Chapter One

Introduction to Biotechnology and the Law

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Since we first published *Biotechnology and the Law*, many things have changed, but the basics have remained. Technology, or "tech," still is a driving force in our culture and economy and will be for the foreseeable future. Beginning in the late 1950s with the development of television, the invention of the transistor, and the launch of Russian satellite Sputnik, and extending to today, Americans evolved into a culture of technophiles. We drank Tang instant breakfast drink (supposedly a mainstay of the astronauts) while watching Walter Cronkite count down the minutes to the next nail-biting space launch. We listened to major news and sporting events, such as the Cassius Clay/Sonny Liston title fight, on our miniature transistor radios. Even our automobiles took on design elements of jet airplanes and rocket ships.

During this same time frame, advances in health care also leapt into our lives. The mass production of vaccines and the inoculation of millions of schoolchildren put to an end many devastating diseases that ravaged the previous generations. We witnessed the first heart transplant, now a common occurrence. Increased medical sophistication gave women a new level of reproductive and economic freedom. It is no wonder that we began to believe in better living through chemistry.

These technological advances were, at least in part, driven by two foundational scientific events that foretold the future of the tech culture and the tech economy. The first was Bell Labs' invention of the transistor, which resulted in a Nobel Prize for the research team in 1956. That simple, almost inert, replacement for the vacuum tube was the initial and necessary step that made possible powerful microprocessors, each containing millions of circuits. Increasingly smaller chunks of silicon and copper, in turn, led to the development of the modern computer, the creation of the Internet, the invention of previously impossible scientific instruments and processes, and the mass production of electronic consumer devices that pervade virtually every aspect of our lives and have created a global tech economy.

The second, equally breathtaking, scientific development was the discovery of the DNA double helix by Francis Harry Compton Crick (Cambridge University), Maurice Hugh Frederick Wilkins (London University), and James Dewey Watson (Harvard University), which earned them the Nobel Prize in 1962. This first glimpse at the source code of life fueled a research explosion in the biological and medical sciences. It foreshadowed the mapping of the human genome. Biotech joined semiconductor technology as a potential driver of the new economy and culture.

While the semiconductor revolution (consistent with "Moore's law" that microprocessor power doubles every 18 months) blazed along at geometric speed, biotech seemed to linger as the great unfulfilled promise. Biotech discoveries and developments progressed incrementally, at least from the consumer point of view, but biotech did not seem to have the same raging momentum. There are many reasons for this perceived disparity in developmental speeds. Chief among these is that even the most sophisticated microprocessor does not approach the mysterious complexities of living systems. Biotech often involves direct or indirect application to human life, so there is little room for error. It is one thing for an office computer to crash and quite another for an inadequately tested medical application to impair life and physical well-being. In other words, "Intel Inside" is simpler than "Got DNA?"

While the benefits of biotech are too numerous to list, it has also been a source of great controversy. Most recently, developments regarding stem

cell research (a biotech poster child), cloning, and athletic performance-enhancement drugs have created public debate that goes far beyond pure science into the realms of ethics and religion, and to the basic definition of what it is to be human. At the concrete level, more serious are the examples of biotech innovation gone wrong, resulting in death and disabling conditions, such as the thalidomide babies of the 1960s.

Many things have changed during the 12 years since we first published *Biotechnology and the Law* in 2007. We are in a very different place, technologically. Genetic treatment for diseases was still experimental 12 years ago, and completely out of favor as a result of the death of Jesse Gelsinger. Now it is more common, if not quite mainstream. Personal DNA reports are readily available. Tests for specific genetic traits are common, and relatively inexpensive. Stem cell treatments are becoming common, and dendritic cells show promise. Big data is driving bioinformatics to improve the efficiency of drug development. Mobile technology and personalized medicine are changing how we conduct trials and how we treat people. The cat-and-mouse game of performance-enhancing drugs continues, but the cat seems to be gaining ground. Medical devices are accelerating the machine-human interface, with implications we can only imagine, but the possibilities are both exciting and frightening.

