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## Outlook 2010

*Life Sciences Law & Industry Report* editorial advisory board members and other experts were asked to list the top issues for the life sciences industry for 2010. The economy, health reform legislation, follow-on biologics, comparative effectiveness research, patent law reform, Medicare reimbursement, and changes at the U.S. Patent and Trademark Office and the Food and Drug Administration topped their lists. Following is a discussion of the experts' leading 12 topics.

## Experts Predict Top Life Sciences Issues in 2010

**W**hile *LSLR's* 2009 list of top 10 topics focused on the effect of the new Obama administration on life sciences and on alternative methods for funding life sciences research and product development, the 2010 list highlights the importance of the economic recovery, industry consolidations, changes in emphases at two key federal agencies, and epic pending health reform legislation.

Two issues that figured prominently in anticipation of 2009 (3 LSLR 50, 1/16/09) are missing from the 2010 list: personalized medicine and stem cell policy. It could be that stem policy was left out because President Obama's March 9, 2009, executive order lifting the stem cell research funding restrictions of his predecessor President Bush (3 LSLR 233, 3/13/09) and approval by the National Institutes of Health Dec. 2, 2009, of the first set of human embryonic stem cell lines now eligible for federally funded research under guidelines resulting from the executive order (3 LSLR 1201, 12/4/09) effectively settled the matter. In fact, none of those con-

tacted included anything specifically about stem cell research in their lists.

As for personalized medicine, respondents suggested that its prominence on last year's list likely was the result of the 2008 passage of the Genetic Information Nondiscrimination Act (GINA) and a flood of articles on the great promise genetic research holds for individualized medicine—which made personalized medicine stand out against other, gloomier predictions. But a year later, the fact that there are no significant regulatory actions in the works concerning personalized medicine but there are significant questions—relating, for example, to how the Food and Drug Administration will approve individualized drugs and how their effectiveness for a small number of patients or even one patient can be demonstrated—indicate that its effect on health care may be years away.

However, Judith A. Hasko of Latham & Watkins LLP, Menlo Park, Calif., told BNA, "With health care reform likely to prompt more interest in targeted applications

of expensive treatments, personalized medicine will be a part of the path to more efficient use of health care resources. People need to see what the new health care landscape will be before they know exactly what role personalized medicine will play in achieving such efficiency.”

The clear repeats from the 2009 list in 2010 are follow-on biologics, comparative effectiveness research, patent law reform, and conflicts of interest.

**1. Economic Recovery.** Virtually all of those LSLR contacted said that whatever other issues were at the top of the list, all were tied in some way to economic recovery.

Jill E. Uhl of Arizona Technology Enterprises, Scottsdale, Ariz., told BNA, “If the recovery is slow or less vibrant than we all hope it is, we could see additional life science companies disappearing. The research to drug timeline is very long and that makes it difficult for new companies to survive and maintain investment. Partnering that with a dull economic recovery can only increase the number of failures we are likely to see.”

Kevin E. Noonan of McDonnell Boehnen Hulbert & Berghoff, Chicago, agreed. “Biotechnology companies were hard-hit by the financial crisis, because many of them are extremely dependent on venture capital and other forms of investment (since they are typically years away from a commercial product). How the industry recovers in 2010 will affect innovation in the sector, as well as whether promising biotechnology companies become takeover targets for big pharma,” Noonan said.

**2. Industry Consolidations, Collaborations.** Hasko predicted that consolidation in the life sciences industry will not subside, as major biopharmaceutical players will merge with or acquire other companies to enhance their pipelines and to take advantage of synergies.

“While private biotechnology companies will continue to seek an M&A exit in 2010 given the still chilly IPO [initial public offering] markets, M&As involving these companies will occur where the larger biopharmaceutical company perceives a strategic fit for the smaller company’s more advanced stage products, or, less often, if that biopharmaceutical company seeks the smaller company’s enhanced technology platform,” Hasko said.

She suggested that mid-size biopharmaceutical companies still will be attractive targets for larger biopharma companies for a variety of reasons, such as geographic reach, complementary or synergistic pipelines, and technical capabilities. “Mergers of the industry titans are a possibility in any market conditions, but given the strain of the last year there may be particular pressure in 2010 on the larger companies to spur consideration of mergers,” Hasko said.

J. Mark Waxman of Foley & Lardner, Boston, said that upcoming patent expirations for blockbuster drugs and the need of large pharma to continue to develop their pipelines will make merger and acquisition activity in 2010 more likely. “Small companies that have good products are running short of cash, may well get acquired, and get acquired sooner than they otherwise might have, by larger entities who have the cash or stock values to make strategic acquisitions,” Waxman said.

