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Life Sciences Law & Industry Report™

Life Sciences

Bloomberg BNA asked noted life sciences attorneys for their top issues for 2016. While concerns about patent eligibility for natural and diagnostic products and other patent-related issues took up six of the top 10 spots, the attorneys gave high importance to the potential impact of approvals of more biosimilars, the growth of integrated digital health and continuing megadeals and partnering.

Biosimilars, Digital Health, Patents Called Top Issues for 2016

Biosimilars, integrated digital medical innovations and the momentum from recent high sales for drugs and devices took center stage in the top issues for 2016 as selected by attorneys contacted by Bloomberg BNA.

Last year's Outlook article labeled 2015 as the year of the patent, and that prediction proved accurate with important court decisions coming down on patent eligibility as well as rulings from the Patent Trial and Appeal Board. And patent concerns aren't expected to abate in 2016. Patent-related issues take six of the 10 spots for top issues for 2016, and even biosimilars has a patent component.

And yet, as life sciences attorneys struggle to break through the fog of uncertainty about patent eligibility, there is in the attorneys' comments a renewed sense of excitement about the possibility of more and more biosimilar approvals, continued innovation in integrated digital health devices and other innovations that are helping to make personalized medicine a reality, and the financial growth of life science companies.

The year 2016 will bring, the attorneys suggested, clarification of patent-related issues and continued life sciences advancement in innovation, in patient health and in company growth.

Biosimilars—the Real Story. Kevin Noonan of McDonnell Boehnen Hulbert & Berghoff LLP, Chicago, said that biosimilars has become a big story now that the Food and Drug Administration has licensed the first U.S. biosimilar to Sandoz for Zarxio, a filgrastim biosimilar to Amgen's Neupogen product (9 LSLR 328, 3/20/15).

Almost all of the attorneys interviewed by Bloomberg BNA listed biosimilars as their top issue for 2016. Thomas J. Quinlan of Reed Smith LLP, San Francisco, said, ''After a few years of waiting for the regulatory path to be clarified, Zarxio entered the market with a 15 percent discount. There appear to be at least 50 more applications in the FDA review'' pipeline.

Top Life Sciences Issues in 2016

- Biosimilars—The Real Story
- Integrated Digital Health—The Biggest Trend
- Megadeals Surge, IPOs May Cool
- FDA's LDT Plan Moving Forward
- Patent Eligibility—Continued Concerns
- Eligibility for Diagnostic Claims in Particular
- Inter Partes Review—Heating Up
- TPP Agreement—Not a Disaster
- University Licensing Revenues Could Increase
- EU Unitary Patent System—High Hopes

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For 2016, then, the focus will be a greater understanding of the provisions of the Biologics Price Competition and Innovation Act (BPCIA) that made the first biosimilar approval possible, the attorneys said.

''The real story is, perhaps, not in the FDA's approval but rather in the U.S. Court of Appeals for the Federal Circuit's approval of Sandoz's strategy for avoiding the so-called 'patent dance' provisions of the BPCIA,'' Noonan said (9 LSLR 828, 7/24/15).

Under the BPCIA, the maker of a biosimilar—a biologic product that is approved for market by the FDA based on a showing that it is highly similar to an already-approved biologic product, known as the reference product—files a biologics license application (BLA) to take advantage of the BPCIA's abbreviated approval pathway using the data of the reference product. Under the statute, the BLA applicant is to supply the reference product sponsor (RPS) with the BLA, manufacturing information and a list of patents that could be infringed by the biosimilar, as well as 180 days' notice of commercial marketing of the biosimilar.

Noonan said, ''Sandoz's strategy was simple: refuse to disclose its biosimilar application to Amgen and also refuse to disclose the manufacturing information also mandated (''shall'') by the law. Their argument was clever: because the law contains provisions permitting the RPS to immediately sue on any patent, this 'remedy' converted the seemingly required to the merely optional, and thus Amgen is left without the information only Sandoz possesses that would permit it to sue on the most relevant patents. The consequence of the Federal Circuit's affirmance of this ploy is that it is hard to see how any biosimilar applicant would ever disclose, if a lawsuit (which the biosimilar applicant is anticipating) is the only penalty.''