Changes in law impact development and acceptance of biotech products. The America Invents Act changed our patent system from "first to invent" to "first to file." Recent court decisions appear to clear the way for the patenting of some form of human genes and to protect against copying those "products." Attempts to streamline the process and accommodate generic biologics are challenging the Food and Drug Administration (FDA). Life science business plans rely even more heavily on international sales, which means that laws in the European Union, Japan, Australia, and the so-called BRAC nations have an impact on development of most products. Initial clinical testing often is done in other countries, such as Australia and China, which provide many benefits. The lasting power of the Affordable Care Act still is unknown, but it or a successor may impact development substantially. Finally, the Great Recession, occurring soon after our first edition published, made capital scarce for many years, which made

creditors' rights, bankruptcy, and business plans that require less capital all critical to modern planning.

Biotech industries are largely about money and the race for that money. The actual applications may be altruistic, such as creating vaccines to avoid pandemic outbreaks of deadly diseases. Even so, with an aging population of baby boomers who are determined to live forever, a great deal of money will be made by the successful competitors in the consumer market. Some of these opportunities create clear ethical concerns, such as a new product that can save lives but at first is restricted to those who can afford it. As is true of most new technologies, such as the Internet, the initial commercialization that provides the necessary capital to go forward often does not come from the most sophisticated and erudite uses of the technology, but, instead, from consumer applications catering to more superficial wants and desires.

After years of very little money flowing into the system, investors returned. It is the potential for great riches that causes biotech investors and inventors to seek each other out. University technology transfer offices, many in their infancy a dozen years ago, now are firmly entrenched to increase university funding through the commercialization of academic research. In some cases, universities count on revenue from this source. Investors now will take a risk with biotech development despite the high failure rate of new biotech ventures, and the great costs and exceedingly long time frames required for a biotech product to reach the market.

A. The Biotech Primer

What does this all have to do with a primer on biotechnology law? The answer is this. Biotech has expanded from the largely exclusive realm of a few major corporations and research organizations to include a multitude of biotech startups and other entities looking for a stake in this next boom. In fact, some pharmaceutical companies and medical device makers appear to use these startups as a kind of minor league, supplying the larger company with new products. As a result, legal practitioners, particularly in university towns, who previously never faced biotech issues, are now representing these new players. Biotech legal practice involves specialized subject matter and regulatory schemes that, generally, are not part of the business lawyer's

repertoire. Because of this expansion of the biotech practice beyond the traditional organizations and their representatives, the American Bar Association's Biotechnology Committee determined 12 years ago that the time was right for a book to help lawyers find their way through the biotech maze. Now, we believe that an update to that book is needed.

This primer was never meant to be the last word on biotech law. Instead, it is intended to serve as a starting place for lawyers faced with the challenge of identifying the legal issues and processes that must be faced by their clients in building, marketing, and protecting a biotech business. The authors of the individual chapters, all of whom are accomplished in their respective fields, have provided thorough, yet accessible, overviews of biotech subspecialties with an eye to practical application. Unexpected for the editors, this book also has been used to teach law school classes on the subject. For that reason, we also include a case study that the authors have used. (See Appendix A.) We hope you will find this primer a useful and often-consulted resource in your biotech practice.

B. Biotech Defined

Before going any further, we must establish what this book covers, providing a working definition of "biotechnology." In its narrowest and most traditional sense, "biotech" is a term of art that encompasses the alteration and application of living matter—for example, the genetic manipulation of microbes—for a human use. With growth of the industry and the integration of many different technologies, however, a working definition becomes more elusive. As the field grew, the term evolved to include research, development, and application of medicines, devices, analytical aids, and therapies intended to contribute to the health and physical well-being of humans. Our working definition includes fields, activities, and subject matter that indirectly impact or contribute to wellness or lifestyle. For example, the broader definition of biotech includes activities such as the development of pesticides, altered or improved agricultural plants and animals intended for food or other uses, microbes engineered to perform specific tasks such as the breakdown of wastes and hazardous substances or the creation of chemical compounds, and even veterinary science aimed at the well-being of the family pet. It is this definition of biotech that is exemplified by the

broad-based membership of many biotech industry groups. This is also the definition applied in this primer.

