

Life Sciences Law & Industry Report asked attorneys and biopharma executives on its editorial advisory board and other experts, including ones from the United Kingdom, Canada, and Japan, to predict the top issues for 2013. In years past, legislation and regulations concerning the abbreviated approval pathway for biosimilars, patent reform, and health care reform figured prominently, and they were cited again for 2013 relating to their implementation. But those commenting paid the most attention to the impact of court rulings from the previous year and anticipated 2013 rulings on issues such as whether isolated DNA and diagnostic methods are patentable subject matter. Two attorneys indicated that the Supreme Court's ruling in the *Myriad* "gene patent" case will be remarkable in that its impact will be immediate.

Gene, Method Patent Rulings Said Top Issues for Life Sciences This Year

For 2013, much of the focus in the life sciences industry will be on patents, experts in life sciences predicted for BNA. Patentable subject matter in the United States and Europe, the scope of the patent infringement "safe harbor" provision, and "patent exhaustion" will be the top issues for 2013 as a result of the impact of past and anticipated court rulings, they said.

In addition to court cases, those commenting for BNA also cited as important this year the implementation of patent reform, increased collaborations between industry and academia, and changes in the patent approval system in the United States and abroad.

In contrast to the year preceding, interviewed experts offered almost no comments regarding developments at the U.S. Food and Drug Administration and the National Institutes of Health. Only one commented in detail about personalized medicine, acknowledging that it may not be commercially feasible but stressing that the life sciences industry will pursue "mass customized therapies" because they will be more effective and therefore more valuable. The abbreviated approval pathway for biosimilars, which had figured so prominently in last year's Outlook, was mentioned, but mostly to indicate that it could be some time, if ever, before it was actively utilized.

Top Life Sciences Issues in 2013

1. Supreme Court's *Myriad* ruling.
2. Patentability of diagnostic method patents.
3. Self-replicating organisms and the doctrine of patent exhaustion.
4. Scope of the "Safe Harbor" from patent infringement provision.
5. European Unitary Patent.
6. Patentability of inventions related to hESCs.
7. Implementation of U.S. patent reform.
8. Off-label promotion as commercial speech.
9. Patent cliff and increased collaborations.
10. Biosimilars.
11. Economics of personalized medicine.
12. Patent changes in Canada, the U.K., Europe, and Japan.

In recognition of the increasing global reach of the industry, BNA asked for forecasts not only from attorneys and industry representatives from the United States but also from Europe and Asia.

1. The Supreme Court's *Myriad* Ruling

Overwhelmingly, those commenting ranked the upcoming decision in *Association for Molecular Pathology v. Patent and Trademark Office*, commonly known as the *Myriad* case, as No. 1.

The court granted certiorari on Nov. 30, 2012 (6 LSLR 1227, 12/14/12). J. Mark Waxman of Foley & Lardner, Boston, said the court's ruling "could upend the biotechnology industry depending on how the justices rule."

Kevin E. Noonan, of McDonnell Boehnen Hulbert & Berghoff LLP, Chicago, told BNA that the Supreme Court did not grant certiorari in *Myriad* to affirm the ruling of the U.S. Court of Appeals for the Federal Circuit that isolated DNA, cDNA, and one DNA-related method for detecting the BRCA1 and BRCA2 genes associated with breast cancer are patent-eligible (6 LSLR 857, 8/24/12).

"Taking a clue from the [Supreme Court's] *Mayo* decision [in which the high court found that claims directed to a method of determining the dosage of a drug given to a patient was unpatentable] (6 LSLR 284, 3/23/12), we can expect that the court will once again try to define what is "enough" patent protection regarding genes and DNA. The prospects are for many amici to argue that permitting genes to be patented is immoral, unnecessary, and will impede progress in areas like personalized medicine. Whether the court is persuaded by these arguments will depend on their own internal biases—Justice [Stephen] Breyer is particularly susceptible to these arguments—and whether a sufficient number of people who actually know what they are talking about file amicus briefs."

The "smart money," Noonan said, is on the Supreme Court finding that the cDNA molecules are patent-eligible as something that is manufactured and because they do not occur in nature. He added though, that, if co-plaintiff American Civil Liberties Union persuades the court that what matters is the unpatented sequence, these "embodiments" may also be at risk. Genomic or isolated DNA likely will be found to be ineligible for patent protection, Noonan said, based on the standard of "enough" being added to nature in accordance with *Mayo*.

It is uncertain whether oligonucleotides—short fragments of nucleic acids with defined chemical structure—will be found to be different "enough," Noonan suggested. He said this will depend on whether the Department of Justice weighs in strongly with some version of the "magic microscope" test—denying patent eligibility if one could zero in on a gene and determine if one was looking at the same thing that could be seen in the isolated DNA—that it had argued when *Myriad* was before the Federal Circuit.