Nicholas K. Mitrokostas of Goodwin Procter LLP, Boston, said, ''There are a number of BPCIA interpretation issues left open and unanswered, including whether notice of commercial marketing is mandatory for biosimilar applicants who have engaged in the patent dance.''

The U.S. District Court for the Southern District of Florida answered that question in the affirmative on Dec. 9 (9 LSLR 24, 12/11/15), and Amgen filed its appeal to the Federal Circuit two days later.

''These issues are percolating in the district courts, and it will be interesting to see how the Federal Circuit addresses them in the near future,'' Mitrokostas said.

Integrated Digital Health—Biggest Trend. Asher Rubin of Hogan Lovells, Baltimore, said, ''Integrated digital health is the biggest thing for me. If you're looking for trends, this is the way I see things coming together. We are seeing high tech and biotech devices being blended. Those who learn how to combine the two different modalities will be ahead of the curve.''

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—ASHER RUBIN, HOGAN LOVELLS

An example of an integrated digital health device is a point-of-care, hand-held diagnostic that can be used with traditional printer technology and that can scan an obtained biological sample to be read at a medical center.

According to Carol A. Pratt of K&L Gates LLP, Portland, Ore., such a device could be used in traditional settings as well as remote areas, developing areas and battlefields.

Pratt said that the FDA has indicated that it will exercise a light touch on software and hardware and that some devices one could assume would be considered subject to medical device regulations won't be. ''This has been a relief to the digital health industry, which can now move forward,'' Pratt said.

She added that some companies are still choosing to obtain FDA medical device approval for their medical applications so they can be more competitive in the marketplace. ''Many health care entities that purchase medical devices will give preference to devices that are eligible for reimbursement by insurers. That requires data showing clinical benefit. So, an interesting aspect of development in this product space is that market pressures, not the FDA, are pushing companies to do clinical studies and get a approval for their mobile medical apps,'' Pratt said.

And yet, while it may seem that from the FDA's perspective it is done with digital health regulation, that might not be the case, Pratt said. ''The agency is becoming more involved at the cybersecurity front, and it is possible that digital health devices could be hacked, intentionally or unintentionally. Consequently, the FDA may have to come back to these devices that it has said it doesn't want to regulate.''

Pratt said that there are a number of startups in this space as well as Fortune 500 companies ''who have never been anywhere near the digital IT space'' and are now targeting the fitness and wellness areas with new product lines. ''They have to create an appropriate infrastructure and obtain the appropriate regulatory experience,'' she said.

Rubin added, ''Eventually, we're going to have to find out how to promote it on the provider side, as in what's in it for them. The hard part will be how to get people to pay for it, how to bundle services in a way that makes sense from the payment perspective.''

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There is also the issue of protection of patient data to be dealt with, Quinlan said, from artificial intelligence and diagnostic models, through personalized medicine and into identification of genetic predispositions and back again to simple protected health information under the Health Insurance Portability and Accountability Act (HIPAA).

''How much can you collect, how (and how long) can you use it, who owns it, how do you protect it and when can you delete it will continue to be asked in 2016,'' he said. ''Consumers want more limits on collection and use but will continue to want the benefits of data analysis and breakthrough technologies. A genetic predisposition will be the justification for a treatment path and the reason for coverage under health insurance but the insurance industry will be prevented from using the genetic data for underwriting purposes. How will this tension play out? How will this all be protected?''

Megadeals Increase, IPOs May Cool. Some attorneys that Bloomberg BNA contacted emphasized that 2015 had produced a good amount of drug and device sales that will serve as a platform in 2016.

Judith Hasko of Latham & Watkins LLP, Menlo Park, Calif., said that, with the amount of cash flowing into life sciences companies in the last few years, collaborations will continue to reflect greater value built by those companies in their platforms and products.

