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Outlook 2018: Pharma/Life Sciences Law and Policy

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Will the 21st Century Cures Act further its aim to boost drug and device development in 2018? That's one of the questions the life sciences industry and attorneys are asking for the new year. The law provides extra money for research and development—including ambitious research into cancer and a landmark precision medicine project involving 1 million Americans—and spurs more use of real-world evidence to support product approvals.

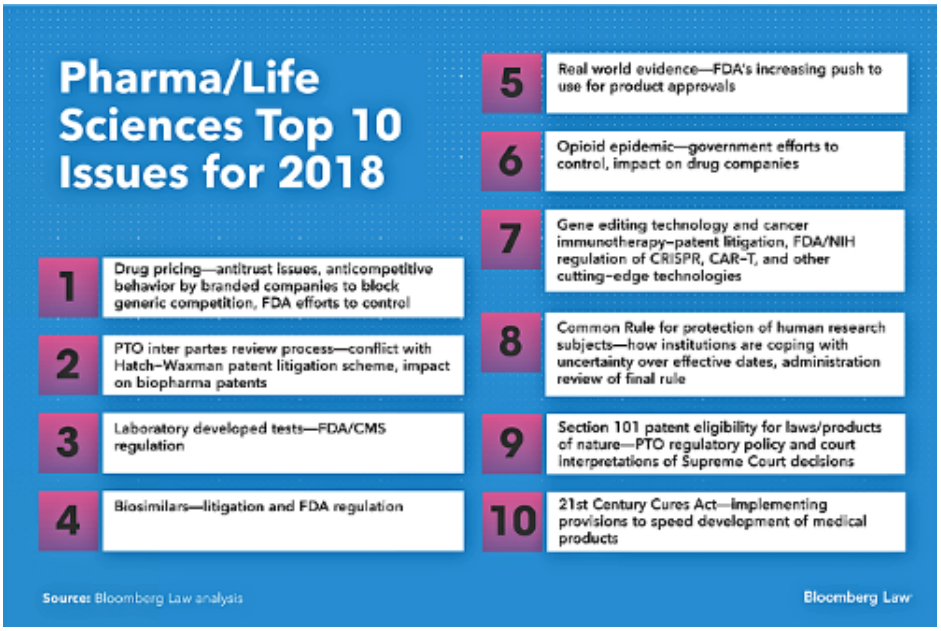
Other issues to watch in 2018 include what the HHS and the NIH will do to help fight the nation's opioid epidemic. In Congress, after a year of no action, there is still plenty of talk about prescription drug prices, and that debate could affect the midterm elections. Scott Gottlieb starts his first full year as commissioner of the Food and Drug Administration and says approving more generics will help keep prices down.

Patents stay in the spotlight as companies fight over the rights to potentially highly profitable new technologies and look for changes in what discoveries are patentable and how existing patents can be challenged. On other fronts, gene editing, cancer immunotherapy, and other new technologies will be tested as they move toward market approval.

PHARMACEUTICALS

Drug Pricing

Efforts to find a way to lower drug prices will continue to be a big issue in 2018.



"While drug pricing took a back seat to Republicans' Affordable Care Act-repeal efforts in 2017, the issue will likely re-emerge as a key campaign theme in 2018," Bloomberg Intelligence analyst Brian Rye told Bloomberg Law in an email.

"Democrats are eyeing the possibility of regaining control of the House and/or Senate in the upcoming midterm elections; doing so would enhance their ability to advance measures aimed at giving the federal government more control over

prescription drug prices," Rye said.

There is interest in Congress and at the state level in doing something on drug costs, Allan Coukell, Pew Charitable Trusts' senior director for health programs, told Bloomberg Law. On the state level, there has been interest in increasing the transparency of drug prices and legislation that would create a supplemental rebate or claw-back mechanism for drugs whose prices increase beyond a certain rate.

"Federally, I think one of the programs to watch is Medicare Part B, in particular because that is where a lot of the growth in spending is just by the nature of Part B-type products," Coukell said. Intravenous biologics and cancer drugs, some of the most expensive products, are often administered through that program.