Belinda M. Juran of Wilmer Hale, Boston, said that consolidation and reorganization of priorities among the large pharma companies will have an effect on the

industry and specifically on opportunities biotech companies have to obtain funding through collaborations. “The Pfizer/Wyeth and Merck/Schering mergers and the Roche/Genentech acquisition mean there are fewer large large/medium-size pharma companies with which to collaborate. In addition, pharma companies engaging in consolidation, as seems to be the case with Roche/Genentech, may terminate certain collaborations as they reconcile their priorities as consolidated enterprises,” Juran said.

Waxman added that there may be an increased number of bankruptcies by start-up companies that simply run out of cash and are not able to negotiate an acquisition on acceptable terms.

But Hasko suggested that the situation will produce different strategies and a new type of collaboration. She said more biopharmaceutical companies will evaluate and pursue application of their technologies to various aspects of the clean technology industry, given the financial support available for such projects from government and private sources, and there will be more interest in collaborations between energy companies, universities, and biopharmaceutical companies in developing certain clean technologies.

**3. University Budget Cutbacks.** “University budgets may have a negative impact on the available technology for start up companies,” Uhl said.

“Most universities are being forced to cut back their patent budgets. This results in fewer patents being filed on work coming from university labs. This also translates into fewer technologies being marketed to the investment community. Fewer start-ups mean fewer successes,” Uhl said.

“With success stories already so limited in the life science space, any decrease in the number of available technologies will have a direct effect on the number of new company formations. Of course, this may then feed into the lack of a robust economic recovery and magnify the effects we already are feeling,” Uhl said.

**4. Follow-on-Biologics/Comparative Effectiveness.** Virtually all of those commenting acknowledged the importance for 2010 of pending health reform legislation that by its very nature will change many aspects of drug development and reimbursement. The House passed its version of the bill Nov. 7 (3 LSLR 1155, 11/20/09) and the Senate its version Dec. 24. Negotiations to reconcile the provisions of the two bills in both houses of Congress are ongoing.

Lacking a final bill on which they could comment, LSLR’s experts zeroed in on particular aspects of the legislation that, even if they did not remain in the final bill, likely would be splintered off and passed as separate bills. Noonan noted that both bills contain provisions for a follow-on biologics approval pathway to be administered by FDA with data-exclusivity terms of 12 years, “which have been opposed by many consumer groups as well as the White House and the FTC [Federal Trade Commission]. It is possible that this term will become part of the negotiations during the conference committee work to reconcile the bills, but in any case there will be follow-on biologics provided a reform bill is passed.”

Saying that FOB legislation “is ripe for action this year,” Uhl expressed the hope that it “would end up with the 12 years of data exclusivity that is currently

part of both the House and Senate bills and that would provide excellent protection from generics.”

Looking further down the road, Teresa Stanek Rea of Crowell & Moring, Washington, said, “Every major and mid-size pharma company is either trying to reinvent itself to focus on biologics or is spending more of its research and development dollars to get a piece of the action. The distinction between ‘generic’ and ‘brand’ will get murkier as more big pharma companies develop biosimilars.”

Rea said that there is an ongoing shift or repositioning in the industry by all types of pharma companies either in the form of increasing collaborations or outright acquisitions of biosimilar companies. “The market demand for biosimilars is great and the prices for those products will remain high compared to generic small molecules. Implementation of the FDA regulations for biosimilars will probably be a bit bumpy at first, but the industry will adjust and patients will benefit,” Rea said.

Wendy L. Krasner of Manatt Phelps & Phillips LLP, Washington, said that the Senate health reform bill includes provisions to establish a private nonprofit entity—the Patient Centered Outcomes Research Institute—to develop comparative clinical evidence through research while the House measure would provide for such initiatives through existing Agency for Health Research and Quality authorities. She added that comparative effectiveness research (CER) “has taken on a life of its own” thanks to the \$1.1 billion included for CER funding in the economic stimulus legislation and the ongoing efforts of the private sector.

“Indeed, CER efforts broadly defined can be viewed as emblematic of the nonstop pressure from health-care payers, both governmental and private, and both domestic and international to control costs. At the same time, the CER movement also reflects the increasingly tougher scrutiny of benefits and safety of life sciences offerings, which of course will be accelerated by health reform. Regardless of the form or the terminology, there will be new funding and new institutions to perform CER, which will provide new and improved information to consumers, providers, and other stakeholders focused on better measurement of value. The life sciences industry will be particularly affected by these initiatives as it tends to offer the newer products that may have to prove themselves both before and right out of the gate,” Krasner said.

