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Life Sciences Industry

Bloomberg BNA's Life Sciences Law & Industry Report asked attorneys in the field to discuss their top issues for 2014. Personalized medicine, including topics ranging from mobile medical devices used for on-site diagnostics to contracts for data and tissue mining to regulation of nutraceuticals and medical foods, reemerged as a hot issue. Patent-related issues also again were seen to be of strong importance, with predictions that disputes over the patent eligibility of genetic materials will continue and that conflicting Federal Circuit decisions on patent-term adjustments will be resolved.

Personalized Medicine, Patents Top Issues for 2014, Life Sciences Attorneys Say

Patent eligibility for genetic material and diagnostic methods and other patent-related topics will continue to be major issues in the life sciences industry in 2014, attorneys contacted by Bloomberg BNA said. But another area reemerged to be of equal, if not superior, importance to patents for the life sciences: personalized medicine.

In the Life Sciences Law & Industry Report 2013 Outlook, the focus was on patent issues: patent eligibility; self-replicating organisms and the doctrine of patent exhaustion; the impact of the new European Unitary Patent; the patentability of inventions related to human embryonic stem cells; and the implementation of U.S. patent reform (7 LSLR 63, 1/11/13). All of these issues did indeed play an important role for life sciences in 2013.

Personalized medicine was only mentioned in the 2013 LSLR Outlook in passing. It had been highly ranked in previous LSLR Outlooks, but its relative absence among the Outlook issues in 2013 appeared to reflect a concern that the promise of personalized medicine continued to be out of reach. The topic also may have been swamped by the concerns about patent eligibility and patent legislation.

Only one attorney, Asher Rubin of Hogan Lovells, Baltimore, commented about personalized medicine in the 2013 LSLR Outlook. He said at the time that the area may not be commercially feasible yet but that the life sciences industry will pursue "mass customized therapies" because they will be more effective and therefore more valuable.

Top Issues in 2014

Personalized Medicine

- Mobile Medical Devices, Upside and Down
- Companies Move to Wellness
- Data and Tissue Mining Create Contract Issues
- Comparative Effectiveness Funding in Demand
- Nutraceuticals, Medical Foods
- Health Claims Litigation Changes Model

Patents

- *Myriad* Ruling Leads to Paradox
- Diagnostic Patent Eligibility Undermined
- Patent Term Adjustment Resolution?
- Reverse Patent Settlements Still in Flux
- Patent Exhaustion Debate Not Over?

Other Issues

- Biosimilars
- Strategic Alliances

Patent-related issues having been addressed, although not completely resolved, in 2013, those offering their top issues for 2014 gave a strong emphasis to personalized medicine.

LSLR advisory board member Carol Pratt of K&L Gates, Portland, Ore., said her top issues were about emerging markets seeing new activity. She noted that, as part of personalized medicine, life sciences companies are moving more into wellness products, mobile devices are finally being utilized to achieve the telemedicine that was envisioned two decades ago, and life sciences entities are pursuing the comparative effectiveness research funding coming from the Affordable Care Act.

Those contacted by Bloomberg BNA indicated that disputes over the patent eligibility of genetic material and diagnostic methods also will continue, the patent exhaustion debate concerning self-replicating technologies may not be over, and the conflict between two different Federal Circuit decisions over patent term adjustments is likely to be resolved by the full U.S. Court of Appeals for the Federal Circuit.

Other issues mentioned as important in 2014 were biosimilars and strategic alliances.

Personalized Medicine

The President's Council of Advisors on Science and Technology defines "personalized medicine" as the tailoring of medical treatment to the individual characteristics of each patient to classify individuals into subpopulations that differ in their susceptibility to a particular disease or their response to a specific treatment.

Judith A. Hasko of Latham & Watkins LLP, Menlo Park, Calif., said, "We are seeing increased consideration of the need or desirability of developing pharmacogenomic products and companion diagnostics for certain types of therapeutic products." Pharmacogenomics is the technology that analyses how genetic makeup affects an individual's response to drugs.