"The risk is for the court to enunciate some broad prohibition on patenting 'products of nature,' a position advocated by certain academics. The penchant for Justice [Stephen] Breyer to rely on misconceptions like those of Rebecca Eisenberg of the University of Michi-

gan Law School concerning the *Mayo* decisions gives me pause to hope similar fantasies are not the basis for such a decision," Noonan said. Eisenberg's major thesis, set out in an article by Michael A. Heller and Eisenberg, "Can Patents Deter Innovation? The Anticommons in Biomedical Research," *Science*, Vol. 280, pp. 698-791, May 1998, which was cited by Breyer, has been the "tragedy of the anti commons"—a coordination breakdown where the existence of numerous rightsholders frustrates achieving a socially desirable outcome—with regard to gene patents. "This is a 'tragedy' that has not appeared in the more than 15 years since she proposed it," Noonan said.

Ronald M. Daignault and Matthew B. McFarlane of Robins, Kaplan, Miller & Ciresi LLP, New York, said, "What's remarkable about *Myriad* is its immediacy—it will have instant commercial and legal impacts on biotechnology innovation, regardless of whether the impacts will largely maintain the status quo or alter in fundamental ways the patentability of DNA-based inventions. There will be an immediate reaction."

They suggested that the court may use its ruling to issue its first broad pronouncement of the law regarding patent-eligible subject matter under 35 U.S.C. § 101 since the court's decision in *Diamond v. Chakrabarty* in 1980. "Indeed, *Chakrabarty's* pronouncement that patentable subject matter includes 'anything under the sun that is made by man'—already cast in doubt with other recent Section 101 decisions—may have little life left. The question presented in the certiorari petition—'Are human genes patentable?'—asks the court to consider the scope of patent eligibility against a backdrop of potentially politically-charged consequences: whether health care providers can test for the presence of genetic mutations in a patient linked to an increased prevalence of certain cancers without infringing valid patents."

If the sentiment expressed in Justice Breyer's unanimous opinion in *Mayo* is any guide, Daignault and McFarlane suggested, the court may view the patent eligibility of human genes skeptically. "On the other hand, the court is being asked to establish clear rules that will guide patent practice for inventions based on DNA sequences for years to come, and coming up with a rational, workable rule to govern such a broad technological area may prove difficult."

Howard W. Bremer, emeritus patent counsel for the Wisconsin Alumni Research Foundation, Madison, Wis., said that the university/nonprofit sector relies on a motivation factor in its technology transfer effort to take the results of research to the public for its benefit, which is the thrust and goal of the Bayh-Dole Act, which became law the same year as the *Chakrabarty* decision.

"With much technology involving isolated molecules, as are being considered in the *Myriad* case, already having been transferred to the private sector for the benefit of the public, a bright line decision by the court in the case that is negative to patentability would put at risk extant patents," Bremer said. "It would also have a

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major chilling effect, not only in upsetting property rights which have existed for many years and which the private sector has relied upon, but also stifle the motivation of the private sector to engage in product development and therefore to the potential for successful transfer of technology from the university/nonprofit sector to the private sector. The ultimate result would be detrimental to the public welfare. The private sector could readily conclude that the risks would greatly outweigh the potential for reward!”

Deborah L. Lu of Vedder Price PC, New York, said, “I think the Supreme Court certified the wrong question: the subject matter should have been isolated genes. By inserting the word ‘human,’ the court appears to be trying to feed into public perception, and perhaps public paranoia, that anything human should not be patentable.”

2. The Patentability of Diagnostic Method Claims

Many of those contacted by BNA also said they believed that the aftermath of the *Mayo* ruling, specifically how the Patent and Trademark Office and the Federal Circuit would interpret the Supreme Court’s decision, was the No. 2 issue for 2013.

The Supreme Court in *Mayo*, Noonan said, held that Prometheus’s method claims for adjusting a drug dosage after observing a patient’s reaction to a drug administration were not patentable because they recited a law of nature and didn’t add “enough.” Jill E. Uhl, director of intellectual property for Johns Hopkins University Tech Transfer, told BNA, “Basically, no one knows what will happen or whether or not diagnostic and personalized medicine claims will remain patentable subject matter. The stakes are high. There are quite a few companies that specialize in diagnostic tests and/or personalized medicine. How can they guarantee that their products will be protected?”

Don J. Peltó of Sheppard Mullin Richter & Hampton LLP, Washington, said, “This decision could result in increased litigation in the medical diagnostic space and a lot of existing patents could go down.”

