr/2006/October/06_civ_722.html.
- 135 *See, e.g.*, FLA. STAT. ANN. § 817.505 (2009).
- 136 42 U.S.C. § 1395nn (2006).
- 137 Office of the United States Attorney, Southern District of Illinois, Augustine Medical Sentenced to \$5,249,910 Fine (Sep. 8, 2005), *available at* <http://www.integriguard.org/corp/newsevents/pressreleases/2004/2004-09-08.html>.
- 138 *See* SSA §§ 1860D-2(d)(2), -15(b)(2) and -15(e)(1)(B) (as added by the MMA) (*codified at* 42 U.S.C. §§ 1395w-102(d)(2), -115(b)(2), and -115(e)(1)(B) (2006)).
- 139 CAL. HEALTH & SAFETY CODE § 119402.
- 140 105 CMR 970.000 et seq. (2009).
- 141 H.R. Rep. No. 5605, 110th Cong. (2008).
- 142 APHIS Fact Sheet, Biotechnology Regulatory Services, October 2008; Importation, Interstate Movement, and Release Into Environment of Certain Genetically Engineered Organisms, 73 Fed. Reg. 60008 (proposed Oct. 9, 2008) (to be codified at 7 C.F.R. pt. 340).
- 143 7 C.F.R. § 340 (2005).
- 144 Importation, Interstate Movement, and Release Into Environment of Certain Genetically Engineered Organisms, 73 Fed. Reg. at 60,011.
- 145 *Id.* at 60,012.
- 146 *Id.* at 60,024.
- 147 *Id.*
- 148 13 DRAKE J. AGRIC. L. 457, 469 (2008).
- 149 *Id.*
- 150 *Id.* at 470.
- 151 *Id.* at 471.
- 152 *Id.* at 472.
- 153 FDA, Guidance for FDA Reviewers and Sponsors: Content and Review of Chemistry, Manufacturing, and Control (CMC) Information for Human Gene Therapy Investigational New Drug Applications (INDs) (Apr. 2008) at 1, *available at* <http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/CellularandGeneTherapy/ucm072587.htm>.
- 154 *Id.*

155 *Id.*
156 45 AM. BUS. L. J. 775, 775 (2008).
157 41 N.Y.U. J. INT’L L. & POL. 1, 27-28 (2008).
158 Agreement on the Application of Sanitary and Phytosanitary Measures,
available at http://www.wto.org/english/tratop_e/sps_e/sps_agreement_cbt_e/c1s1p1_e.htm.
159 45 AM. BUS. L. J. at 786; N.Y.U. J. INT’L L. & POL. At 29-30.
160 <http://stemcells.nih.gov/policy/legislation>.
161 MINN. STAT. § 145.422 (2005).
162 MINN. STAT. § 145.421 (2009) *see note* 175, *infra*, and corresponding text
163 https://www.revisor.leg.state.mn.us/revisor/pages/search_status/status_detail.php?b=Senate&f=SF0100&ssn=0&y=2007.
164 <http://www.cirm.ca.gov/>.
165 Conn. Gen. Stat. §§19a-32d - §19a-32g; §4-28e(c)(3) (Supp. 2006); *see also* <http://www.iascr.org/docs/CT-Apr2008.pdf>.
166 Connecticut Department of Public Health, Stem Cell Research Program—Grants (Apr. 16, 2009), <http://www.ct.gov/dph/cwp/view.asp?a=3142&q=389700>.
167 <http://www.idph.state.il.us/irmi/index.html>.
168 *Id.*
169 Stem Cell Research and Human Cloning Prohibition Act, 410 ILL. COMP. STAT. 110/1 (2008).
170 <http://www.mscref.org/>.
171 MASS. GEN. LAWS ch. 23I (2009).
172 2008 Mass. Acts ch. 130.
173 <http://www.umich.edu/stemcell/>.
174 Adrienne Lu, *Budget Cuts Endanger Stem-cell Research in N.J.*, PHILADELPHIA ENQUIRER, Mar. 4, 2009.
175 *Id.*
176 *Id.*
177 Press Release, Lieutenant Governor David Patterson, A New Stem Cell Research Fund, (May 8, 2008), *available at* http://www.ny.gov/governor/press/lt_stemcell.html.
178 <http://www.lsdfa.org/home.html>.
179 Peter Hamby, *Kaine Blocks Funding for Embryonic Stem Cell Research*, CNN POLITICAL TICKER, Mar. 31, 2009, <http://politicalticker.blogs.cnn.com/2009/03/31/kaine-blocks-funding-for-embryonic-stem-cell-research/>.
180 Minn. Stat. §§ 145.421-422 (2009).
181 § 145.422.
182 720 ILL. COMP. STAT. 510/6-12.1 (2009); 410 ILL. COMP. STAT. 110/1, et. seq.
183 CALIFORNIA HEALTH AND SAFETY § 123440 (2009) (making it “unlawful for any person to use any aborted product of human conception, other than fetal remains, for any type of scientific or laboratory research or for any other kind of experimentation or study, except to protect or preserve the life and health of the fetus.”); *see* CALIFORNIA CONST. art. 35 (establishing the California Institute for Regenerative Medicine and permitting stem cell research).