Hasko, a LSLR advisory board member, said that the drivers behind this trend vary according to the situation. "Such pharmacogenomic products or companion diagnostics may be required by regulatory authorities for approval of the therapeutic, desirable for reimbursement purposes for the therapeutic, or otherwise determined to be useful for optimizing product use after approval is obtained."

Other attorneys Bloomberg BNA talked to focused on new technologies and products that are the result of the personalized medicine approach.

Kevin Noonan of McDonnell, Boehnen, Hulbert & Berghoff LLP, Chicago, however, said that personalized medicine "remains a future prospect, if not a pipe dream." He referenced the Dec. 30, 2013, New York Times article, "I Had My DNA Picture Taken, With Varying Results," by Kira Peikoff that described the different and conflicting performance of three genetic testing services on the same DNA sample.

Mobile Medical Devices, Upside/Downside. Pratt said that the use of mobile medical devices is revolutionizing medical diagnostics.

"The upside is that this is the realization of the telemedicine that was briefly explored in the 1990s but the technology wasn't there. Now the technology is here, and, as a result, care can happen anywhere. This tre-

mendously expands the delivery of health care. The downside is the regulatory issues haven't been resolved, and this is affecting the investment needed to the extent that a whole new business model is needed for companies utilizing the combination of mobile medical devices and in vitro diagnostics," she said.

According to Pratt, when mobile applications first became available, there had been uncertainty about what software the Food and Drug Administration would regulate. The FDA then issued guidance and began clearing mobile medical applications under the 510(k) program, referring to the 510(k) form required from medical device manufacturers as pre-market notification that they intend to introduce a device into commercial distribution for the first time or reintroduce a device that will be significantly changed or modified to the extent that its safety or effectiveness could be affected.

"The industry then settled down," Pratt said. "But in the past year or so there has been an explosion of applications based on what people understood the FDA to be approving. What has changed, though, is the new ability for a health care professional to take, say, an iPhone and have the data at the site of the patient uploaded into the cloud and be read by someone else some place else who closes the loop with feedback on a diagnosis. It's basically the use of companion products, a hardware device with an assay of some sort. It becomes patient-side care using off-the-shelf equipment and proprietary software in a cloud-based environment."

"We are seeing increased consideration of the need or desirability of developing pharmacogenomic products and companion diagnostics for certain types of therapeutic products."

—JUDITH A. HASKO, LATHAM & WATKINS LLP

The problem is, Pratt said, that companies have been "sailing through thinking that the FDA would clear their approach as 510(k)s and that they could focus on the diagnostic part. Only they then find that their use of the software is more complicated than what the FDA had been clearing since the software is actually participating in the analysis. And then they find they might need to do clinical research to support the 510(k) or move to a PMA [pre-market approval]."

This has led to financial issues because the company may have raised hundreds of thousands of dollars from investors only to find it needs millions of dollars for the clinical research, Pratt said, adding, "This requires a whole new business model, and there is some uncertainty still. We are able to find out what gets through the FDA but don't know as much about what is getting stalled at the FDA."

Companies Move to Wellness. Pratt said that big pharma and big food companies have been opening wellness divisions. She gave as examples Nestle and GlaxoSmithKline.

“It’s an interesting phenomenon in that they are basically developing the same category of product aiming at the functional food category, but they are coming at it from different directions. Wellness is a hot commodity. The movement to wellness is a natural progression from the emphasis on personalized medicine.”

Robert H. Underwood of McDermott Will & Emery, Boston, characterized this as the nutraceuticals market that includes foods and beverages that are intended to have health benefits to consumers and encompasses dietary supplements, functional foods and nutraceutical ingredients.

“There has been dramatic growth in these markets in the U.S. and internationally as consumers become more health conscious and as populations age,” Underwood said. “This has been accompanied in recent years by Big Pharma and food companies actively acquiring smaller companies and by the development of new products and technology by small and large companies.”

These business activities and several legal developments indicate that this industry may experience significant changes in 2014, Underwood said. “The growth in the nutraceuticals market has attracted investment to support development of new products and new technology. The lines demarcating one type of nutraceutical from other products—dietary supplement, functional food, nutraceutical ingredient—are sometimes unclear, and the regulatory and compliance issues vary for the different types of products.”