Lu, however, said, “I do not believe that *Mayo v. Prometheus* spells the end of diagnostic patents, as stated in an article I co-wrote earlier this year (6 LSLR 845, 8/10/12), although method claims in diagnostic patents are subject to increased scrutiny.”

3. Self-Replicating Organisms and the Doctrine of Patent Exhaustion

Bremer, Lu, and Noonan cited the potential importance of *Bowman v. Monsanto* (U.S., No. 11-796, review granted 10/5/12), which deals with harvesting self-replicating seed produced from patented plant technology and for which the Supreme Court granted certiorari Oct. 5, 2012, to the appeals court’s ruling finding infringement.

Monsanto argued that letting the Federal Circuit’s ruling stand would create an exception to the patent exhaustion doctrine for self-replicating technologies. The “first sale” or “patent exhaustion” doctrine provides that the first unrestricted sale by a patent owner of a patented product exhausts the patent owner’s control over that particular item. The questions presented to

the court are whether the Federal Circuit erred in refusing to find patent exhaustion in patented seeds even after an authorized sale and by creating an exception to the doctrine of patent exhaustion for self-replicating technologies.

Lu said, “The question as to whether dealing with a self-replicating organism makes a difference with respect to patent exhaustion will hopefully be answered, or at least clarified in 2013.”

Noonan said that the case is “worrisome” because the solicitor general specifically told the court that defendant Vernon Hugh Bowman, whom Monsanto contended infringed its patent, was wrong in asserting that the Federal Circuit based its decision on the discredited line of cases in *Mallinckrodt Inc. v. Medipart Inc.*, 976 F.2d 700 (Fed. Cir. 1992). That decision arguably was overruled by the high court’s ruling in *Quanta Computer v. LG Electronics*, 553 U.S. 617 (2008), which extended the principle of patent exhaustion, he said. The court granted certiorari anyway.

“This is not a ‘patent exhaustion’ case, but Bowman is arguing that it is,” Noonan said. “Now, the court could merely take the opportunity to vacate and remand with a strong warning that the Federal Circuit should disclaim any aspects of the case based on patent exhaustion because arguably the district court may have based its decision on exhaustion. But there is a risk that the court could come out with some rubric that patent rights on a seed are exhausted upon sale, and that the only way to restrict their use is by contract—which of course would prompt someone to argue an antitrust violation or at a minimum patent misuse. This concept could certainly bleed over into other areas.”

There also is a risk, Noonan said, that “the court could adopt Bowman’s scientifically ludicrous position that a recombinant seed—or any other recombinant ‘thing’—is ‘made’ when a gene is introduced, so that growing more of the recombinant seeds—or any other recombinant ‘thing’ is not a making under 35 U.S.C. § 271(a). (Shudder).”

Bremer suggested that the fact that the court granted certiorari despite the solicitor general’s brief may not mean that the court is seeking a new and different solution to or modification of the opinion of the Federal Circuit because it requires only four justices to grant certiorari. “It may well be that at least those four justices might wish to clarify the exhaustion doctrine in some way. In my view, affirmation of the Federal Circuit would be the simplest solution and would be acceptable to the university community. It would continue to be the motivation factor for the private sector to license self-replicating technologies for development and marketing under the auspices of licensing arrangements with universities and thereby serve the public interest.”

4. The Scope of the ‘Safe Harbor’ From Infringement Provision in Section 271(e)(1)

Sharon Roberg-Perez of Robins, Kaplan, Miller & Ciresi LLP, Minneapolis, told BNA that biotechnology litigants should expect continued uncertainty as to the scope of the safe harbor provision under 35 U.S.C. § 271(e)(1), a provision intended to shield companies from patent-infringement liability in certain circumstances. Under the statute:

[i]t shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the

United States a patented invention . . . solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products. 35 U.S.C. § 271(e)(1).

“The Federal Circuit’s jurisprudence on precisely which activities are protected is in flux, with Chief Judge Randall R. Rader and Judge Kimberly Ann Moore squaring off in an unresolved debate,” Roberg-Perez said. In *Classen Immunotherapies Inc. v. Biogen IDEC*, 659 F.3d 1057 (Fed. Cir. 2011) (5 LSLR 856, 9/9/11), the patentee asserted claims directed to a method of immunization according to an immunization schedule optimized to decrease the risks of later development of certain chronic diseases. Defendants Biogen and Glaxo-SmithKline both were accused of infringement because they had participated in studies to evaluate the association between the timing of childhood vaccinations and the development of type 1 diabetes. Defendants were successful in front of the district court in arguing that their activities fell within the safe harbor provision. On appeal, patentee Classen argued that the safe harbor provision applies only to activities undertaken to obtain pre-market approval for generic drugs, which are carried out before expiration of the branded company’s patent.

