INSIDE THE MINDS

Understanding Legal Trends in the Life Sciences Industry

Leading Lawyers on Complying with Regulatory Changes and Keeping Abreast of Supreme Court Decisions

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Life Sciences IP: Current Concerns and Challenges

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Introduction: Major Current IP Issues

From an intellectual property (IP) perspective, the legal issues in the life sciences industry are many. Probably the most important current question is what can and cannot be patented. A secondary topic of interest is what can and cannot be agreed to in settlement of the major IP cases in life sciences—namely, cases under the Hatch Waxman Act between branded and generic pharmaceutical companies. The former touches every patent case in the life sciences from beginning to end; while the latter emerges from the settlement of a patent case and has consequences in antitrust, *qui tam,* and enforcement litigation.

On the former, until recently, you could patent almost whatever you wanted. That is not the case anymore, as the Supreme Court has stepped in and begun to limit patentability, primarily from a subject matter perspective.[1] As far as settlement goes, until recently, it was generally free reign on settlements, as well. You could agree to anything you wanted if you had a patent right. The courts and government (especially the government) have now begun to restrict these agreements in various ways, particularly with respect to so-called reverse payments, where a branded drug manufacturer might pay a generic manufacturer some compensation to remain out of the market during the manufacturer's period of patent exclusivity.[2] Other issues, such as false claims and off-label marketing, touch the IP space, but from an IP perspective, patentability and what can be agreed to in a settlement are the top two.

The overriding cost of health care is a main factor driving these trends. The cost has gone up, and people are looking for ways to lower costs or at least to give the appearance of lowering costs. In 2008, it was permissible to patent just about any discovery made in the life sciences space, if it was a genuine discovery and not something anyone could have done. That is not the case anymore.

The Supreme Court has taken a great interest in what is and is not patentable in all industries, but with particular emphasis on life sciences. In the *Mayo* case, for example, the cost of patent enforcement intruding on

[1] *See e.g., Mayo Collaborative Sers. v. Prometheus Labs Inc.*, 132 S. Ct. 1289 (2012).
[2] *See F.T.C. v. Actavis Inc.*, 133 S. Ct. 2223 (2013).

medical care was a prime issue in the background of the case. Numerous *amici* filed briefs in the case describing, in the opinion of the individual *amicus*, the detrimental effect certain patent rights could have on the cost and quality of health care. For example, it was said in the case that a doctor might worry about patent enforcement in the routine treatment of patients, thus potentially deterring the doctor from utilizing the best care. Alternatively, if the doctor chose to infringe a questionable patent, the hospital or physician would be subject to expensive patent enforcement, which, ultimately, would have to be passed on to the consumer.

Similarly, in the context of settlement, there is a perception among some that settlements that pay a generic provider to stay off the market for some period of the patent term drive up consumer costs by keeping lower-cost generic goods from the market. Whether this perception is correct is hotly debated by the government, the pharmaceutical industry, and economists. Nonetheless, the dominant view in the government is that settlements between branded and generic manufacturers that are "win-win" for those two groups are losses for the consumer.

Another factor driving these trends is the maturation of the appellate courts in dealing with IP and the life sciences. I think there was a perception in the latter part of the twentieth century—probably rightly so—that biotech and pharmaceutical inventions needed protection and needed to be less subject to being invalidated, so industries could grow and prosper. In my view, that perception has weakened now, as, for example, the biotech industry has begun to reach maturity, and there are large, prosperous biotech and diagnostic companies with products on the market that, it is believed, ought to be allowed to compete successfully without any special protections under the law. Thus, treating those inventions the same ways as all other inventions are treated is now perceived to be appropriate, and biotech/pharma patents are no longer sacrosanct.

A final factor is general competition—our economy works that way. More competition has come from everywhere, including foreign competition. Foreign competition is taking advantage of the larger market here in the United States and bringing more challenges under various aspects of the law to gain entry to the market. That includes challenging patents and previously agreed to settlements. The US market is No. 1 in the world for

pharmaceutical/biotech inventions, and breaking into it can support a company around the world. As this occurs, we will start to see these issues migrate to other jurisdictions, the beginning of which I have seen already.