**5. Medicare Reimbursement.** Krasner said that Medicare reimbursement will be of increasing importance in 2010.

She noted that the Senate health reform bill contains provisions that could affect Medicare pharmaceutical and biologic reimbursement. “As of the second calendar quarter after enactment, Part B payment for a biosimilar biologic product and for the reference biological product [brand name product] would be the average sales price plus 6 percent. The CER provision in the final Senate bill will not totally preclude the Centers for Medicare & Medicaid Services from using CER data in Medicare reimbursement and coverage determinations, although it would impose certain limits on using such research. And the Senate bill includes authority for an Independent Medicare Advisory Board, which would recommend ways to reduce Medicare per capita growth rate,” Krasner said.

She said CMS would be required to implement the board’s recommendations unless Congress enacts legislation achieving the same savings. “The concern of life sciences companies regarding the board is to what extent the board could recommend on its own initiative new authorities that could become part of the Medicare statute unless Congress does not act.”

Krasner said there has been some speculation that the board’s authority could be so broad as to enable it to recommend something like a “least costly alternative” reimbursement methodology. This speculation has increased in light of the recent U.S. Court of Appeals decision in *Hays v. Sebelius* (D.C. Cir., No. 08-5508, *aff’d* 12/21/09), she said. That case affirmed a lower court ruling that Medicare is required to pay for covered items or services at a statutorily prescribed rate and cannot use a lower cost alternative approach.

Krasner added that on Dec. 30, 2009, CMS released a proposed rule on Medicare and Medicaid payment incentives for “meaningful use” of electronic health records (EHRs) that will be available to hospitals, physicians, and certain non-physician practitioners (*see related item in the Federal News section*).

“CMS proposes a phased approach with ‘meaningful use’ criteria becoming more robust over time. Life sciences companies will recognize increasing value as functionality and use of EHRs develop under this approach,” Krasner said.

Giving an example, Krasner said that under CMS’s criteria for 2011, providers must utilize clinical decision support tools that support quality goals, and in later years, CMS expects to require reporting of adverse events to public health databases, which will be invaluable to surveillance activities. Eventually, providers will more broadly report standardized data that potentially could be used for research or other secondary purposes. “So while technically this may not kick in until 2011, this is perhaps the biggest sleeper issue with major long term and ongoing consequences for the industry,” Krasner said.

**6. Patent Reform Legislation/PTO Changes.** Both Uhl and Philip T. Chase, vice president of legal for Alnylam Pharmaceuticals Inc., Cambridge, Mass., placed patent reform legislation high on their lists.

Chase said, “It is critical that we create an environment in this country that stimulates biomedical innovation by protecting biomedical inventions. Patent reform legislation under consideration in the U.S. Congress is of great importance to the biotech industry, and the U.S. Patent and Trademark Office has been quite outspoken about the need to pass this legislation as soon as possible. There have been active discussions in the Senate, and there appears to be momentum to bring the Senate Judiciary [Committee] version of the bill to the Senate floor for consideration.”

Chase said that it will be important that the legislation “not compromise future biomedical innovation, particularly with respect to assigning damages to cases where patent infringement has occurred.” He commented that the Senate version of the legislation appeared to strike “a fair balance between different industry concerns on this issue whereas the House bill includes language regarding the apportionment of damages that could effectively stifle innovation, which is very expensive in biotechnology, and reward infringers.”

Uhl said, "This may be the year when we actually get something done. Apportioning damages could be disastrous for pharma companies and, of course, any change that weakens patents or makes them easier to challenge will have a negative impact on life sciences companies."

In a related matter, Jane M. Love of Wilmer Hale, New York, noted that changes at the PTO may positively affect the life sciences.

"The new director, David J. Kappos, has instituted a number of changes at the PTO—a pilot program for green innovations, a patent pendency model, the SPE [Supervisory Patent Examiner] Performance Appraisal Plan-Award Task Force—that appear to be immediately beneficial to the applicant. In addition, he has put to rest the question whether the 'new rules' regarding limitations on continuations and claim number would be instituted. He has begun a public blog and it appears he will continue to make changes to the PTO that will assist prosecution of patent applications and affect the prosecution of life sciences-related subject matter in a positive way," Love said.

Rea, who is the immediate past president of the American Intellectual Property Law Association, agreed, commenting, "Director Kappos really hit the ground running in 2009 and made a number of decisions that were applauded by the stakeholder community."