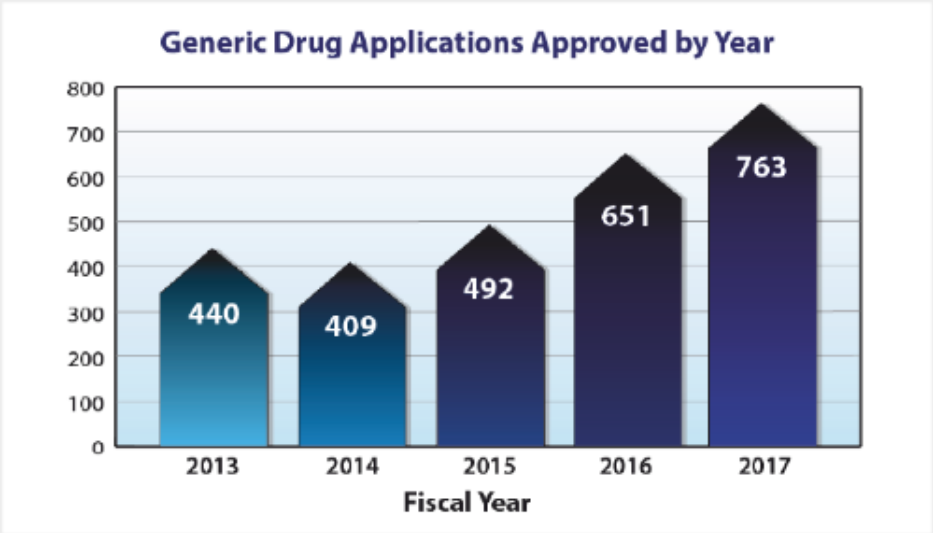
Coukell said Part B doesn't have formulary or utilization management tools, and "there's certainly policy options for Congress to consider and things the administration could do."

"Democrats and Republicans are starting to agree there is a problem," Rep. Peter Welch (D-Vt.) told Bloomberg Law. "But there continues to be a challenge with coming up with a solution that can get bipartisan support."

Welch said he's hopeful legislation will be considered "to address the broken market in pharmaceutical pricing." He said he plans to pursue legislation to allow Medicare to negotiate drug prices with manufacturers and to allow imports of less expensive drugs from Canada. Sen. Bernie Sanders (I-Vt.) also plans to pursue such legislation, Josh Miller-Lewis, Sanders' communications director, said.

The FDA also will look for ways to bring more competition to the market to lower prices, Commissioner Scott Gottlieb said at a November conference in response to a question from Bloomberg Law on his priorities for 2018.

While the FDA has increased the number of generic drug approvals in recent years, there are still some things that could be done to increase generic competition. In 2017, the FDA approved 763 generic drug applications, compared to 651 in 2016 and 492 in 2015.



One issue the generic industry has faced is obtaining samples of branded drug products needed to do the testing required to submit a generic drug application, Chip Davis, president of the Association for Accessible Medicines, a generic industry group, said.

Generic companies can't do the pharmacovigilance testing needed to submit an application because brand companies are abusing risk evaluation and mitigation strategy (REMS) systems and REMS-like distribution systems to deter competition, Davis said. The FDA sometimes imposes a REMS on a drug to ensure its benefits outweigh its risks.

To fix this problem, the AAM supports the Creating and Restoring Equal Access to Equivalent Samples (CREATES) Act, Davi s said. The bill would prevent branded drug manufacturers from using REMS to keep generic drug developers from obtaining samples.