Challenges in the Life Sciences Industry

Innovation and Cost Management

A key challenge in the life sciences industry is how to incentivize innovation and manage costs at the same time. The two things are inherently in tension with each other. If you innovate, our system says you have exclusivity, and exclusivity is not consistent with lowering costs. This is rightly so because companies want a return on their investment. People sometimes wishfully think that innovation should be free of charge—particularly life-saving medicines—but that is just not how it works in the real world. It would be great if innovations could be brought to market free, but companies are not exaggerating when they say that for every good drug they develop, twenty or thirty or more fail. The average cost is in the billions for each drug, if you add up all the failures.

Off-Label Issues

It is important for lawyers and their clients to pay attention to issues surrounding off-label use of drugs. Drugs are typically approved for sale for just one (or more) labeled use, but doctors and medical research almost always find other uses for the drug that are unapproved, some of which can result in substantial sales.

From an IP perspective, off-label use has been raised as an issue by generic manufacturers in patent litigation. One prominent issue is infringement—if a drug has significant off-label use, does that use provide a defense to a suit over a patent for an on-label use? The courts are sorting this issue out.[3] Another prominent issue is in the validity context, where generic manufacturers have argued that success of a drug might not be due to the patented use, but rather to off-label use, and, potentially, illegal off-label marketing. While little can be done about the former—i.e., the sales of the

[3] *See, e.g., AstraZeneca LP v. Breath Ltd.*, CIV.A. 08-1512, 2013 WL 1385224 (D.N.J. Apr. 3, 2013).

drug are either for an off-label use or not—the latter is on every company's list of issues, particularly outside the IP context.

If off-label sales of a drug are significant, the temptation to market off label can be very high, but the consequences also can be severe for companies that go over the line. It is important for attorneys and their clients to pay attention to investigations to make sure that their compliance issues are in order. These issues include things like maintaining proper sales promotion, continuing medical education, and even internal communications over such sales.

Off-label marketing is a common occurrence that can cause a company to be investigated by governmental authorities. Often, a whistleblower will trigger an investigation. The government pays large dollars for drug reimbursements, for example, and whistleblowers incentivized by the False Claims Act alert the government to practices that violate permissible marketing. The government may then make a claim that reimbursements for uses of drugs that were off-label were unlawful under Medicare and the like. Whistleblowers can then share in any eventual recovery—hence, the incentive for them to report violations.

It is a challenge to control off-label marketing where there is significant off-label use of a product. Companies have both a financial and a legal incentive to distribute information about off-label uses. While the financial incentive is straightforward, companies also want to distribute information about their products to avoid being sued for failure to warn, but they are not allowed to market those drugs for uses that are not on their labels. A well-known example of a drug with extensive off-label use is gabapentin. In one court case, it was estimated that 75 percent of the use of gabapentin—then known as Neurontin—was off-label.[4]

International IP Coordination

The European space is hospitable to branded life sciences companies. Japan is also hospitable—really the western countries. Other less hospitable countries include China and India, which are very large markets; however,

[4] *See Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348 (Fed. Circ. 2003).

they are changing over time. India is not a highly hospitable place to branded life sciences companies. It is, however, very hospitable to generic life sciences companies, so it depends on your perspective.

Each international actor has its own laws. The trans-Pacific countries (Unites States, Japan, etc.) are negotiating a treaty, a specific trade deal. The deal may be for or against patent rights, but there is question about how the deal will come out. That is a very important agreement being negotiated.

Aside from this deal, I do not spend much time worrying—from an IP perspective—about treaties. You tend to have to deal with the laws of the country or the laws of the organization that you are in. In the United States, we spend little time worrying about foreign laws. In Europe, we are worried about the European laws. In Canada, we do not spend much time worrying about European and US laws. No over-arching treaty in this space governs what I do in IP.

There are additional challenges associated with IP use in other countries. It is difficult to have a consistent approach across all of the different countries where multi-national corporations function. The laws vary widely country-to-country, even with next-door neighbors, like the United States and Canada. What can be patented in Canada is quite different from what can be patented in the United States. The two countries share many aspects, but also have a great number of differences.

Trying to bridge those differences is difficult. The popular perspective is that US litigation is unique, as well, so there are different regimes around the world, different laws, different things are patented, and then the US litigation process is unique in the world in terms of its depth and breadth. You have to worry uniquely in the United States about everything you say in the world coming back to haunt you, then trying to explain either to a judge or to a jury that you said something in this or that country because the laws there are different.