''Many such companies have used financing revenues to move their platforms or product pipeline forward to a more advanced stage before partnering. Accordingly, when these companies are ready to partner, they've got a more valuable product, and they can garner a higher value from the partner in a collaboration, both in terms of revenues they can receive and in terms of retaining valuable rights such as profit sharing, co-promotion or territorial rights,'' Hasko said.

Quinlan said that mergers and acquisition activity will continue to be robust as life science companies and others try to make use of cash that has accumulated and debt that has become more available in the market. ''Other factors such as tax strategies and the need to expand or consolidate product portfolios will continue to drive M&A in life science companies in 2016,'' he said.

Rubin commented, ''In the M&A world, I see there being more acquisitions of companies that fill in for big biopharmas, narrowly focused companies like those in gene editing doing things big biopharmas don't.''

Quinlan said that the market for initial public offerings (IPOs) in 2016 is said to be looking flat due to factors such as comments from the investment community over the past six months regarding the market caps for tech companies and concerns over the softness in the global economy.

''Despite this, many commentators believe that IPOs in biotech and health care could continue to be strong. In the recent 2016 BDO IPO Outlook, BDO reported that a majority of the executives it surveyed believe that health care and biotech IPOs will increase during 2016 [9 LSLR 1269, 11/13/15]. The JOBS Act [of 2012] [6 LSLR 443, 4/20/12] has of course facilitated the entry of health care and biotech companies into the public markets by reducing obstacles for companies with revenues of less than $1 billion [through the easing of certain securities regulations],'' Quinlan said.

Rubin said that the IPO market for biopharmaceuticals ''seems to be cooling thanks to claims of inflated pricing by a few of them. I'm seeing a vibrant market in the world of university spin-offs and university partnerships. It might turn out to be an alternative market if the IPO market continues to cool. In the meantime. we may see universities trying to hop over with a sort of slow-moving angel financing.''

Sarah Korman, senior counsel for intellectual property and litigation for Amgen Inc., Thousand Oaks, Calif., noted that the high cost of drugs has led to scrutiny of U.S. drug pricing that will surely continue in 2016.

''A rising tide of public discontent along with the U.S. presidential race is likely to spur a more interventionist approach to drug pricing. For example, an investigative panel from the House Committee on Oversight & Government Reform has indicated that it plans to hold a 2016 hearing on skyrocketing drug costs,'' she said.

In the short term, however, drug pricing reform is unlikely and the majority of pharmaceutical companies won't be affected, Korman said. ''Certain companies are more at risk in 2016. Specialty pharmaceuticals and biotech companies that rely on drug pricing rather than research and development, as well as companies with a high percentage of sales in the U.S., are likely to experience pricing pressure.''

FDA's LDT Plan Moving Forward. The FDA's plan to increase oversight of laboratory-developed tests (LDTs) created controversy in 2015 that those contacted by Bloomberg BNA said likely could be resolved in the new year as the FDA's risk-based, phased-in approach heads to a final version after it looks at input from comments and workshops (8 LSLR 773, 8/8/14).

Nathaniel Beaver of Foley Lardner LLP, Washington, noted that in November, the FDA published a report of 20 case studies demonstrating the need for FDA oversight of LDTs. The report highlighted the agency's contention that laboratories offering LDTs that follow only the regulatory requirements of the Clinical Laboratory Improvement Amendments, which the Centers for Medicare & Medicaid Services oversees, still experience significant problems that ''illustrate, in the absence of compliance with FDA requirements, that these products may have caused or have caused actual harm to patients.''

The FDA's proposed LDT regulations are "draconian, comprehensive in scope, ambitious and dense, easily one of the longest and most dense that I've ever seen from the FDA."

—Carol Pratt, K&L Gates

Pratt called the FDA's proposed LDT regulations ''draconian, comprehensive in scope, ambitious and dense, easily one of the longest and most dense that I've ever seen from the FDA. And there has been push-back from industry.''

