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Pharmaceutical Law & Industry Report®



# OUTLOOK 2016: Drug Prices, User Fees, Biosimilars Among Key Topics

In 2016, the key concerns for drug and biotech companies will include the reauthorization of drug user fee programs, drug pricing, the ongoing implementation of the FDA approval pathway for biosimilar drugs and the continuing evolution of what drug companies can say about the off-label uses of their products.

Bloomberg BNA contacted stakeholders and interviewed members of the *Pharmaceutical Law & Industry Report* advisory board to identify the important 2016 issues for drug and biotech companies in the courts, Congress and regulatory agencies.

Other key issues to watch will be drug compounding, Medicaid reimbursements and medication therapy management.

**User Fees, Drug Compounding.** The top priorities for the Food and Drug Administration's Center for Drug Evaluation and Research (CDER) in 2016 include the reauthorization of the drug user fee programs, which expire in September 2017, and implementing the statutory provisions on drug compounding, Janet Woodcock, director of CDER, said Dec. 14.

In 2016, CDER will be working on negotiating the sixth reauthorization for the Prescription Drug User Fee Act (PDUFA), the second authorization for the Generic Drug User Fee Amendments (GDUFA) and the second authorization for the Biosimilar User Fee Act (BsUFA), Woodcock, who spoke at the FDA/CMS Summit for Biopharma Executives, said.

Additionally, Woodcock said CDER is continuing to put in place a regulatory structure for drug compounding. The Drug Quality and Security Act (Pub. L. No. 113-54), which was signed into law in November 2013, distinguishes between compounders engaged in the traditional pharmacy practice of making customized drugs for specific patient needs and those compounders making large volumes of compounded drugs without individual prescriptions. Compounders outside the scope of traditional pharmacy practice can voluntarily register with the FDA as ''outsourcing facilities'' and become subject to federal oversight like traditional drug manufacturers.

Cathy L. Burgess of Alston & Bird LLP in Washington said that ''pharmacy compounding will continue to be a top issue in 2016 as compounders offer to make low cost compounded drugs available to compete with higher priced approved drugs.''

''It is likely that FDA will continue to focus on establishment inspection of outsourcing facilities, as these facilities adapt to pharmacy compounding in a [current good manufacturing practice] environment,'' she said.

''An open issue is whether the agency will take steps to promulgate regulations on cGMP requirements for outsourcing facilities, or will continue to issue warning letters that are informed by FDA draft guidance'' on cGMP for drug compounding outsourcing facilities, Burgess added.

FDA's Woodcock said her office also will continue to implement multiple statutes, including the Food and Drug Administration Amendments Act (FDAAA) of 2007, the FDA Safety and Innovation Act of 2012 (FDASIA) and the Drug Quality and Security Act.

Additionally, she said CDER will be working on issuing a guidance on generic versions of abuse-deterrent formulations of opioids and establishing the FDA-European Union mutual reliance initiative for facility inspections.

Woodcock said the FDA has made ''significant'' progress on the FDA-EU mutual reliance initiative. This initiative would allow the FDA to rely more on the results of European inspections of manufacturing facilities, she said. This would free up FDA resources so that the agency could concentrate on inspections in other parts of the world, Woodcock said.

Woodcock said other priorities for CDER in 2016 include:

- taking a new look at drug advertising and promotion in light of current jurisprudence around the First Amendment (the FDA has suffered court case losses in its efforts to prevent certain types of drug promotion);
- continuing to plan and build the new information technology system, called Panorama, for the drug review process and other regulatory functions;
- improving staffing (the agency has more than 600 vacancies);
- developing a process and ultimate policy documents on the evaluation of a biomarker as a surrogate endpoint for accelerated approval; and
- working on the final version of the quality metrics guidance (the draft guidance was released July 27, 2015).

**Rising Rx Drug Prices.** Experts say rising drug prices and related attempts to contain drug costs will continue to be huge issues in 2016, particularly in the ramp-up to the 2016 presidential election.

The drug industry has been under fire for its prices, with Gilead Sciences Inc. taking much of the criticism for its hepatitis C treatment Sovaldi. Sovaldi came on the market in December 2013 bearing the promise of a cure and a price tag of about $1,000 a day for 12 weeks. Gilead has argued that Sovaldi can save the health-care system costs by keeping people with hepatitis C from eventually needing a liver transplant or getting liver cancer.

The fundamental pricing decisions that pharmaceutical manufacturers make when they launch new, innovative drug products, particularly those that address chronic, rarer diseases and cancer and often are biological, and then adjust those prices (usually upward) over time will be a central piece of the debate on drug prices, said Larri A. Short of Arent Fox LLP in Washington. These drugs often are priced in the thousands and sometimes hundreds of thousand of dollars a year, she said.

But recent price spikes on older, off-patent drugs acquired by drug companies that didn't develop them are also sparking public outcries, and recent jumps in the prices of many generic drugs also are drawing concern about access to affordable health care.

The pricing discussion on generic drugs likely will include discussions of shortages and whether issues such as the backlog of generic drug applications at the FDA, tighter requirements for FDA inspections and industry consolidations are contributing factors to the spikes in the costs of some generic drugs, Short said.

These ''hot button issues'' are ''likely to heat up further as the presidential campaigns wear on and candidates address the [pricing] issue; Congress holds hearings; the [Government Accountability Office], the AARP, the Kaiser Family Foundation and other groups issue reports; and the press gives more coverage to personal impact stories,'' she said.