Against this backdrop, Underwood said, the stage was set in 2013 for increased industry regulation and oversight. “The FDA announced that it intends to finalize draft guidance on new dietary ingredients and to update the post market surveillance system for regulating dietary supplements in 2014,” Underwood said. “This will be something to monitor closely.”

Data, Tissue Mining Create Contract Issues. Pratt said that the sudden surge of interest in data and tissue mining are both related to personalized medicine.

“Personalized medicine means figuring out subsets of patients for targeted therapies. To do this, you need large volumes of clinical data and tissue. These areas have been of regulatory interest for years, but now they are becoming a commercial issue. People want to buy and sell tissue. And this opens up not only regulatory concerns but transactional ones on an international scale that also brings in the ownership of intellectual property.”

Attention must be paid to privacy laws, the Health Insurance Portability and Accountability Act (HIPAA), and the European Union privacy directive, which have differences, Pratt said.

“You have to create a matrix of local, federal and international laws. Tissue is the most interesting because it is tied to patients’ informed consent forms, which can be 10 or more years old, and their provisions for future, unspecified use of tissue. For both clinical data and tissue mining, you begin to focus on the pedigree of what is being sold. We’re seeing contracts trying to hammer out who has ownership of the data and tissue and, once the sellers get the data or tissue, what they can do with them. We’re seeing built on the front end of deals a lot of due diligence concerning ownership and limitation of use,” Pratt said.

Comparative Effectiveness Funding in Demand. Pratt said that the pursuit of wellness that is generating these products and services also is spinning off comparative effectiveness research. The Patient-Centered Outcomes Research Institute, which was created in 2010 under the Affordable Care Act, has \$1 billion in 2014 to spend on comparative effectiveness research, Pratt said (7 LSLR 1190, 11/29/13). PCORI is charged with examining the relative health outcomes, clinical effectiveness and appropriateness of different treatments by evaluating existing studies and conducting its own.

“It’s natural that companies are saying, ‘I want some of that,’ and are pursuing it maybe rather than National Institutes of Health funding. We’re seeing health care networks who have the ability to mine their data to determine what interventions are being effective, and then they make a pitch to the PCORI for comparative effectiveness funding. They’re capable of producing cost-cutting longitudinal studies, which are another aspect of personalized medicine, although this is an epidemiological approach.”

Pratt said that people are lining up for research dollars. “It’s exciting, but drug companies are getting nervous about this kind of research that says Company A’s product is better than theirs. It’s an unusual position for drug and medical device companies to be in, sitting on the bench and seeing health care networks collating data about their products.”

Nutraceutical Health Claims Litigation. Pratt said that the movement by Big Pharma into conventional food and beverages also is generating litigation concerning health claims for these products.

“Traditionally, the only thing companies making, say, dietary supplements had to worry about was not crossing the line into where what they were making was a drug the FDA would regulate. The Federal Trade Commission and the FDA monitored these types of products, with the FTC being more active for targeted areas, but the oversight was generally weak,” Pratt said.

What has been happening in the last year or so is that private litigants have been suing companies for lack of substantiation for their claims, Pratt said. “The motivation is largely monetary. Individuals have gone to attorneys, and there have been class action suits in state courts in California, Florida, New York and New Jersey, all states that have unfair business practices laws and that are generally pro-consumer. The plaintiffs are not asserting that the claims are inappropriate but are saying they are unsubstantiated. They are arguing, ‘You haven’t tested your product on humans, so how do you know it will work?’ ”

According to Pratt, the FTC has established criteria, which include that the product must be tested on humans and the companies can’t rely on animal studies. “Now, companies making dietary supplements and the like have become comfortable with the fact that this area has had low regulatory approval issues. Suddenly, these lawsuits are having a huge impact. If a company is sued, there is no cheap way to get out of it. They can fight it, which is expensive, or they can settle, which is expensive.” Pratt said she has seen settlements as high as \$2 million.