Pratt said that the FDA's proposed LDT plan always would have been considered an important event but that it is even more interesting because of the timing: The FDA wasn't able to move it forward fast enough to avoid its being sucked into the 2016 election year cycle,

which has prompted congressional hearings and alternative proposals.

''I favor the proposal that would create a division for all in vitro diagnostics, including both LDTs and those diagnostics that are sold. I have concerns with the FDA applying its traditional approach to LDTs and find having a division focused on IVDs intriguing,'' Pratt said.

She said, in spite of suggestions that the FDA could abandon the plan in an election year, the fact that Jeff Shuren, director of the FDA's Center for Devices and Radiological Health, has indicated that the agency is targeting the final version of the plan for release in early 2016 rather than late 2016 means that the agency is committed to getting the plan done and out (9 LSLR 23, 11/27/15).

Beaver said, ''Should FDA finalize the proposal early in the year, I would expect this will not be the final say on this matter, as both industry as well as Congress will influence the final outcome.''

Patent Eligibility—Continued Uncertainty. Concerns about the patent eligibility of natural products and diagnostic methods will continue in 2016, attorneys said.

Jill Uhl, director of intellectual property for Johns Hopkins University Technology Transfer, said, ''Unfortunately, a string of Supreme Court decisions has changed the way life science companies look at patentable subject matter'':

■ *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, which held that claims for methods for administering a drug are patent ineligible as laws of nature unless there is an ''inventive step'' (6 LSLR 404, 4/6/12);

■ *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, which held that composition claims for isolated DNA are patent ineligible because they recite the judicial exception to patent eligibility of products of nature (7 LSLR 622, 6/14/13); and

■ *Alice Corp. Pty. Ltd. v. CLS Bank Int'l*, which dealt with business method and software patents and expanded on the two-part test the court provided in *Mayo* (7 LSLR 622, 6/14/13).

''If we look at the trend over the last decade, for better or worse, these decisions cap a decade long trend away from the patentability of the human body, human embryonic stem cells, human physiology, diagnosis of human disease, human thoughts and now human genes. As the collection of patentable subject matter is narrowed, how long will it be before the available investment in life science companies begins to be negatively impacted by this contraction?'' Uhl asked.

''Such uncertainty cannot be good for encouraging investment in life science companies,'' Uhl said.

Eligibility for Diagnostic Claims. A number of commentators focused on the impact of a 2015 Federal Circuit panel decision in *Ariosa v. Sequenom*, which concerned the discovery that a pregnant woman's blood plasma/serum contains fetal DNA that can be teased out by amplifying paternally-inherited sequences from the cell-free plasma of the mother's blood (9 LSLR 715, 6/26/15).

Applying step one of the two-step *Mayo*/*Alice* test, the panel found that the claims were directed to a natural phenomenon, lacked an inventive step and were therefore patent ineligible.

Noonan said, ''The Federal Circuit affirmed a truly awful district court decision in *Ariosa v. Sequenom* and what may be worse is that even the Federal Circuit knew the decision was a problem but felt their hands are tied by the Supreme Court's equally difficult *Mayo*, *Myriad* and *Alice* decisions.''

He noted that the Federal Circuit's Judge Richard Linn wrote a concurring opinion that read like a dissent from the panel decision, while Judge Alan D. Lourie, joined by Judges Kimberly A. Moore and Timothy B. Dyk, wrote concurrences from the court's denial for reconsideration en banc, similarly strongly hinting that the court believed its decision complied with Supreme Court mandates (9 LSLR 24, 12/11/15).

''Loose language in the Supreme Court's opinions, and how the lower courts have interpreted that language causes the problem, along with this Court's unwillingness to roll up its sleeves and decide with some rigor whether *Parker v. Flook* [437 U.S. 584 (1978)] or *Diamond v. Diehr* [450 U.S. 175 (1981)] is the right way to interpret claims,'' Noonan said.