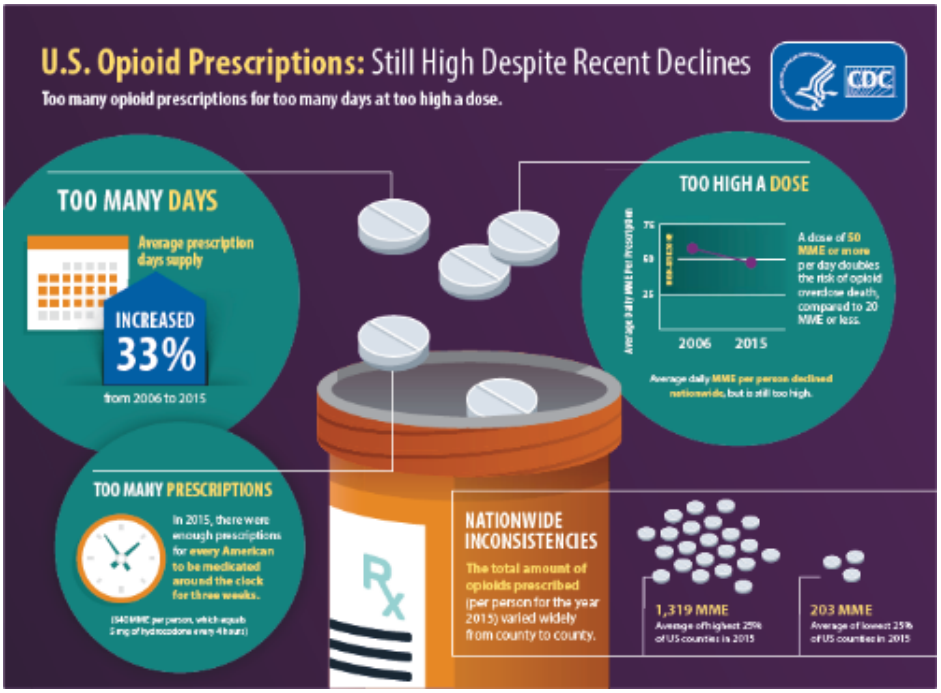
Rep. Welch also said he plans to pursue the REMS issue through the Fair Access for Safe and Timely (FAST) Generics Act,

which is similar to the CREATES Act.

Opioid Epidemic

Combating the opioid abuse epidemic also will be a top priority for 2018, Coukell said.

Ninety-one Americans die every day from an opioid overdose, and the number of overdose deaths involving opioids has quadrupled since 1999, according to the Centers for Disease Control and Prevention. A November report from the White House Office of Economic Advisers also estimated the opioid crisis cost $504 billion in 2015—equal to 2.8 percent of gross domestic product that year. The report calculated the economic cost of deaths caused by opioid overdoses using conventional economic estimates for valuing life routinely used by federal agencies.



The FDA plans to take additional steps to address the crisis, Gottlieb said at the recent conference. He said the agency will focus on the treatment side to provide more medical therapies to help patients who are addicted.

> ***"This opioid crisis is something that's affecting the constituents of all members of Congress and these price explosions are hurting their first responders." Rep. Peter Welch (D-Vt.)***

Welch also said Congress is looking into the explosion in the price of Adapt Pharma Inc.'s Narcan (naloxone), a drug that reverses overdoses, and other life-saving drugs used by first responders. "This opioid crisis is something that's affecting the constituents of all members of Congress and these price explosions are hurting their first responders" and "there's more sympathy about trying to get affordable access to drugs like Narcan."

The AAM's Davis said it's important to make sure there's a comprehensive and systemic approach from everyone in the system to address the epidemic, including generic companies. "We need to make sure we're focusing on appropriate treatment modalities and options for patients, but we also need to make sure we're doing our role on awareness and prevention," he said.

21st Century Cures

New drugs are needed for illness and epidemics, and one law might promote their development. The lawmakers who wrote the 21st Century Cures Act said they will continue to refine the law, although there is no new legislation on deck.

Looming in 2018 are about 30 deadlines and requirements agencies such as the FDA and the National Institutes of Health must meet, according to a bill tracker created by think tank Faster Cures. They range from reducing administrative burdens on researchers to a public meeting by June 13 on novel clinical trial designs to an NIH plan for improving research rigor and reproducibility.

The law also provides $5.3 billion as part of a 10-year innovation fund. In fiscal year 2018, the NIH will receive $496 million and the FDA will receive $60 million to fund projects such as the cancer moonshot to double the rate of progress of cancer therapies and prevention. One focus of the moonshot is immunotherapy, which trains the immune system to attack cancer cells. With immunotherapy products by Novartis and Kite Pharma Inc. already approved, this emerging area likely will continue to advance in 2018.

Cures also adds funding for precision medicine, and the NIH's centerpiece effort in the field, the All of Us Research Project, is to begin this spring. “This is a really big positive to get more and more people engaged in taking part in clinical trials,” Mary Woolley, president of Research America, said.

Real-World Evidence

Under a Cures mandate, the FDA must implement by Dec. 13, 2018, a framework on real-world evidence, which is the use of data collected outside a randomized, controlled trial. It is a move to harness existing data sources to accelerate treatments to market while understanding better how patients actually use these products.