Often someone like me is asked to try to coordinate actions in the United States, Australia, Germany, England, Canada, and Japan all at once. Coordinating such work requires close communication between in-house and outside counsel. Most important is fostering a spirit of teamwork, lest

the lawyers from various countries become bogged down in disputes over which position to take where. Frequently, I suggest to my clients that they appoint one trusted person to oversee the team in-house, as well as one from outside. An in-person "summit" led by these two individuals can be an invaluable tool in managing this kind of complex coordination.

Key Recent Court Decisions on Life Sciences IP Protection

The US Supreme Court has issued several recent significant decisions in the life sciences IP sector.[5] In *Mayo* and *Myriad*, the Supreme Court rules on subject matter eligibility of medical diagnostic inventions; *Actavis* concerns antitrust scrutiny over patent settlements. The *Mayo* case reaffirms that laws of nature and natural phenomena cannot be patented by themselves or in combination with steps that were known in the art already. I represented Mayo in that case.

The *Myriad* case concerns the permissible patenting of genes. The Supreme Court's decision in that case was a split one. The court ruled that you cannot patent a gene simply because you remove that gene from the body, but that gene constructs known as cDNA are patentable because they are created in the laboratory. I am representing Myriad now in the cases that have resulted from competitive companies entering the market upon the ruling from the Supreme Court.

Both of these cases raise many issues for the lower courts to sort out, including what must be added to a newly discovered natural law or phenomenon to make it patentable. Until there are more cases, I think it is going to be very difficult to know the precise impact. The perception is that it will have a broad impact, and there is no doubt that there will be winners and losers. However, by the time a case makes it to the Supreme Court, it typically is addressing technology that may be as much as twenty years old. How these cases might relate to patents on something new—stem cells, for example—is unpredictable. Any patent practitioner worth his or her salt will need to consider these decisions in working for their diagnostic clients.

[5] These include *Mayo Collaborative Services v. Prometheus Labs Inc.*, 132 S. Ct. 1289 (2012); *Ass'n for Molecular Pathology v. Myriad Genetics*, 133 S. Ct. 2107 (2013); *and Federal Trade Comm'n v. Actavis Inc.*, 133 S. Ct. 2223 (2013).

The *Actavis* case provided some guidance on the permissible scope of settlements in patent cases where consideration is transferred to the infringer (as opposed to the patent holder). Neither side could claim victory, with the Supreme Court saying that such settlements need to be looked at from a "rule of reason" point of view. If they are reasonable and do not have an anti-competitive purpose and effect, then they will be okay. But if they are simply agreements in restraint of trade, then they will not be. This is compromise between the government's position—all such settlements presumptively violate the antitrust laws—and industry's—all such settlements are fine, so long as they are within the patent right. For those in my line of work, I do not think the decision was surprising; the Supreme Court tends not to like hard and fast, bright-line rules. Nonetheless, it provides important guidance for practitioners in the life sciences space and may end the call for any further Congressional action on these settlements.

Non-IP Issues that the Life Sciences IP Attorney Will Confront

Outside of the IP context, from time to time, I deal with products liability issues, though it is not my area of practice. These come up because of the technical competence one masters in practicing life sciences IP. Those same technical issues tend to surface in products liability cases. These cases arise because life sciences companies may face a variety of penalties if their products are found to be harmful, and these harmful effects were not disclosed. Companies can face criminal violations, but also civil and statutory violations. Sometimes company executives can face personal liability for such claims.

Most product liability claims result from an injury to a person by a drug or a medical device. Often, the device or drug was defective in some way, and there was a failure to warn before the injury occurred. The drug inherently had the problem that caused the injury, and there was no warning of it. Or there was a warning, and it was inadequate in some way. For example, side effects may have been listed, but not discussed in detail. Users then take the drugs, which make them sick in a way that was not warned about, or if it was warned about, that warning was inadequate. In other cases, devices are just defective.

I get involved because products liability cases can involve some of the same technical issues that IP cases involve: How does a drug work? What are its effects? What are its side effects? How was it discovered? In addition, companies' responses to products liability issues may implicate IP. For example, companies may be required to disclose and say things are routine or expected to comply with federal regulations. This has impact on whether those same things might or might not be patentable—that which is routine or expected may not be patentable, depending on the context.