“I tell these companies, some of which are small to medium in size, that their new concern is being targeted for private litigation. They never used to think of human

studies, and now the lack of them is a significant litigation risk,” Pratt said.

This situation is affecting entry into the market, she said. “To mitigate the risk and do human subject research for conventional foods and dietary supplements, a whole industry of contract research organizations [CROs] is springing up. From a scientific point of view, it is very difficult to design a study that measures maintenance of the status quo. In a yogurt study, for example, you could test the effect of yogurt on healthy people, but what would you measure this against?”

And there are regulatory issues as well, Pratt said. “You have to be careful not to do a study that FDA will construe as a drug study. If so, then you’ll need to go to an IRB [institutional review board] and get an IND [investigational new drug application].”

Pratt also noted that this becomes a huge factor in due diligence. “I’ve seen the deals that are no longer focusing on market share but on whether the company being sold has substantiation for product claims. It can taint the deal or devalue it. I had mentioned that both food and pharma companies have developed wellness divisions, coming from different perspectives. The food industry doesn’t have a clinical study background. Biopharmas do and have backgrounds of working with CROs. But then the food industry is hiring people from biopharmas. In the end, the whole situation is challenging for both biopharmas and food companies in that neither has an advantage in doing studies that don’t cross the line into drugs.”

Patents

When asked if three important recent Supreme Court decisions on biotechnology issues mark the end of the “gene patent,” diagnostic method patent and self-replicating technology-patent exhaustion stories, attorneys contacted by Bloomberg BNA said, “Not really.”

In *Ass’n for Molecular Pathology v. Myriad Genetics, Inc.* (7 LSLR 622, 6/14/13), the Supreme Court found that “genes and the information they encode are products of nature and not patent eligible under [35 U.S.C.] § 101 simply because they have been isolated from the surrounding genetic material,” while complementary DNA doesn’t exist in nature and therefore is patent eligible.

In *Mayo Collaborative Servs. v. Prometheus Labs., Inc.* (6 LSLR 284, 3/23/12), the court held that a correlation that occurs in nature, such as the relationship between the concentration of a blood metabolite and the response to a therapeutic drug, is a law of nature. A claim directed to such a law of nature without more, or that only adds well-understood, routine, conventional steps specified at a high level of generality, isn’t patent eligible.

In *Bowman v. Monsanto Co.* (7 LSLR 530, 5/17/13), the court unanimously held that seeds as a form of self-replicating technology that were harvested by a farmer from one crop were “additional copies” of patented genetically modified seeds and thus weren’t subject to the patent exhaustion doctrine.

Myriad Ruling Leads to Paradox. Noonan, a LSLR advisory board member, who had anticipated the Supreme Court’s ruling in *Myriad* in his 2013 LSLR Outlook comments, said that the lack of clarity in the decision likely will have repercussions for 2014 and beyond.

Noonan said that until *Myriad* there never had been a case where the Supreme Court clearly enunciated a standard for when a compound that occurs in nature isn’t patent eligible. “Unbiased review of cases like *Brogdex [American Fruit Growers v. Brogdex, 283 U.S. 1 (1931)]* and *Funk Bros. [Funk Brothers Seed Co. v. Kalo Inoculant Co., 333 U.S. 127 (1948)]* reveals that the court was not addressing these issues as products of nature categorically,” he said. “Cases of earlier precedent, such as *Cochrane v. Badische Anilin & Soda Fabrik, 111 U.S. 293, 311 (1884)* and *American Wood-Paper Co. v. Fiber Disintegrating Co., 90 U.S. (23 Wall.) 566, 595 (1874)*, were clearly concerned with novelty issues—removing compositions from the public domain,” Noonan said.

“Previously, an antibiotic made by a microorganism could be patent eligible upon purification, and *Myriad* throws that standard into doubt.”