Real-world evidence “is going to continue to be a very signature event in 2018,” Carol Pratt, an FDA regulatory attorney with Lee & Hayes, PLLC, said. She likened it to the impact of the Health Insurance Portability and Accountability Act (HIPAA) in the early 2000s. “Everyone knew that it was going to change life, but they didn't know exactly how it was going to change life. And I think that's where we are. There are a lot more questions than there are answers.”

Biologics Issues

Look for several developments in the biologics and biosimilars arena in 2018, observers said.

Biosimilars are “highly similar” but less expensive copies of complex name-brand biologic drugs, while an interchangeable product produces the same clinical result as the branded drug and can be substituted by pharmacies without a physician's approval.

An interchangeable product has yet to be approved, but “the FDA has at least surmised” that within the next year one could be granted, said **Deborah Shelton**, a partner with McCarter & English LLP who leads its food and drug law practice.

“[I]t certainly looks like there are some biosimilar developers out there that look to be doing the kinds of switching studies you would expect to see” to get an interchangeable approved, said Shelton, a Bloomberg Law advisory board member.

Other regulatory developments she is following include comments to interchangeability draft guidance the FDA issued in 2017. She noted the guidance doesn't address labeling, as it has done for biosimilars.

The agency might also start the process of amending its regulatory definition of biological products, Shelton said.

“I'm not sure if notice and comment rulemaking will get underway, but FDA has signaled that they do intend to amend their regulatory definition of biological products,” she said.

On the litigation front, Amgen Inc. and Genentech Inc. are battling over where a biosimilar patent dispute should proceed. Amgen, the reference product holder, alleges it complied with the Biologics Price Competition and Innovation Act “patent dance” information exchange, and sued Genentech for infringement in California. Genentech sued Amgen the next day in Delaware.

“That's something certainly everybody is following because it leaves open the question of who gets to choose where these cases happen,” said Elaine Blais, a partner with Goodwin Procter. “Is it only the reference product sponsor that gets to choose, or is there a path through the statute that would allow the biosimilar maker to make that choice?”

PATENTS

CRISPR Legal Battle

On the intellectual property front, an important legal battle is underway between the Massachusetts Institute of Technology's Broad Institute and the University of California at Berkeley. California claims the U.S. Patent and Trademark Office issued overly broad patents on gene-editing technology called CRISPR-Cas9 to Broad.

The PTO's Patent Trial and Appeals Board (PTAB) found California's patent application didn't overlap with the Broad patents, so there was no reason for it to decide who invented which technology first.

California is appealing the PTAB's ruling to the U.S. Court of Appeals for the Federal Circuit.

The case is the biggest interference case in decades, Brent Babcock, an intellectual property lawyer with Knobbe Martens, told Bloomberg Law. Because the interference battle is just the first of many fights between the parties, who have already spent millions on litigation costs, it's likely the case will settle at some point, he said.

Future of Inter Partes Review

Patent experts are also keeping their eyes on Oil States Energy Services LLC v. Greene's Energy Group LLC, a case pending at the U.S. Supreme Court that could upend the PTAB's inter partes review (IPR) process. The high court is expected to decide the case by June.

The question for the Supreme Court is whether Congress properly established the IPR procedure in a 2011 patent law overhaul known as the America Invents Act. Oil States argued patents are private property rights that can only be taken away through a jury trial in a court sanctioned under Article III of the Constitution—not in an administrative trial-like proceeding at the PTO.

“It seems unlikely to me that the court will find IPR unconstitutional,” Bloomberg Law board member Jake M. Holdreith of Robins Kaplan LLP said. “I think the court would have a hard time drawing a line between reexamination, which was conceded to be constitutional at the argument, and Inter Partes Review, which is challenged,” he said.

If the high court does find the popular IPR process unconstitutional, “it will be a dramatic sea change in how we conduct patent litigation,” Babcock said.

Congress to Step In?

However the high court comes out, the PTO and Congress likely will figure out how to reshape IPR procedures to comply with the decision.

Sen. Orrin G. Hatch (R-Utah) recently said Congress may need to examine whether the IPR procedure is affecting the balance between innovation and lower-cost generic entry his namesake Hatch-Waxman Act of 1984 tried to strike.