The Federal Circuit agreed, with Rader joining Judge Pauline Newman, announcing that the safe harbor provision “does not apply to information that may be routinely reported to the FDA, long after marketing approval has been obtained.”

In reaching this conclusion, Roberg-Perez said, the court relied on the fact that the safe harbor provision was intended to correct for an unintended distortion of the patent term that is a result of pre-market regulatory requirements. Moore dissented, stating, “Nowhere does the statute limit the safe harbor to pre-approval uses.”

Roberg-Perez added, “Moreover, when the Supreme Court considered the boundaries of the safe harbor provision in *Merck KGaA v. Integra Lifesciences I Ltd.*, 454 U.S. 193 (2005), it had reversed the Federal Circuit’s narrow interpretation of 35 U.S.C. § 271(e)(1), repeatedly stating that the text of the statute makes clear that all uses of patented inventions that are reasonably related to the development and submission of information for submission under federal law fall within the exemption.”

Less than a year later, in August 2012, the Federal Circuit appears to have done an about face in *Momenta Pharmaceuticals, Inc. v. Amphastar Pharmaceuticals Inc.*, 686 F.3d 1348 (Fed. Cir. 2012) (6 LSLR 821, 8/10/12), Roberg-Perez said. In a case between generic manufacturers of blood clot medication, the court vacated a district court’s grant of a preliminary injunction. “The basis: Patent holder Momenta was unlikely to succeed on its infringement claim because its competitor’s post-market approval activities fell within the scope of the safe harbor provision,” she said.

In an opinion authored by Moore, to which Rader dissented, the court cited *Merck KGaA* to conclude that the text of the safe harbor provision exempted from infringement “all uses” of patented inventions that are “reasonably related to the development and submission of any information” to the Food and Drug Administration. Further, the information need not actually be submitted to FDA, but only of the type that would be appropriate to include in a submission. Rader dissented, rely-

ing on legislative history to discuss how the safe harbor provision had only been enacted because it was “limited in time, quantity and type.”

Bremer said, “In my view the language in the legislation itself provides a basis for interminable argument about the scope of the provision. To use the term ‘reasonably related’ in any piece of legislation invites dispute and disagreement since definitive scope is completely absent. In that regard it is unfortunate that there seems to be no room embraced by the statutory language for excluding certain information from the exemption on the basis of the phase of research or the particular submission in which it could be included. The non-definitive language of the statute is a lesson in poor legislative drafting which has many, perhaps unintended, consequences which would appear to potentially establish a complete defense to a claim of patent infringement for the life of the patent with regard to use of the patented technology to develop information for both pre and post market approval as well as in response to any statutory requirements under the FDCA [Federal Food, Drug, and Cosmetic Act].”

Roberg-Perez concluded, “As biotechnology research leads to more and more commercial applications and regulatory oversight, the scope of the safe harbor provision under Section 271(e)(1) will be tested, and the debate between Judges Rader and Moore will continue.”

5. European Unitary Patent

Some of those picking the top issues for 2013 for BNA turned to the unitary patent in Europe and its potential effect on life sciences companies that manufacture or plan to manufacture globally.

Under the European Union patent regime, patent protection is obtained separately in each EU country, and obtaining a patent that is valid across the EU costs an average of \$47,000, the majority of which is related to translation costs. Hugh Goodfellow of Carpmaels & Ransford, London, told the BIO IP Committee Conference in Charleston, S.C., that he has seen translation costs for EU patents reach \$500,000 (6 LSLR 1166, 11/16/12).

On Dec. 11, 2012, the European Parliament voted in favor of proposals to create a single patent valid in all but two—Spain and Italy—of the EU’s 27 member nations (6 LSLR 1266, 12/14/12). The move would establish accepted languages for patents and create a Unified Patent Court (UPC), with headquarters in Paris, for hearing patent disputes. According to the European Commission, an EU unitary patent may cost as little as \$6,100. The system also would reduce litigation costs, as patent holders no longer would need to file suit in multiple EU member countries to enforce their rights.

Paul Chapman of Kilburn & Strode, London, said that, assuming that the Court of Justice for the European Union (CJEU) follows the EU advocate general’s opinion to reject Spain and Italy’s challenge to the approval of the unitary patent system, the Unified Patent Court Agreement would take effect on Jan. 1, 2014, or after 13 states, including the United Kingdom, France, and Germany, have ratified it.