—KEVIN NOONAN, McDONNELL, BOEHNEN, HULBERT & BERGHOF LLP

Myriad makes it plain that, at least for DNA, there is a level of modification that doesn’t meet the standard for patent eligibility, Noonan said. “While the Court tried mightily to avoid speaking to anything other than DNA, its rationale could be extended to other natural products. This would be a shift from prior policy. Previously, an antibiotic made by a microorganism could be patent eligible upon purification, and *Myriad* throws that standard into doubt. ‘Mere’ purification may not be enough, particularly in view of the scientific reality that purification of a natural compound may often involve less chemical change to the compound than the changes incumbent upon isolating a genomic DNA fragment.”

Noonan said that this also leads to the paradox that the more similar to the natural compound the claimed invention is, the less patent eligible it may be. “In view of the subtleties involved in even small changes in biologically active molecules, this result seems to place the patent system as viewed by the court at odds with the best pharmaceutical practices. It also remains unclear whether merely claiming such compositions as pharmaceutical compositions—that is, comprising pharmaceutical adjuvants and excipients and the like—will be enough, in view of the *Mayo* prohibitions against ‘routine, conventional and well-understood’ activities not being ‘enough’ to render a natural law (extended to natural products) patent eligible,” Noonan said.

Underwood suggested that *Myriad* may affect the nutraceutical companies he referred to earlier.

“Some are being run and/or financed by biopharmaceutical veterans and are pursuing a traditional biopharma-type strategy that involves securing venture capital financing to fund early stage development and then seeking strategic partnerships. Traditionally, acquiring strong patent rights has been a key component of this strategy. However, it is unclear if this will hold true for nutraceutical companies in view of the *Myriad*

decision. The *Myriad* decision was limited to a holding that naturally occurring nucleic acids are not patentable, but defendants will certainly try to extend that holding to cover other naturally occurring compounds. Further legal developments following *Myriad* will have a significant impact on nutraceuticals, since the key ingredients in nutraceuticals are generally naturally occurring compounds that are found in naturally occurring food products,” Underwood said.

Stephen A. Bent of Foley Lardner, Washington, told Bloomberg BNA that the *Myriad* ruling represents a decade-old debate between more inclusive or liberal and less inclusive or conservative viewpoints.

“The liberal-to-conservative continuum has graduated in terms of the ‘appropriate’ balance of structural versus functional claim limitations,” Bent said. “For inventions that turn on information content or information manipulation, including many business methods, software and informational macromolecules, we’ve seen in recent years a replay of arguments that courts addressed over 25 years ago, but now the conservative perspective seemingly has the upper hand.”

Bent said that the implications of this tilting in the debate favor more narrowly drawn patent claiming strategies, such as in the personalized-medicine arena, and more numerous patent filings made later in the developmental cycle of a given technology.

Deborah L. Lu of Vedder Price, New York, said, “In view of the attacks on Section 101 in *Mayo* and *Myriad*, there may be more clarity on 35 U.S.C. § 101 (patent eligibility) with the *Alice Corp. v. CLS Bank Intl.* case [U.S., No. 13-298, cert. granted 12/6/13] that has been granted certiorari by the Supreme Court.”

Appellee CLS Bank in its petition against granting cert cited the Supreme Court’s ruling in *Mayo*, arguing that, absent an inventive concept, a method of performing well-understood economic activity is not patent eligible under 35 U.S.C. § 101. The risk management economic concept at issue in this case is merely an abstract idea, the brief said.

According to Lu, a LSLR advisory board member, “Even though it is a software and business method case, it could lead to ‘abstractness’ affecting bioinformatics patents.”

Diagnostic Patent Eligibility Undermined. Sheppard Mullin Richter & Hampton LLP attorneys Don Pelto, a LSLR advisory board member, and Joy Nemirow and Anthony Marshall said that while *Myriad* garnered a tremendous amount of mainstream media attention, it isn’t the decision with the largest impact on patent-eligible subject matter for the life sciences industry. “That distinction goes to *Mayo*, which has significantly affected patent applications in the area of diagnostics and personalized medicine.”

In *Mayo*, they said, the Supreme Court shifted away from determining whether the steps of a claim are transformative or are tied to a machine toward determining whether the steps of a claim consist of more than merely “well-understood,” “obvious,” “routine,” or “conventional” activities.