“I think we need to examine IPR's effect on the Hatch Waxman branded-generic balance,” Hatch said. “If reforms to IPR are needed to preserve that balance, we should think carefully about how best to make those reforms.”

Under Hatch-Waxman, the FDA won't grant a generic company final approval of its product for 30 months after it has been sued by a branded drug company for patent infringement. Some commentators have said that stays granted in the IPR process can delay Hatch-Waxman litigation and “frustrate the intent of the provision by drawing out litigation for more than 30 months,” Hatch said.

Sovereign Immunity Switcheroo

Allergan Plc's clever but criticized sovereign immunity “rental agreement” to avoid PTAB proceedings is sure to face continued scrutiny in court and in Congress.

Allergan announced in September it transferred ownership of patents covering its Restasis dry eye medication to the Saint Regis Mohawk Tribe in New York, which in turn granted Allergan exclusive licenses to them. The tribe then moved to dismiss an inter partes review proceeding challenging the patents’ validity, citing sovereign immunity.

The gambit made headlines and drew bipartisan howls from lawmakers, who vented at a House Judiciary Committee subcommittee hearing in November. A Senate bill introduced in October would bar the tactic.

“If Congress took up the issue, it could resolve it pretty quickly,” William Jay, a partner with Goodwin Procter LLP and co-chair of its appellate litigation group, told Bloomberg Law. Jay testified at the hearing on behalf of the generic trade group AAM.

Absent a legislative fix, “there might be quite a wait until the Federal Circuit and perhaps the Supreme Court decides the issue,” Jay said.

"'Here's an incredibly valuable patent, we will pay you to take it' is a very suspicious transaction." William Jay, partner with Goodwin Procter LLP

The PTAB has allowed outside parties to submit friend-of-the court briefs as it considers the tribe's motion to terminate.

In announcing its agreement, Allergan noted the PTAB has dismissed IPR proceedings against state universities based on state sovereign immunity.

However, the Constitution protects state sovereign immunity, Jay said, whereas tribal sovereign immunity exists only to the extent Congress grants it.

And state universities engage in research and development efforts leading to challenged patents, while here the tribe has been paid to take patents it didn't develop, he noted.

"'Here's an incredibly valuable patent, we will pay you to take it' is a very suspicious transaction," Jay said.

Patentability Problems

Don't expect great clarity to emerge from the PTO in 2018 on what constitutes patentable subject matter under 35 U.S.C. § 101, said Deborah Lu, a shareholder and intellectual property attorney with Vedder Price P.C. Her hopes for resolution in 2017 were dashed, she said.

"I don't think we've really shifted all that much from last year, to be honest," said Lu, a Bloomberg Law advisory board member. "I don't think we've gotten any clear guidance since this time last year."

The Supreme Court says laws of nature, natural phenomena, and abstract ideas aren't patentable under Section 101 without novel or useful application of them. Since the Federal Circuit's 2015 Ariosa decision applying Supreme Court precedent, lower courts and the PTO have regularly invalidated biotech patents as covering ineligible subject matter, frustrating the biotech industry and patent bar.

"I think it's frustrating for practitioners, I think it's frustrating for clients, and I think it's frustrating for the patent office," Lu said.

The mishmash of decisions and absence of clear criteria for patent examiners to apply leads to "a situation of 'we'll know it when we see it,'" Lu said. "It's like the test for pornography."

The PTO did issue a report in July summarizing public views on Section 101 eligibility in light of recent judicial precedent. And the office updates resources on its subject matter eligibility page, including charts and reference sheets summarizing key decisions.

MEDICAL RESEARCH

Cutting-Edge Technology

Gene editing and CRISPR-based therapeutics will continue to garner attention as both the products and the intellectual property landscape relating to them evolve.

Gene editing refers to a group of technologies that give scientists the ability to change an organism's DNA. A method known as CRISPR-Cas9 (clustered regularly interspaced short palindromic repeats) has enabled gene editing to be faster, cheaper, more accurate, and more efficient than other methods. It essentially allows scientists to cut out unwanted sections of DNA and replace them with desirable sequences.