“The Unitary Patent Regulation and the applicable translation arrangements will apply from Jan. 1, 2014 or the date when the Unified Patent Agreement enters into force, whichever is the later. Therefore, in 2013 we are likely to see moves to ratify the treaty in many member

states,” Chapman said. “Although there has been intense lobbying over certain aspects of the treaty, it is now unlikely that further changes will be accepted.”

Goodfellow told BNA, “The notion of a European Unitary Patent must be welcomed. What has met with less enthusiasm is the manner in which Unitary Patents will be enforced. Hand-in-hand with the Unitary Patent Regulation comes the UPC, created by a separate inter-governmental agreement.”

Current users of the system will over the next few years need to decide whether the Unitary Patent and the associated UPC is a good or a bad thing, Goodfellow said. “One imagines that many will sit and watch developments from the sidelines, in the meantime opting out—at least during the initial seven year transition period—until it is clear where the wise money is going. But even seven years is probably not long for a sufficient bolus of case law to accumulate to give users confidence that the court knows what it is doing. In the short term, it may be that the national patent system becomes resurgent, as companies decline to have their patents litigated before the UPC, and prefer the existing system where as plaintiff you can decide your forum of choice. But of course, defendants sued for infringement will not have that luxury, and so sooner or later large companies are likely to experience the system whether they like it or not,” Goodfellow said.

Looking at the new patent system from a U.S. perspective, Sarah Rouse Janosik, corporate IP counsel for Onyx Pharmaceuticals, which is based in South San Francisco, Calif., said, “It remains to be seen whether life science companies will utilize this unitary patent. Given the high stakes, companies may seek to avoid the risk of a single ruling invalidating their patents across Europe. Those that can afford to apply for patents and litigate in multiple countries may continue with an individualized member country strategy.”

6. Patentability of Inventions Related to hESCs

In the United States, on Jan. 7, 2013, the Supreme Court denied certiorari and therefore ended the challenge by the plaintiffs/petitioners in *Sherley v. Sebelius* that federally funded hESC research violates the Dickey-Wicker Amendment, which bans federal funds for research that destroys human embryos (*see related item in the Court Proceedings section*). In Europe, according to Chapman, the controversy regarding hESCs concerns the patentability of hESC-related inventions.

The CJEU ruled Oct. 18, 2011, in the case of *Brüstle v. Greenpeace* that a process developed for medical research that involves the removal of a stem cell from a human embryo but also leads to the destruction of the embryo cannot be patented, which was interpreted in some quarters as imposing a blanket ban on patenting in the field (5 LSLR 994, 10/21/11). The CJEU was asked by the German Supreme Court to consider a set of questions designed to assist in the interpretation of what exactly was meant by the term “embryo” as used in the EU Biotech Directive and implemented in German national law (and by extension elsewhere in the national law of the other EU member states). The CJEU decided that it was use of a human embryo as a “base material” for a hESC invention that would place the practice inside the definition of subject matter excluded from pat-

entability by the terms of the Biotech Directive. The decision also was seen widely as influencing the revised *Guidelines for Examination* issued by the European Patent Office in June 2012 (6 LSLR 966, 9/21/12).

On Dec. 22, 2012, the Federal Court of Justice of Germany (BGH) issued its ruling in the *Brüstle* case following the return of the answers from the CJEU. The full decision is not yet available. “However, it is clear from the BGH press release that the court also shares the EPO view that nondestructive procedures for derivation of hES cells are not excluded from patentability,” Chapman said. “Further, it seems that a cell taken from a blastocyst is also not considered to be an embryo since it is not possible to commence the process of development into a human being. An unanswered question from the CJEU ruling in the *Brüstle* case is whether the CJEU was right in its answer to the question posed by the BGH on the definition of an embryo as including a parthenogenetically activated oocyte. Such parthenotes are, in essence, an oocyte which has been caused to enter into a limited cycle of cell division, but where the parthenote ultimately fails to develop into a viable embryo.”

In a case now pending before the U.K. high court, it is being asked to hear this question, and an answer is expected in 2013, although it too might result in a further referral to the CJEU, Chapman said. “The case law is moving but struggling to keep up with the science at times. Fact specific cases such as *Brüstle* at the CJEU are also not generating lasting precedents as some might have imagined. Inevitably, given the hopes invested in stem cell therapy the research is proceeding in both hES and the alternative non-embryonic derived areas of adult mesenchymal stem cells and induced pluripotent stem (iPS) cells. There are other appeals pending before the EPO and national courts which could lead to further important rulings also. It will remain to be seen how the national patent offices, the European Patent Office and national courts will apply the BGH ruling in the *Brüstle* case. Further amendments and clarifications may be issued as a result,” Chapman said.