Flook held that an invention that departs from the prior art only in its use of a mathematical algorithm can only be patent eligible if the implementation is novel and nonobvious with the algorithm itself considered as part of the prior art. *Diehr* held that mathematical formulas in the abstract can't not be patented but that the mere presence of a software element doesn't make an otherwise patent-eligible machine or process patent ineligible. Noonan said, ''I think the *Diehr* 'claim as a whole' approach is the better one.''

He also said, ''If the Supreme Court appreciates the mess it has made and how inimicable these decisions are to progress in the diagnostics space they may grant certiorari (review).''

Neeta Thakur of Sheppard Mullin Richter & Hampton, Palo Alto, Calif., said, ''The decision sets up a petition for writ of certiorari to the Supreme Court with several members of the Federal Circuit calling for review. The decision shows that the court's hands are tied by the Supreme Court precedent set by *Mayo*. It also suggests significant hurdles to obtain patent protection of new diagnostic methods, which can significantly impact the personalized medicine industry. It is clear that any further guidance on patent eligibility under 35 USC § 101 will probably now come from the Supreme Court. I hope the Supreme Court does review it.''

Carl Gulbrandsen, managing director of the Wisconsin Alumni Research Foundation, said the focus of a Supreme Court review of *Ariosa* would be whether there remains some exception for pharmaceutical, medical and biotechnology inventions under the judicial exclu-

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sion from 35 U.S.C. § 101 eligibility for natural principles and products of nature.

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—CARL GULBRANDSEN, WISCONSIN ALUMNI RESEARCH FOUNDATION

''The uncertainty that exists today over whether newly discovered and non-obvious natural products or natural principles can be patented continues to seriously threaten innovation in this country,'' Gulbrandsen said.

While universities still file patent applications for inventions that involve natural products and natural principles, it is becoming more and more difficult to license such applications given the existing uncertainties as to whether such applications will survive § 101 rejections,'' he said.

''Startup companies based on fundamental technologies that are under the *Myriad/Mayo/Alice* cloud find it harder to attract investment dollars,'' Gulbrandsen said. ''And this present situation puts the U.S. at a decided disadvantage with regard to the rest of the world where exceptions to the natural product/natural principle exclusion do exist.''

Inter Partes Review—Heating Up. Deborah Lu of Vedder Price, New York, said that inter partes review (IPR) by the PTAB continues to be a hot topic.

''Three years after it went into effect under the America Invents Act, the IPR process is frequently utilized as an alternative, a prelude, or to delay patent litigation and the process has been meeting the goal of a decision within a year. But there have been complaints from patent owners that if your patent is challenged through an IPR it stands a good chance of being partly or completely invalidated,'' Lu said.

Some PTAB decisions are being appealed to the Federal Circuit, and there is proposed legislation to revamp the IPR process, Lu noted.

''However, many decisions have not been overturned by the Federal Circuit, leading some to believe that the IPR process is effective and more efficient than district court litigation,'' she said. ''And all of this is before the PTAB considers patents that may touch on patent eligibility issues under *Mayo*, *Myriad* and *Alice*, which could happen in 2016 and heat up the discussion even further.''

Noonan said, ''The PTAB continues to be a convenient avenue for patent challengers of every stripe, and the lack of any standing requirements, as are found in other post-grant review provisions, has been controversial. While becoming less of a 'patent graveyard' than some complained it might become, including former Federal Circuit Chief Judge [Randall R.] Rader, continued use of the 'broadest reasonable interpretation' standard for claim construction coupled with procedural (at least) hurdles to amendment makes it an attractive target for congressional intervention in the latest round of patent 'reform' legislation. Whether Congress can assemble the consensus that such a measure requires for passage is at best problematical.''