Analysts call it one of the most important inventions ever and cite a potential value of billions of dollars. The first U.S. clinical trials applying gene editing technology to mutations causing serious diseases could be up and running in 2018.

The Vote

The partisan environment during a midterm election year will make it especially difficult for Congress to follow the normal process for passing bills known as regular order, Research America's Woolley said.

"It's inescapable that next year it's going to be even more intensely political than the one we're in right now," Woolley said. "But this year, trying to get to anything close to regular order is like climbing Mt. Kilimanjaro."

When Congress doesn't act, it creates a ripple effect throughout the federal government, as agencies remain uncertain about whether they will be funded on endless continuing resolutions or face reorganization.

What does that mean for research? “The relatively easy stuff is not going to necessarily get done so that people can't work on the emerging challenges,” she said.

These challenges come amid some of the largest statutory and regulatory changes affecting the biomedical industries.

Common Rule

Few situations highlight this unpredictability better than the status of the Common Rule revisions, the biggest changes in three decades to regulations governing human research subjects. Those changes kick in Jan. 19—possibly.

A proposed rule to delay the effective date to 2019 is under White House Office of Management and Budget review. “The current effective date stands unless there is a final change to the rule,” Lisa Nichols said. She is the director of research and regulatory reform for the Council on Governmental Relations, which represents research institutions. Most institutions are preparing to comply with the revisions by January.

There's no further guidance from the HHS on the Common Rule revisions other than the revised rule itself, which includes some complex changes, such as broad consent for future research on biospecimens and a new exemption if the Health Insurance Portability and Accountability Act privacy rule applies. “There are parts of the rule that are very hard to implement without guidance,” said Heather H. Pierce, the Association of American Medical Colleges’ senior director of science policy and regulatory counsel. “That doesn't mean they can't be implemented, but they won't be implemented consistently.”

At the same time, the FDA hasn't updated its regulations. “If it does go into effect as intended on Jan.19,” Pierce said, “a federally funded clinical trial that is FDA regulated will be under [both] the old and new Common Rule because the FDA regulations are so closely aligned with the old Common Rule.”

21st Century Cures (Pub. L. 114-255) requires the HHS and the FDA to harmonize their regulations, and FDA officials have said they are working on it.

Regenerative medicine, which also has Cures money, will continue to be important as researchers are recruiting for gene therapy trials. Emergence of the CRISPR-Cas9 technology has advanced the field by making gene editing faster, cheaper, and more accurate.

MEDICAL DEVICES

Still Waiting on Diagnostics

For the medical device industry, what the FDA should do regarding laboratory-developed tests is pressing, but remains unsettled.

“The federal government, as a whole, including Congress, has been unable to come up with an appropriate regulatory pathway that both protects patients and advances innovation,” Bloomberg Law board member Bradley Merrill Thompson of Epstein Becker & Green said.

“It's rather unbelievable that such an important issue should take so long to resolve,” he said.

Historically, the regulation of diagnostics such as LDTs has been under the purview of the Centers for Medicare & Medicaid Services under the Clinical Laboratory Improvement Amendments, while the FDA has exercised enforcement discretion in the field.

The FDA has repeatedly said it intended to phase out its policy of enforcement discretion over LDTs and start actively overseeing at least some of the tests. In 2016, it had to withdraw a proposal to strengthen that oversight. Clinical lab groups opposed the proposal, saying it would subject them to double regulation.

But the agency is expected to announce a new pilot plan soon to certify laboratories that develop diagnostic tests in lieu of drafting rules for the tests themselves, according to Sean Khozin, associate acting director of the agency's Oncology Center of Excellence. The approach will be modeled after the FDA's pilot approval process for digital health products, Khozin said.

There also may be legislative action on the topic early next year. Reps. Larry Bucshon (R-Ind.) and Diana DeGette (D-Colo.) introduced a draft bill for an LDT regulatory pathway—an area that the 21st Century Cures law didn't address. The FDA has been providing technical assistance on the draft bill and agency head Gottlieb has said his agency is eager to work with Congress on the issue.

Meanwhile, Gottlieb said in a Dec. 11 blog the FDA would take steps to reform and modernize its review of medical device applications, known as 510(k) applications, including publishing a draft guidance to help manufacturers demonstrate their devices are substantially equivalent to already marketed devices.

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