The *Mayo* decision “affects the life science industry in that investors and companies are unsure whether their diagnostics and personalized medicine products have or can acquire adequate patent protection.”

—DON PELTO, JOY NEMIROW AND ANTHONY MARSHALL,
SHEPPARD MULLIN RICHTER & HAMPTON LLP

“What the court leaves patent holders with is a very subjective standard for determining patent eligibility. As a result, the stability and clarity of the U.S. patent system with respect to the patent-eligible subject matter has been undermined. This affects the life science industry in that investors and companies are unsure whether their diagnostics and personalized medicine products have or can acquire adequate patent protection,” Pelto, Nemirow and Marshall said.

Noonan agreed, noting that the consequences of the *Mayo* case continue to reverberate, particularly when applied in the context of the *Myriad* decision.

“It is an open question what this combination will do to diagnostic methods, but there is at least one district court that has combined *Myriad* with the Supreme Court’s ‘law of nature’ precedent (in this case, *Parker v. Flook* [437 U.S. 584 (1978)]) to find such a method patent ineligible,” he said. “This case, *Ariosa v. Sequenom* (7 LSLR 1114, 11/15/13), will be one to watch at the Federal Circuit because the U.S. District Court for the Northern District of California made several logical leaps to craft a rule not mandated by either *Myriad* or *Mayo*, or *Flook*, for that matter,” Noonan said.

Noonan said that the court based its preemption analysis on the availability of commercially viable alternatives. “This has never been the standard. Indeed, the point of patenting is to leave room for competitors to enter the market—if at all—in a commercially disadvantageous position, until the patent expires, of course. Here, the district court was able to apply its subjective view regarding the patent because the Supreme Court’s recent decisions provide no objective analysis or analytical tools for courts to use. It is Justice Stewart’s pornography test applied to patent law,” referring to Supreme Court Justice Potter Stewart’s statement in *Jacobellis v. Ohio*, 378 U.S. 184 (1964), that hard-core pornography was hard to define but “I know it when I see it.”

Patent Term Adjustments Resolution? Another patent-related issue that will affect life sciences in 2014 is patent term adjustments, Pelto, Nemirow and Marshall said.

A PTA is additional time added to a patent term when prosecution doesn’t progress according to statutory deadlines due to Patent and Trademark Office delays and “is essential to patent life cycle longevity in the pharmaceutical and biotechnology industries,” they said. “Each day of patent life for pharmaceutical and biological products can equate to millions of dollars in revenues.”

There are two conflicting Federal Circuit decisions concerning PTAs on which the legal spotlight will be focused in 2014, they said.

In *Exelixis Inc. v. Kappos (Exelixis I)* in 2012, the U.S. District Court for the Eastern District of Virginia held that under the correct interpretation of the PTA statute, 35 U.S.C. § 154(b)(4)(A), “requests for continued examination [RCE] have no impact on PTA if filed after” the three-year statutory deadline that triggers the “B delay” period for purposes of PTA calculation (6 LSLR 1135, 11/16/12).

B delay occurs when prosecution hasn’t been completed within three years after the application was filed. Under this holding, the proper measure of B delay is from three years after the application filing date to the date the patent issued. Under *Exelixis I*, if an RCE is filed after the three-year period, the patent application continues to accrue PTA time during the B delay period.

In 2013, in *Exelixis, Inc. v. Kappos (Exelixis II)*, a different district court judge from the Eastern District of Virginia reached the opposite conclusion (7 LSLR 137, 2/8/13). In *Exelixis II*, the court found the idea that an RCE filed before the three-year deadline should be treated differently from one filed after three years to be an “absurd result.” Accordingly, the court determined that the PTO’s interpretation of the PTA statute and the resulting regulation (37 C.F.R. § 1.703(b)(4)), which disallows PTA for any time an RCE is under consideration regardless of when the RCE was filed, to be correct.

“Patent applicants and owners, therefore, will need to follow these [patent term adjustment] cases closely in 2014, as the result could extend the life of their patents, potentially increasing their revenues.”