**7. FDA/DOJ Enforcement.** Carol A. Pratt of K&L Gates, Portland, Ore., predicted more aggressive FDA enforcement.

She said that FDA Commissioner Margaret Hamburg announced soon after her appointment that the agency would be more aggressive in using its enforcement tools to protect the public health. If needed, Hamburg said, FDA would take action first and then worry about whether the agency had legal authority.

"Hamburg removed the requirement that all warning letters be approved by the Office of Chief Counsel before being issued by the relevant division and said that FDA could take enforcement action following a warning letter without giving companies additional notice. While actual enforcement actions by FDA have not been overwhelming, Hamburg's focus early in her tenure on enhanced enforcement foreshadows an uptick in enforcement activities in the future," Pratt said.

Pratt also predicted increased FDA enforcement of clinical trial regulations, saying that FDA has been scolded for taking so long to take action against investigators in clinical trials being investigated for debarment. "These investigations can go on for years without resolution. The FDA recently issued a guidance clarifying the responsibilities of investigators and sponsors in clinical trials with the intent of increasing accountability. Of particular note was the FDA's position that industry sponsors are ultimately responsible for making sure that investigators in clinical trials have the necessary training and expertise to conduct the trials in compliance with applicable laws. This will increase the burden on sponsors to conduct suitable due diligence before contracting with investigators and appropriate monitoring during clinical trials."

Stephanie King, corporate counsel of Gilead Science Inc., Forest City, Calif., noted that the Department of Justice has turned its attention to target the pharmaceutical industry specifically in its criminal enforcement of the Foreign Corrupt Practices Act (FCPA).

"In several speeches in November 2009, the assistant attorney general stated that government is inexorably intertwined with the health care system in many other countries, and as such, many of the individuals with whom pharmaceutical companies interact in foreign countries may be considered foreign officials under the FCPA. The DOJ has indicated that any arrangements that would violate the Anti-Kickback Act in the United States would most likely be viewed as violating the FCPA outside the United States," King said.

King also said that the Obama administration has increased its fraud and abuse budget for 2010 by 50 percent, a significant portion of which is dedicated to enforcement. King said that in her view companies, faced with increased enforcement, should, in addition to reviewing and testing their codes of conduct and related procedures, address their records retention policies and procedures and assess the data management systems they have in place to prepare themselves to efficiently, accurately, and cost-effectively answer any inquiries.

**8. Conflicts of Interest.** Waxman said that conflicts of interest will continue to be an important life sciences issue.

"Look for continued legislative activity, as well as informal rule tightening by the academic medical community, such as the Partners Health Care System in Boston, to force more transparency, or enhance restrictions on interactions or compensation arrangements," Waxman said.

King agreed, noting that in addition to state actions and the Physician Payment Sunshine Provisions in the House and Senate health reform bills, she sees medical centers and academic institutions themselves increasingly putting restrictions in place to address real and perceived conflicts of interest.

"Many of them have severely limited and even banned access to their facilities for sales reps and even medical scientists employed by commercial entities, consulting arrangements their employees can enter into with commercial entities, and educational events sponsored by commercial entities. The effect of these increased restrictions will force change in how life sciences companies interact with physicians and others who have traditionally been an important source of guidance, advice, and information," King said.

**9. Decisions in *Bilski*, *Ariad*, *Myriad*.** LSLR's patent experts cited a number of upcoming patent cases that could have great importance to the life sciences industry.

Love said that the implications of the forthcoming Supreme Court decision in *In re Bilski* could have important effects on the availability of patents to protect certain subject matter. On Oct. 30, 2008, the U.S. Court of Appeals for the Federal Circuit held a patent applicant's claims were ineligible for patent protection under 35 U.S.C. § 101 because they involved a nontransformative process encompassing purely mental steps unaided by a computer or other device. The decision was perceived as having a negative effect on life sciences, and that effect can already be seen, Love said. "For example, in the case of *Classen Immunotherapies v. Biogen IDEC* in December 2008 (3 LSLR 9, 1/16/09), the Federal Circuit relied on *Bilski* to render invalid a patent claim for a method of determining whether an immunization schedule affected the incidence or severity of a disease," Love said.

Noonan was more ambivalent. “The Supreme Court’s decision in the *Bilski* case may be anything from extremely significant to the exact opposite, depending on how the court decides to address the issue of patent eligibility. There are at least two members of the court—Justices [Stephen] Breyer and [John Paul] Stevens—who believe method claims in the diagnostics area may be outside the bounds of patent-eligibility, being no more in some cases [than] comparing numbers (assay data) with a standard reference. On the other hand, the justices seemed genuinely inclined to avoid using the *Bilski* case to make any grand pronouncements, although they are highly unlikely to reverse the ultimate decision in the case that *Bilski*’s claims are not patent-eligible. But there is almost no likelihood that the court will let the Federal Circuit’s ‘machine or transformation’ test stand, since it is another ‘bright-line’ rule that the court has been disinclined to permit the Federal Circuit to use.”