7. Implementation of U.S. ‘Patent Reform’

Noonan noted that the changeover in the America Invents Act from first-to-invent to “first inventor to file” (FITF) goes into effect on March 16 (5 LSLR 923, 9/23/11), and said there are many questions about how the PTO’s proposed implementation will play out. “I predict a flood of continuation and divisional applications will be filed just prior to the effective date, because the PTO has set out a minefield that will convert applications to a FITF regime if there are any claims that the office deems are not supported by the original application.”

Uhl said, “At least from the university perspective, becoming a first to file country will have dramatic effect on our patent filing and management. The patent office has already begun to insist that provisional applications are fully supportive of any later written claims. Even though this has always been the law, in the past the patent office has been willing to grant priority to you when the provisional description is less than complete. Now, however, since the first inventor to file will be granted the patent (as opposed to the true first inventor), the patent office is insisting that the provisional be fully enabling and fully describe your invention before they

grant you priority for a later filed application. As a university, we used to file virtually all of our inventions as cover page provisionals. We took the year provided to continue to work on those inventions and at the 12 month mark, knew a lot more about our invention, including whether it was worth pursuing by filing a utility or PCT [international Patent Cooperation Treaty] application. Having to file fully drafted provisional applications is costing us approximately \$5,000-10,000 more per application. This means that we will have to make decisions about what we file much earlier and certainly before we really know which inventions are best suited to improve public health.”

8. Off-Label Promotion as Commercial Speech

Janosik noted that in the Dec. 3, 2012, ruling in *United States v. Caronia* (6 LSLR 1230, 12/14/12), the U.S. Court of Appeals for the Second Circuit held that the FDCA should be construed as not prohibiting off-label promotion of an FDA-approved drug that is neither false nor misleading. The decision vacated the criminal conviction of a pharmaceutical sales representative for off-label promotion on the basis that the sales representative was impermissibly prosecuted for his speech in violation of the First Amendment.

“The full impact of the Court’s decision remains to be seen,” Janosik said. “It is important to note that the decision is currently binding only within the Second Circuit. Moreover, a petition for a hearing by the full panel of Second Circuit judges, and, eventually, for writ of certiorari to the U.S. Supreme Court may lie ahead. The FDA and federal government have frequently relied on off-label promotion as the basis upon which the government has achieved substantial monetary settlements under the False Claims Act. It is unknown whether the FDA will refine its post-market regulatory and enforcement activities to focus more closely on prosecutions that are based on off-label promotion that the agency regards as false and misleading.”

The effect of the decision on the government’s application of the False Claims Act to promotional activities is also yet to be determined, she said, although this decision is likely to influence the willingness of companies to settle for substantial amounts, or for corporate executives to plead guilty to strict liability misdemeanor offenses under the FDCA relating to truthful, off-label promotion.

9. The ‘Patent Cliff’ and Increased Collaborations

The patent expiration of various big-selling drugs, or the “patent cliff,” will continue throughout 2013, Janosik said. “While overall losses associated with it are projected to be less in 2013 than 2012, a number of blockbuster drugs will go off patent this year.”

The 2013 expiration list includes patents covering Eli Lilly’s anxiety and depression drug Cymbalta; Purdue Pharma LP’s OxyContin, an opioid for pain management; Novartis’s Zometa injection, a treatment for hypercalcemia of malignancy caused by high calcium blood levels due to cancer; Genentech/Roche’s Xeloda, an oral chemotherapy treatment for metastatic colorectal and breast cancer; Warner Chilcott’s Asacol for the

treatment of ulcerative colitis symptoms; and Novartis’s osteoporosis treatment Reclast, among others.

“The patent cliff is generally portrayed as a negative event for the pharmaceutical industry, and it will be interesting to see how companies respond,” Janosik said. “Revenue lost through patent expiry will likely be broadly offset by sales of new products. Pharmaceutical companies will also likely strengthen their presence in emerging markets and seek growth strategies based on smaller or medium-sized acquisitions.”

Asher Rubin of Hogan Lovells, Baltimore, said that in 2013 he expects that the life sciences industry will see more, and more creative, collaborations between academic medical centers and research universities and industry. “More specifically, I expect industry of all types—large pharma, biotech, biopharma and device companies—to bypass the more traditional route of partnering with research-stage companies, which previously had licensed pre-clinical technologies from the academic community, and to license and collaborate directly with universities.”

Rubin said he believes this changing dynamic is occurring for several reasons. Since venture funding was not available for earlier stage investments during the fiscal crisis, many academic researchers were left with few options to develop their discoveries other than through use of government grants, venture philanthropy, and similar funding mechanisms. “Consequently, academic institutions may have advanced their technologies to a stage—pre-investigational new drug application or phase 1 trials—where industry is provided with data that is far more advanced than it would have been provided [with] historically. Accordingly, industry can better assess a technology in order to partner directly with the academic institutions,” Rubin said.