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SHEPPARD MULLIN RICHTER & HAMPTON LLP

Pelto, Nemirow and Marshall said, “If the Federal Circuit affirms *Exelixis I*, it will be significant for patent applicants. Applicants who would otherwise not be eligible for PTA because of RCEs filed after the three-year deadline could in some cases increase the length of their patent terms by days, months, or even years. Patent applicants and owners, therefore, will need to follow these cases closely in 2014, as the result could extend the life of their patents, potentially increasing their revenues.”

Reverse Payment Settlements Still in Flux. Pelto, Nemirow and Marshall noted that even though the Supreme Court ruled in June in *Federal Trade Commission v. Actavis, Inc.*, 133 S. Ct. 2223 (2013), that drug patent litigation settlements are subject to a rule-of-reason analysis, it still left several issues unresolved. They also are known as reverse payment settlements because they involve payments from branded drug companies to generic drug companies in exchange for the generic staying off the market.

In analyzing whether the reverse payment settlement runs afoul of antitrust laws, the Supreme Court provided the following factors for courts to consider: the reverse payment settlement’s size, its scale in relation to the payer’s anticipated future litigation costs, its independence from other services for which it might represent payment and the lack of any other convincing justification. The court further said that it will leave to the lower courts the structuring of the present rule-of-reason antitrust litigation.

“With only this vague listing of factors and without any further elaboration, district courts will be grappling with how to apply these factors,” Pelto, Nemirow and Marshall said. “For example, district courts will have to consider how much weight each factor should be given: Should a larger size induce closer scrutiny for other factors like ‘any other convincing justification?’ What are other convincing justifications? How will ‘anticipated future litigation costs’ be calculated? Several issues, such as what qualifies as a payment, should a smaller universe of factors or more broad-ranging factors be considered, how to handle the underlying patent issues and effects of the generic company’s delay, are already being debated.”

District courts also may vary in their applications of the *Actavis* ruling until further clarification from circuit courts or the Supreme Court, they said.

“Prior to *Actavis*, the Second, Eleventh and Federal Circuits had held that reverse payments do not violate antitrust laws unless the exclusionary effect of the settlement exceed the scope of the patents at issue. By contrast, the Third Circuit held that reverse payment settlements were presumptively unlawful, and the Sixth Circuit held that reverse payment agreements were a per se violation of antitrust laws. District courts, in making their multi-factored *Actavis* analysis, may be influenced by their respective circuit courts’ pre-*Actavis* viewpoints, and thus reverse payments may have a more difficult time passing scrutiny within the Third and Sixth Circuits even under *Actavis*. A consistent application of the *Actavis* holding will likely require further clarification from the Supreme Court,” they said.

Pelto, Nemirow and Marshall advised that parties involved in abbreviated new drug application litigation will have to proceed with caution in their settlement talks because the law still appears to be in a state of flux.

Noonan said that in *Actavis*, while both the FTC and the biopharma industry, both branded and generic, could claim at least a partial victory, the FTC got closer to what it wanted than biopharma did.

“Courts are now empowered to assess antitrust liability for these types of settlement agreements and to do so without addressing the underlying validity or enforceability of the patents at issue,” Noonan said. “As a consequence, it is unlikely that ANDA litigants will enter into such agreements and thus the diversion of dollars from R&D to ANDA litigation will be encouraged.”

In addition, Noonan said, while the court was focused on the “payment” part of these agreements, the FTC has made it clear that it will use the *Actavis* decision to challenge other types of “compensation,” such as agreements not to launch an authorized generic by the branded drug company, thus expanding the scope of the decision.

Patent Exhaustion Debate Not Over? While the case before the Supreme Court in *Bowman v. Monsanto Co.* involved the patent exhaustion doctrine and the sale of seeds, life sciences attorneys and companies paid attention to the case because the ruling had the potential to affect self-replicating technologies such as man-made cell lines, DNA molecules and some nanotechnologies.

The court's ruling was heralded as a "big win" for the life sciences industry.