Noonan said that the Supreme Court’s decision is likely to be a “clarification” that the court’s earlier jurisprudence in *Diamond v. Diehr*, 450 U.S. 175 (1981), did not require a patent-eligible method claim to satisfy the machine-or-transformation test and will state that the test will be one way, but not the only way, for a method claim to be patent-eligible—much like the CAFC’s “teaching-suggestion-motivation” test was not abrogated but merely curtailed in the court’s decision in *KSR International Co. v. Teleflex Inc.* (1 LSLR 153, 5/11/07).

Noonan also suggested that if the upcoming CAFC en banc decision in *Ariad v. Eli Lilly* (see 3 LSLR 1226, 12/18/09) reverses 14 years of Federal Circuit precedent it would have a significant effect on the scope of biotechnology claims.

“The Federal Circuit will decide en banc whether there is a ‘separate’ written description requirement in 35 U.S.C. Section 112, first paragraph,” Noonan said, indicating that the outcome was uncertain. “There is a vocal minority of the court who believe the statute does not contain a separate requirement and also several whose positions are unknown. In addition, the en banc panel consisted of only 14 judges, since Judge [Alvin A.] Schall has taken senior status. It may be expected that a decision that there is no separate requirement might be more likely to be reviewed by the Supreme Court than a decision that such a separate requirement exists. But if the CAFC made such a decision it would significantly affect the scope of biotechnology claims,” he said.

Both Love and Noonan agreed that in *Association of Medical Pathologists v. Myriad Genetics*, the American Civil Liberties Union-sponsored lawsuit attempting to have patents on genetic material declared ineligible for patenting, a large portion of biotechnology patent estates would be put in jeopardy should the court rule in the plaintiffs’ favor (see related item in the Court Proceedings section).

**10. Privacy of Genetic Information.** Hasko observed that it is possible today to obtain commercially a list of an individual’s single nucleotide polymorphisms relevant to disease and risk factors and even to have one’s own genome sequenced and that the amount of genetic

data available on an individual level will increase dramatically as these services become more cost effective. “Legal protections for how to maintain the privacy of this information, and legal parameters for permitted uses of this information will be tested on an increasing basis, and relevant laws will necessarily become more fully developed in the next few years,” she said.

King added, “Privacy issues are not new to the life sciences industry because of debate around use of genetic information and electronic medical records, however, all companies will have to deal with the complex and often untested data privacy and data security laws with respect to protecting their own employees’ information as well as information related to clinical trials. With no federal law, states such as Massachusetts and Nevada have enacted their own legislation and countries outside of the United States tend to require more stringent protections for personal information. Companies increasingly need to consider data privacy issues in day-to-day operations such as business continuity preparedness programs and internal investigations.”

**11. Higher Bar for 510(k) Medical Devices.** Pratt said that, in the aftermath of a very public scandal and allegations that FDA was too influenced by industry, the agency has indicated that it will impose more rigorous requirements on companies seeking 510(k) clearance for lower risk medical devices.

“Barbara Zimmerman of FDA’s Office of Device Evaluation recently cautioned companies against relying on past 510(k) clearance requirements for predicate devices and indicated that FDA would rely more on scientific evidence and the best interest of public health. Consistent with this position has been the trend for requiring more clinical data to support 510(k) applications,” Pratt said.

She concluded, “It’s not clear how close the 510(k) bar will be moved to the pre-market bar, but it is clear that the bar is moving and the gap between the two is shrinking.”

**12. Vaccines’ Reemergence.** Krasner ended her comments by noting the reemergence and growth of vaccines.

“Based on the H1N1 epidemic and the resources from the White House, Congress, the Centers for Disease Control and Prevention, CMS, and many other agencies mobilized to get the vaccines out to the public, there is a growing recognition of the value of the somewhat overlooked vaccine industry. As vaccines are under [development] for new key uses including potentially, cancer and Alzheimer’s, it can be expected that all of the action that follows drugs and biologics may move accordingly. So we can expect both more encouragement but also more regulation of vaccines,” Krasner said.

**Coda.** Chase described a theme underlying his list of top trends and issues for 2010 as well as that of LSLR’s other experts: “In order for the biotechnology industry to thrive, we need to continue to encourage and reward innovation and provide a strong and consistent regulatory framework within which to develop novel drugs.”

BY JOHN T. AQUINO