1. Three-Branch Approach

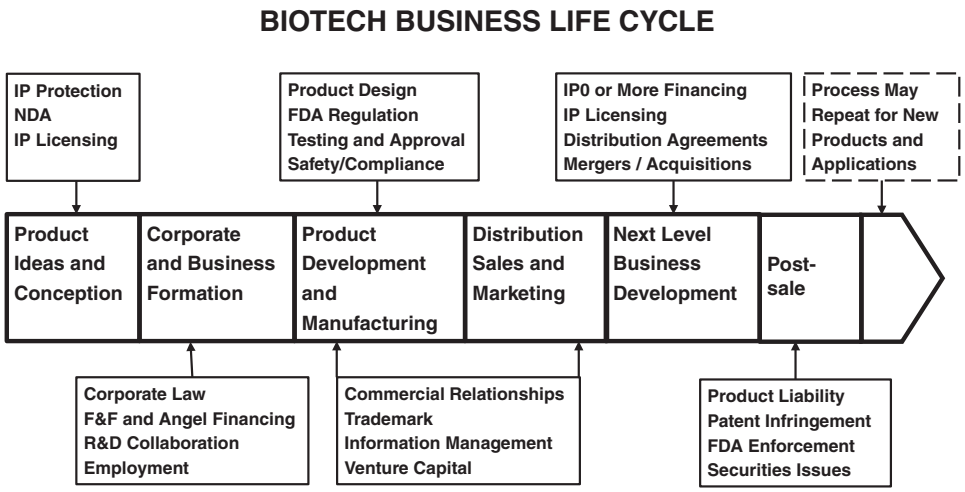
Because of the vastness of biotech development and application, it might be better to define biotech to encompass all things medicinal and/or biological, and then break the area down into three functional branches. The first branch is "pharmacological," referred to in the industry as "pharma," which includes medicines, vaccines, and some diagnostic tools. The second branch is "medical devices," used for research, diagnostics, and the application of medicines and therapies. The third branch might be described as the "genetics," "biologics," or "Jurassic Park" branch and includes DNA technologies to create medical therapies, as well as plants and animals.

While this three-branch approach is a good starting point, the demarcation gets very fuzzy at the edges. So, for example, how do you characterize a therapeutic system involving a device that is implanted in a patient to interact with a mobile device and dispense particular medications to specific cells or parts of the body? Or, what about a semiconductor designed to analyze a drop of a patient's blood (the "lab on a chip") to determine the genetic source of a disease? In the end, for the lack of a better taxonomy method, these examples all fall into the general category of "biotech."

C. The Biotech Company Life Cycle

Before you can understand the application of specific areas of biotech law, you first must understand the overall biotech company life cycle. Figure 1-1 presents a somewhat simplistic, but generally accurate, depiction of that life cycle. Beginning with idea conception and corporate formation, through product development and marketing, next level business development, and postproduct sale, the life cycle is intended to provide the reader with a frame of reference for the issues that arise at various points in the biotech business process. Accordingly, we have attempted to organize this primer in a manner consistent with the biotech life cycle. From a practical standpoint, the biotech company life cycle can be divided into four general phases.

Figure 1-1: The Biotech Company Life Cycle



1. Phase I: Startup

The startup phase is characterized by two distinct elements: idea conception and company formation, which are discussed in Chapters 2–5 of this primer. Biotech is idea-driven, dependent upon creative minds to come up with scientific discoveries that might develop into new products. To succeed economically, however, those ideas and inventions must be backed by sufficient, reliable financial investment within the context of a company structure. Therefore, representation of the startup company requires expertise in both intellectual property protection and corporate formation and financing.

a. Intellectual Property

Fortunes can be lost for failure to take the proper legal steps to protect the intellectual property of discoveries and applications. This step in the legal process is the realm of the intellectual property lawyer with expertise in patent, trade secret, licensing, trademark, and copyright law. This is critical to build a foundation that will contribute to adequate business development funding and maximum profitability at the next major stage of biotech business development.