TPP Agreement, Not a Disaster. In his selection of important issues for the 2015 LSLR Outlook (9 LSLR 868, 7/24/15), Noonan included the Trans-Pacific Partnership Agreement, but added, ''I don't know if this will be an issue because I don't know what it says—nor does anyone. And this is what motivates the conspiracy theorists and anti-patent folks, particularly regarding pharmaceuticals.''

The final text of the TPP was released Nov. 5 (9 LSLR 1297, 11/13/15).

In his list of top issues for 2016, Noonan included the TPP again. He said, ''Well, now we know what it says and while it isn't perfect, it isn't a disaster either. The major provision is that the regulatory exclusivity period has a floor of eight years for biologic products (although other legitimate readings could reduce this to five years). This term isn't a ceiling, however, and doesn't require the U.S. to reduce the 12-year exclusivity period under the BPCIA, which, of course, will happen whenever there is the political will or interest alignment to support it—the Obama administration has been trying to reduce the term to seven years ever since the law was enacted.''

On the plus side, he noted, ''there are many signatory countries that had no exclusivity term, so there is the possibility of some protection in those countries.''

Any such optimism must be tempered by the TPP including ''loophole'' terms like the Doha Declaration, which gives governments flexibility in implementing agreements when they are acting in the interest of public health, Noonan said, and ''which in practice have stripped GATT/TRIPS [General Agreement on Tariffs and Trade/Trade-Related Aspects of Intellectual Property Rights] of much of its intended force in having member countries respect patent rights.''

University Licensing Revenues Could Increase. Gulbrandsen discussed the possibility that university and research organizations will be able to increase their licensing revenues in 2016 as the result of a court decision.

He noted that the phrase ''efficient infringement'' describes the practice of some business sectors of choosing to infringe rather than license a patent because, in most cases, the worst that can happen to an infringer is having to pay a reasonable royalty. ''This circumstance exists today because of the near impossibility of infringed patent owner obtaining an injunction or enhanced damages,'' Gulbrandsen said.

In *Halo v. Pulse*, U.S., No. 14-01513, *petition granted* 10/19/15, the Supreme Court is being asked to consider whether the standard used by the Federal Circuit to determine if an award of enhanced damages may be made under 35 U.S.C. § 284 is too strict.

''Allowing district courts more discretion to award enhanced damages in infringement cases will go part way to reducing the incentive to infringe rather than license,'' Gulbrandsen said, ''Increasing the incentive to license is important to universities and research institutions that depend on licensing to move their discoveries to the marketplace to improve lives. Licensing also encourages collaboration between industry, small busi-

ness and research institutions leading to greater innovation.''

In a Dec. 16 amicus brief filing, the solicitor general and the Patent and Trademark Office urged the court to reject the Federal Circuit's enhanced damages test, asserting that it is ''flawed'' and needlessly restricts these awards. The Supreme Court set oral arguments in the case for Feb. 23 (*see related story in the Court Proceedings section*).

EU Unitary Patent System—High Hopes. Amgen's Korman said that hopes remain high that the EU Unitary Patent System will come into operation in late 2016 and receive its first cases in early 2017.

Under the Unitary Patent System, a single patent, granted by the European Patent Office (EPO), will be offered in addition to already-existing national patents (9 LSLR 24, 12/11/15). This unitary patent will be effective across the EU and enforceable with a single court ruling.

The system would establish accepted languages for patents—English, German or French—and create a Unified Patent Court (UPC) for hearing patent disputes. In addition, a specialized branch of the UPC, located in London, will be established to handle all pharmaceutical and life sciences cases.

Signatures from at least 13 countries are required before the UPC takes effect. The list of signatories includes Germany, Denmark, France, the U.K., Hungary, Luxembourg, Sweden and Slovenia.

''The launch of the EU unitary patent and the UPC will create a single jurisdiction encompassing at least four G8 economies and a total population of more than 600 million people. The impact on pharmaceutical and life science companies that do business in Europe will be profound,'' Korman said. ''Not only will the new system present a series potential risks and strategic challenges, but it will also offer a range of opportunities.''

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