He added that not all academic technologies have advanced to clinical trials, and, without most venture funds being able to commit funding to take these projects to a stage appropriate for “partnering” with Big Pharma, Big Pharma will be reaching directly into the academic lab to find its next generation of innovative products.

10. Biosimilars

The approval of the Biologics Price Competition and Innovation Act of 2009 and FDA’s implementation of its abbreviated approval pathway for biosimilars has been a constant feature of the outlook for the year ahead, and it is included in this one. But the comments seem somewhat muted this time around.

Lu said, “The guidelines promulgated in 2012 [see 6 LSLR 467, 4/20/12] unfortunately provide more questions than answers. The guidelines indicate that the FDA would prefer to work with biosimilar applicants to develop a pathway rather than provide definitive suggestions. It will be interesting to watch how the application process unfolds in 2013.”

Waxman said developments in biosimilars are not yet having a major impact in the United States, but that products seem to be getting closer and closer to market.

Noonan said that FDA will refine its guidances on the biosimilar pathway under the Affordable Care Act, and added, “Whether this is enough to get any applicant to take the plunge remains to be seen.”

11. The Economics of Personalized Medicine

While for others commenting, the importance of the quest for patient-specific drugs may have been implicit, Rubin listed it as a major life sciences issue for 2013 and beyond.

“Although the promise of truly personalized medicine may be commercially not feasible, I think the development of, and transactions for, ‘mass customized’ therapies will become a commercial reality,” Rubin said. “This coincides with the search for, and development of biomarkers to identify the patients and/or patient populations that will respond best to particular therapies. Ultimately, I think industry will pursue these sorts of medicines because they will be more effective and the more effective that a medicine is the more valuable it is to both companies and patients. Put differently, prescribing a six-figure drug for patients looks entirely different from a cost-benefit analysis when payers know that the drug is being used by only the one-percent or two-percent of the patient population for which there is evidence that the drug works. I believe that this coincides with some of the general principles of the Affordable Care Act related to paying for effectiveness.”

Rubin used as an example Abbott’s Vysis ALK Break Apart Fish Probe Kit, which is designed to identify anaplastic lymphoma kinase-positive non-small cell lung cancer (NSCLC) patients for Pfizer’s approved NSCLC therapy, Xalkori (crizotinib), an oral first-in-class ALK inhibitor. “It’s estimated that Xalkori will cost approximately \$80,000 per patient (\$9,600 per month) and the Fish Probe Kit will cost approximately \$1,500. I believe that only a small percentage of NSCLC tumors (less than 5%) are ALK positive. When medicines are prescribed based on specific diagnoses in specified patient populations and patients are not prescribed drugs that will not help them, we eliminate unnecessary expenses and side-effects without primary effectiveness. Looked at from a financial perspective, the health care system can spend its limited resources testing at \$1,500 per test, so that it can spend \$80,000 on patients who will be helped—as opposed to spending \$80,000 on ‘all-comers’ until there is no more money left,” Rubin said.

12. Patent Changes in Canada, the U.K., Europe, and Japan

Those commenting to BNA from overseas on top issues for 2013 noted changes in the patent process in their own countries or regions.

Kilburn & Strode’s Chapman told BNA, “The UK business secretary, Vince Cable, has announced that he will be seeking to bring in some new provisions to aid innovation and allow companies better opportunities to exploit their intellectual property. Many of the provisions relate to education and information initiatives to “spread the word” about the importance of protecting ideas. However, one proposal is to provide for processing of UK patents to take no longer than 90 days, which would be a significant improvement. It is yet to be seen whether any new resources will be made available and also whether this proposal will apply only under special circumstances.”

Another issue that is likely to be important in the EU in 2013 relates to a change in procedure before the

EPO. “It is now more important than ever that applicants make sure they check the text of their European patents carefully before they are granted. This arises because there is now no possibility of correcting any errors in a patent at the EPO after it has granted. The EPO’s Enlarged Board of Appeal has recently ruled that it is not possible to correct errors, however minor, in European patents at the EPO after the patent has granted—unless the patent is in opposition or central limitation proceedings. This means that the onus falls even more heavily on patent proprietors to ensure that they are completely happy with the text of their European patents before they are granted,” Chapman said.