It is very important for a biotech startup to get intellectual property counsel involved early in the process. Patent lawyers, who by definition are required to have technical training in addition to a law degree, generally

have backgrounds that mirror their clients' scientific disciplines. For example, semiconductor patent attorneys also tend to be electrical engineers ("Double Es") or chemical engineers ("Chem Es"), like their clients or their clients' inventors. Similarly, in the world of biotech, patent lawyers tend to come from the life sciences disciplines and often hold advanced degrees in relevant areas such as biochemistry, molecular biology, and biomechanical engineering. Working with such a specialist will help avoid the pitfalls inherent in the intellectual property protection process and also set the stage for a successful business strategy.

b. Company Formation

While company formation is important for any startup business, it is particularly crucial for the biotech startup. In contrast to the Internet startups, which seemed to move from inception to an initial public offering about as soon as the domain name was registered, the biotech company may take more than ten years from idea inception before a product has been approved for sale. Because of this long lead time, strategic company formation is critical to keeping the company, its key executives, and its brain power together for the duration of the life cycle. Therefore, the business lawyer advising a biotech company must be able to think well into the future and to anticipate the types of corporate issues that might be triggered, including long-term corporate governance, key executive longevity, and the allocation of corporate equity.

c. Investment Capital

Taking a biotech product to market costs a lot. The product will not show a profit for years after idea inception. Therefore, the biotech startup needs great amounts of outside investment capital from venture capitalists, sophisticated "angels," or a large pharma or biotech company seeking to purchase or partner with the startup. Once money is at issue, the financial relationships between the startup principles and the outside investors can become complex, as the startup's equity begins to migrate away from the founders to those investors. Therefore, the startup's lawyer must help the client form a company that protects the principles' interests while also

being financially attractive to the initial outside investors. This is doubly true today, as investment criteria has tightened, and other players (pharma) are active. And sometimes, for many years, investment is just not available.

Even though all of the players are focused, more or less, on the money, as with any tech speculation, there is a natural tension between investors and inventors. Typically, the outside money looks for speedy returns on investment. Inventors, on the other hand, and particularly academic inventors, often are driven by an obligation to complete fully the necessary research without shortcuts that could cause professional embarrassment. It is at this early intersection where biotech lawyers can work with their clients by creating business entities specifically tailored to address the need for speed while avoiding unnecessary research and development risks that could lead to exorbitant liability and business failure. Help the client select a strong board of directors and appoint appropriate watchdogs, such as a science advisory board. With this, the company might create a sort of business détente between investors and inventors that may allow them to survive the tumultuous early years of the relationship and see them through to success.

2. Phase II: Early Development

Once the basic foundation of the startup is in place, the new company is now on the long road to development, regulatory approval, and product sale. The early development phase is marked by continuous financing issues, the search for development partners, the beginnings of the regulatory trials process, and the business issues faced by any tech company as it grows beyond a few principles to become a more complex organization. Chapters 5–8 and 11–13 of this primer address many of these early development issues.

a. Additional Investment

If there is one recurring theme throughout the biotech business life cycle, it is financing and the virtually constant need for new capital. These needs increase with each stage of development. Financing issues are not as critical for the larger, established biotech companies with a diversified portfolio of products at different stages of maturity. For the startup, however, finding capital and the right partners often means the difference between a

successful business and early demise. These relationships can take different forms, both public funding and private investment, each of which presents strategic issues for the new company and challenges the biotech business lawyer in helping to shepherd a client to success.

b. The Regulatory Track

The early development phase also is marked by the all-important relationships between the company and the relevant governmental agencies, as well as the beginning of the years of scientific testing and trials necessary to ultimately achieve regulatory approval. Because biotech company development involves inherent tension between time and money, missteps in terms of damage to agency relationships or failure to comply with the required regulatory protocols can cause serious delays that strain the time/money critical path and endanger the company's chances for success. The biotech lawyer, who may be better versed in regulatory compliance and relationship building than a science-driven client, can provide great value.

c. Business Growth and Complexity

Once the fledging biotech company grows beyond the initial principles, it will become a more complex business organization, complete with employees and consultants who may have personal agendas different from those of the founders. As the principles move from the role of researchers to business managers, counsel should help to set up these relationships in a manner that protects the company's assets and mitigates the inevitable tensions. For example, tech companies are typically havens for bright young scientists and engineers anxious to apply their training and make a name for themselves in their respective disciplines. A disproportional degree of the actual idea advancement that occurs in tech companies often comes from young innovators fresh from academia and with exposure to the most recent theoretical developments. When their ambitions motivate them to make their own ways and, perhaps, to start their own companies, there are often disputes about who owns the research and inventions. By anticipating these issues, legal counsel can help clients create employer/employee relations that may not stop the departure of brain power, but could prevent them from leaving with the family jewels.