Future of Life Sciences IP

I think in the next half dozen years, we will see a continuing push of companies looking to take advantage of the new biologics provisions of the Affordable Care Act. More companies will try to develop biosimilars—i.e., drugs that are biologic in origin—e.g., an antibody or protein—that are similar to, but not quite the same as, a marketed biologic drug. One famous example of this is EPO, or erythropoietin, which increases red blood cells in patients, for example, with anemia. Most famously, EPO is mis-used by professional cyclists to obtain a competitive advantage.

The Affordable Care Act directs the FDA to develop regulations to provide a pathway for approval of biosimilars that will be similar to the generic drug pathway. Because they are biologic in origin, though, copying a branded biologic drug will not be as simple as copying a generic drug that is a small molecule. This will lead to a host of patent issues on methods of making drugs that simply do not come up in the generic drug context. In addition, there will be action at FDA on whether regulations surrounding particular biologics are stringent enough.

We also see a greater number of molecules in the small-molecule area being orphaned and then repurposed—i.e., companies that developed drugs for one large particular use give up on the molecules, only to see other, smaller companies enter the fray to improve the drugs by developing newer versions of the drugs. These newer versions are then marketed by the smaller company itself, or that company may partner with another company, including the original developer. Such "repurposing" typically results in a new patent fight surrounding the "old" molecule, but now put to use for a new disease in a new way.

I think we will also see a continued diminishment of blockbuster small-molecule drugs. The 1980s, 1990s, and early 2000s saw the dominance in the market of drugs for "lifestyle" indications—too-high cholesterol, for example—with tens of millions of potential patients. Companies are now setting their eyes on smaller markets—oncology, for example—that many believe are more difficult to serve. Consequently, I expect we will see fewer, but no less valuable, blockbuster drugs.

Advice for Life Sciences IP Attorneys

I have been practicing in this field now for almost twenty years. The most important advice I can give to attorneys new to this field is to learn how to be a lawyer first before trying to learn every nuance of the life sciences. You can learn a great deal about being an effective counselor in the life sciences space by working on anything. Once you have those skills—at least at a certain level—then shift to pure life sciences. Too many people want to specialize right away and do not have the basic knowledge of the legal profession. It does not help to build up the specialty immediately. Doctors have to learn how to be generalists first, and then they specialize. The same is true for lawyers. Law school does not prepare you to be a counselor to a large life science enterprise, whether that is a public company, an academic or research institution, or simply an individual. You need an "internship" or "residency" to learn how to be a lawyer, just as you need it to be a doctor, and law school unfortunately does not provide that.

My second piece of advice is not to wed yourself too early to any particular type of company or client. Try to work with large and small clients and on both sides of the divide—defendant and plaintiff in a litigation practice or licensor and licensee, if you do not do litigation. Learning how the other person thinks is very important: you will be asked the question, "What does the other side believe?" more times than you will be able to count. If you choose one side immediately, you will miss learning the answer from cold, hard experience, and it becomes more of a guessing game.

Conclusion

Overall, working in intellectual property in the life sciences is incredibly challenging and interesting. A practitioner in this area can expect to deal

with all varieties of technology and numerous aspects of the law, including that which is not technically included in intellectual property, such as products liability or government enforcement. Because health care touches all of us in important ways, life sciences IP is constantly evolving to meet the needs of this critical area in our lives. From the highest levels of our government down to the basic doctor-patient interaction in a clinic, IP in the life sciences touches just about everything in our health care system.

Key Takeaways

- IP practitioners should read the *Mayo* and *Myriad* decisions and understand them to serve their clients most effectively.
- Settlements in which compensation is given to an alleged infringer may draw antitrust scrutiny after the *Actavis* case.
- Attorneys and their clients need to pay attention to off-label use, not just for compliance issues, but also for IP significance.
- Attorneys new to this field need to learn how to be lawyers first, before trying to learn every nuance of the life sciences.

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Mr. Singer is annually named one of the nation's finest life sciences trial attorneys, and is an expert in proceedings under the Hatch-Waxman Act. His clients consistently praise his innovative and groundbreaking work in cases like Mayo Collaborative Services, et al., v. Prometheus Labs, In re Cyclobenzaprine, and Allergan v. Barr Labs. In addition to his courtroom work, Mr. Singer teaches life sciences trial and patent practice around the country.

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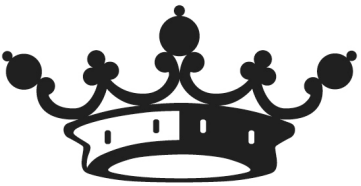

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