184 Human Cloning Prohibition Act, S. 1599, 105th Cong. (1998).
185 Human Cloning Prohibition Act, H.R. 2505, 107th Cong. (2001)
186 Human Cloning Prohibition Act, H.R. 534, 108th Cong. (2003).
187 Human Cloning Prohibition Act, H.R. 2560, 110th Cong. (2007).
188 Center for Veterinary Medicine, United States Food & Drug Administration,
Department of Health and Human Services, *Proposed Risk Management
Guide*, Dec. 28, 2006; Center for Veterinary Medicine, United States Food
& Drug Administration, Department of Health and Human Services, Draft
Risk Assessment, December 28, 2006.
189 See Center for Veterinary Medicine, United States Food & Drug
Administration, Department of Health and Human Services, *Animal
Cloning: Risk Management Plan for Clones and their Progeny*, Jan. 8,
2008, [http://www.fda.gov/AnimalVeterinary/SafetyHealth/AnimalCloning/
ucm055490.htm](http://www.fda.gov/AnimalVeterinary/SafetyHealth/AnimalCloning/ucm055490.htm); Center for Veterinary Medicine, United States Food
& Drug Administration, Department of Health and Human Services,
Animal Cloning: A Risk Assessment, Jan. 8, 2008, [http://www.fda.
gov/AnimalVeterinary/SafetyHealth/AnimalCloning/ucm055489.
htm](http://www.fda.gov/AnimalVeterinary/SafetyHealth/AnimalCloning/ucm055489.htm); Center for Veterinary Medicine, *Guidance for Industry #179: Use
of Animal Clones and their Progeny for Human Food/Animal Feed*,
Jan. 15, 2008, [http://www.fda.gov/downloads/AnimalVeterinary/
GuidanceComplianceEnforcement/GuidanceforIndustry/UCM052469.pdf](http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM052469.pdf).
190 Press Release, USDA, Statement by Bruce Knight, Under Secretary for
Marketing and Regulatory Programs on FDA Risk Assessment on Animal
Clones (Jan. 15, 2008), available at [http://www.usda.gov/wps/portal/!ut/p
/_s.7_0_A/7_0_1OB?contentidonly=true&contentid=2008/01/0012.xml](http://www.usda.gov/wps/portal/!ut/p/_s.7_0_A/7_0_1OB?contentidonly=true&contentid=2008/01/0012.xml).
("USDA fully supports and agrees with FDA's final assessment that meat
and milk from cattle, swine and goat clones pose no safety concerns, and
these products are no different than foods from traditionally bred animals.")
191 Press Release, USDA, FDA's Final Risk Assessment, Management Plan
and Industry Guidelines on Animal Clones and their Progeny, (Jan. 2008),
available at [http://www.usda.gov/wps/portal/usdahome?contentidonly=true
&contentid=2008/01/0011.xml](http://www.usda.gov/wps/portal/usdahome?contentidonly=true&contentid=2008/01/0011.xml).
192 Press Release, USDA, Agricultural Marketing Service (Jan. 31, 2007)
(agency which administers the National Organic Program, stating that food
products from animal clones cannot be considered organic).
193 As of May 2009, the FDA has declined to issue labeling guidelines for food
derived from cloned animals or their progeny.
194 For example, the California Cloned Food Labeling Act was passed
by the California House and Senate in 2007, but was vetoed by Gov.
Schwarzenegger. See Cloned Food Labeling Act, S. 63 (Ca. 2007),
available at [http://info.sen.ca.gov/pub/07-08/bill/sen/sb_0051-0100/sb_63_
bill_20070116_introduced.html](http://info.sen.ca.gov/pub/07-08/bill/sen/sb_0051-0100/sb_63_bill_20070116_introduced.html). Similar bills have been proposed in other
states, including Kentucky, Tennessee and New Jersey.



Printed on Recycled Paper with a
Minimum of 10% post consumer waste

ISBN 1-888404-40-X

positively Department of Employment
and Economic Development
Minnesota