But Bent suggested to Bloomberg BNA that the nature of the *Bowman* ruling still requires careful drafting by life sciences attorneys. "The outcome of *Bowman* was not a surprise. The Supreme Court wasn't likely to sanction unrestrained replication of a patented article by a purchaser of the article," Bent said.

"More interesting for the future," Bent continued, "is the indication by Justice Elena Kagan that certain types of self-replication might not constitute infringement: 'Our holding today is limited—addressing the situation before us, rather than every one involving a self-replicating product. We recognize that such inventions are becoming ever more prevalent, complex and diverse. In another case, the article's self-replication might occur outside the purchaser's control. Or it might be a necessary but incidental step in using the item for another purpose.'"

Bent said that there is a suggestion in Kagan's statement of a different outcome if the patented article self-replicates outside of the purchaser's control or beyond the ambit of the article's primary purpose. "The uncertainty cast by this prospect will elevate the importance of careful drafting of 'conditional sale' agreements, viable in principle under state contract and federal anti-trust laws, which could fill a gap left by an evolving post-*Bowman* infringement exception."

Other Issues

Among the non-patent or personalized medicine issues raised by those Bloomberg BNA contacted, biosimilars and strategic alliances stood out.

Biosimilars. Pelto, Nemirow and Marshall said that biosimilars will remain a hot topic in 2014 as products come closer and closer to market, which will mean that litigation brought under the Biologics Price Competition and Innovation Act of 2009 (BPCIA) also will take up more of the spotlight.

They said that the Nov. 12, 2013, decision in *Sandoz, Inc. v. Amgen, Inc.* by the U.S. District Court of the Northern District of California is being heralded as the first district court decision interpreting the BPCIA statute (7 LSLR 1116, 11/15/13).

The court held that a party seeking biosimilar approval must submit an application with the FDA prior to seeking a declaratory judgment of patent invalidity under the BPCIA provisions. Thus, the biosimilar applicant can't avoid the statutorily mandated patent ex-

change, including an exchange of a list of patents that the biologics license applications holder and the biosimilars applicant believe are at issue in a preliminary injunction suit, and other rules set forth in the BPCIA by the mere filing of a declaratory judgment prior to its application submission.

"Amgen signals the beginning of courts facing issues arising under the BPCIA statute. Whether other district court jurisdictions will follow it when faced with a similar issue or the appeals court will reverse remain to be seen [see related item in the *Court Proceedings* section]. Furthermore, other issues, including various interpretations of the other provisions of BPCIA, relating to biosimilar litigation will likely continue to be evolving during 2014," Pelto, Nemirow and Marshall said.

Hasko added that "in advising life sciences companies developing biologic products, we are constantly challenged to anticipate the degree to which biosimilars will enter a given market, whether in the U.S. or elsewhere. The lack of clarity on biosimilar product development processes in the U.S., and the fact that data regarding biosimilar product availability and competition in Europe and elsewhere are still being collected and analyzed, will perpetuate the life science industry's struggle to understand and manage the implications of biosimilar product introduction and competition in 2014."

Lu said that biosimilars likely will be another hot topic and guidelines may emerge from the FDA. "Perhaps the approval of monoclonal biosimilars by the European Medicines Agency [7 LSLR 752, 7/12/13] may influence the FDA biosimilar approval."

Noonan, however, said there is really nothing happening in biosimilars. "And there won't be until someone actually files an application."

Strategic Alliances. Hasko said that with the economic climate improving, she is seeing an impressive number of high-quality strategic alliances being struck at all phases of life sciences product development.

"In 2013, pharma and large biotechs invested in their pipelines by in-licensing product candidates, structuring deals that reward the licensors well for success. With the IPO [initial public offering] window having been opened in 2013, pharma and large biotech have had to compete for product opportunities with alternative product development funding from public sources to succeed in in-licensing efforts, requiring these transactions to be thoughtfully structured and carefully balanced. Initial indications for 2014 are that these drivers will continue to enable licensors with good product candidates to strike deals that optimize product potential," Hasko said.

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