John Norman and Livia Aumand of Gowlings, Ottawa, told BNA how over the past several years, patents—and particularly pharmaceutical patents—in Canada have been invalidated for failing to meet the utility “promised” in the patent disclosure. “This doctrine is relatively new—from around 2005—and, as such, the methodology by which the courts have construed the ‘promised’ utility has been inconsistent and highly subjective. In the past year, the courts have moved back to the language of the claims in determining whether the patent makes a specific ‘promise’ of utility and, whether that promise had been met as of the Canadian filing date. It will be interesting to see what developments the law brings in 2013 as this problematic doctrine is further developed by the courts,” Norman and Aumand said.

According to Norman and Aumand, the Canadian government and the EU currently are negotiating the terms of the Comprehensive Economic and Trade Agreement (CETA).

Norman and Aumand said that there are three issues in particular that are at issue in the negotiations that have an impact on the life sciences industry:

- ensuring a right of appeal for innovator companies in the proceedings under the Patented Medicines Notice of Compliance to allow an innovator company to institute summary proceedings to obtain an order from the Federal Court prohibiting Health Canada from issuing marketing approval for a generic version of the innovator company’s drug until the patent(s) related to that drug expire;

- a two- or three-year data protection extension in the case of new indications is being sought during the CETA negotiations that would provide for fuller protection for innovators and bring Canada in line with the EU; and

- because in Canada, and unlike in the United States and Europe, no extensions of the patent term are granted if the patentee is unable to exploit its invention due to regulatory approval necessary to market a drug, some degree of patent term restoration is being sought in the CETA negotiations to ensure that a more appropriate period of exclusivity is awarded for those who invest in the research and development of innovative drugs.

Junko Iyoda of Taiyo, Nakajima & Kato, Tokyo, told BNA about changes in examination guidelines for patent term extensions in Japan.

He said that Japanese patent law includes a provision that corresponds to the extension of patent term stipulated in 35 U.S.C. § 156. In the past, the Japan Patent Office (JPO) has permitted registration of extension of

a patent term only in cases in which approval of production and marketing of a pharmaceutical product containing a novel active ingredient or a pharmaceutical product having a novel indication has been granted by the Ministry of Health, Labor and Welfare (MHLW), and registration of extension of the patent term is requested for a patent that protects the pharmaceutical product.

“In other words, in cases in which approval of production and marketing has been granted for a novel production process or a novel dosage formulation of a pharmaceutical product containing the same active ingredient and exhibiting the same pharmaceutical effect as a pharmaceutical product for which production and marketing approval has already been granted, registration of extension of the patent term of a patent that protects the novel production method or novel dosage formulation has not been permitted,” Iyoda said.

However, in 2011, the Supreme Court of Japan upheld a decision by the intellectual property high court that overturned the conventional position of the JPO and concluded that when a previously-approved pharmaceutical product does not fall within the technical scope of any of the claims of a patent for which an application for registration of a patent term extension has been filed, the application for registration of patent term extension should not be rejected due to the existence of the approved pharmaceutical product.

In the case of a patent term extension of a patent directed to a production process of a pharmaceutical product, the claimed production method of the patent and the production method specified in the MHLW approval should be compared when considering an application for registration of patent term extension. If the production method specified in the MHLW approval for production is not within the scope of the claimed production method, the application for registration of ex-

tension for the patent directed to the production method would be rejected.

In addition, registration of a patent term extension is performed with respect to a patent right as a whole, rather than for individual claims. “Therefore, the following case may occur,” Iyoda said. “A patent includes claim A that specifies a pharmaceutical effect of a pharmaceutical product (such as an analgesic containing substance X as an active ingredient) and claim B that depends from claim A and specifies a dosage formulation (such as an injectable solution) of the pharmaceutical product, and approval for production and marketing has already been granted to an analgesic in the form of a tablet containing substance X as an active ingredient. In such a case, patent term extension based on a subsequently granted approval for production and marketing of an analgesic in the form of an injectable solution containing substance X as an active ingredient will not be granted.”

While Iyoda acknowledged that this might seem somewhat inconsistent, he said the reason given by the JPO is that the pharmaceutical product claimed in claim A could already have been practiced after the prior approval of the analgesic in the form of a tablet, and since claim B includes all of the limitations of claim A, the scope of claim B is within the scope of claim A.

“Therefore, when both a pharmaceutical effect of a pharmaceutical product and a dosage formulation of the pharmaceutical product are to be claimed, it is advisable to avoid inclusion of both claims in one application if patent term extension is likely to be sought. This may be achieved, for example, by filing a divisional application including the claim specifying the dosage formulation, or by filing a patent application including a claim specifying the pharmaceutical effect and a separate patent application including a claim specifying the dosage form on the same day,” Iyoda said.

BY JOHN T. AQUINO