According to David A. Balto of the Law Offices of David A. Balto in Washington, ''Pharmaceutical companies are testing how far they can go in terms of raising prices.'' Balto formerly served as assistant director for policy and evaluation in the Federal Trade Commission's Bureau of Competition.

**Congress Gets Involved.** Indeed, Congress has started to get involved in the pricing debate, too. In December 2015, the Senate Special Committee on Aging began what it said will be the first in a series of hearings on drug prices. Sen. Susan Collins (R-Maine), who is leading the committee's investigation into drug prices, has said she would like to include proposals related to how the FDA approves generic drugs that are in competition with monopoly drugs as part of a larger FDA reform bill in the Senate Health, Education, Labor and Pensions Committee in 2016.

The panel also plans to look into the FDA's process for approving new generic drugs, as well as the recent spate of pharmaceutical mergers and acquisitions.

James M. Burns, of Baker Donelson PC in Washington, predicted that 2016 likely will see some legislative activity around the issue of the pricing of seldom-used, off-patent drugs that face little competition. Faster approval of generic drugs has been suggested as one way to address this concern, he said, and ''a legislative response to the issue would not be surprising,'' he said.

Certain industry stakeholders are also concerned about the prices of prescription drugs and are weighing in on the issue. For example, the Healthcare Supply Chain Association (HSCA) and its member group purchasing organizations are urging Congress to give the FDA authority to expedite review and approval for new generic drugs that have the potential to mitigate price spikes and help ensure access to critical medications for health-care providers and patients.

Edith A. Rosato, chief executive officer of the Academy of Managed Care Pharmacy (AMCP), told Bloomberg BNA that containing drug costs is ''an important topic for Americans and the health insurance industry.''

''Containing costs and assessing the value of prescription drugs, particularly specialty medications and biologics, will be important as more medications are introduced to the market that promise cures or significant improvements in treatment for certain conditions, including cancer, MS [multiple sclerosis], rheumatoid arthritis and orphan conditions,'' she said.

''Medications recently introduced for curing HCV [hepatitis C virus] show tremendous promise but are not without issues, including the cost to treat the number of Americans with HCV, rates of re-infection after treatment, and the immediate impact on public and private insurers. These issues will continue for medications for other conditions,'' Rosato said.

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—Edith A. Rosato, Academy of Managed Care Pharmacy

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''It will be more important than ever to assess the value of medications relative to quality of life, outcomes, and cost,'' Rosato said.

Nonetheless, some experts warn that the increasing downward pressures on drug prices could ultimately lead to drug shortages.

''The cost of manufacturing even an old generic drug in full compliance with FDA regulations is very expensive,'' James N. Czaban, of Wiley Rein LLP in Washington, said. ''If companies can't price their drugs according to market demand, it's going to lead to more and more drug shortages.''

The issue is multi-layered and complex, Short agreed. ''The issues and market interactions underlying high drug prices are complex and efforts to rein in such prices will need to take account of that complexity to be effective and to avoid unintended consequences,'' she said.

**BIO Hopes to Focus Discussion on Value.** Meanwhile, Kay Holcombe, senior vice president of science policy at the Biotechnology Innovation (formerly Industry) Organization (BIO), told Bloomberg BNA that BIO's top priority for 2016 and possibly longer will be to change the terms of the debate away from pricing ''so that we are focusing more on the value of our products to patients and on the best ways of providing access to innovative products to patients who need them.''

  PLIR ISSN 1542-9547

Holcombe said BIO is working on developing policy approaches that will allow for interactions between insurance companies, pharmacy benefit managers (PBMs) and pharmaceutical companies to ''satisfy concerns about what is the price on behalf of the payers and satisfy our concerns about finding good insurance designs and contracting designs that allow patients to have access to products.''

''One of the really important things that we've been working on for a few years is to try to talk with providers and payers more clearly about the value of our products, including talking about pharmacoeconomic information that does not specifically appear on the label of the product, as well as talking truthfully and in a nonmisleading way about uses of our products that are happening now'' and that aren't included in the labeling, Holcombe said. ''We have been back and forth with FDA on this multiple times to try and get some statement from the agency that lays out some parameters under which we can discuss truthful information about products so that patients, providers, prescribers and insurers and payers can have the best and the latest information.''

Holcombe said BIO will be continuing that effort in 2016.

**21st Century Cures Legislation.** Holcombe also said that BIO has been involved with the 21st Century Cures legislation from the very beginning and provided ideas that made it into the pending legislation.

The goal of the legislation is to speed the approval of innovative drugs and medical devices.

Holcombe said BIO thinks Rep. Fred Upton (R-Mich.), the chairman of the House Energy and Commerce Committee, ''has done a brave new world kind of approach'' with the legislation.

''It seems as though it's taking a while, probably longer than [Upton] had hoped,'' Holcombe said. ''We will continue to work with the Energy and Commerce Committee on those provisions that already are in the bill, and then we are still working with the Senate [Health, Education, Labor, and Pensions] HELP Committee as they're trying to pull together their version.''

The House passed its version of the legislation (H.R. 6) in July 2015. The Senate is working on its own version of the bill.

**PhRMA's Focus.** Lori Reilly, executive vice president for policy and research at the Pharmaceutical Research and Manufacturers of America (PhRMA) told Bloomberg BNA that PhRMA will be focusing on ''ensuring patients have access to medicines.''

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—LORI REILLY, PHRMA

''We've been engaging a fair amount in the [health insurance] exchanges because of the access concerns that we're seeing there,'' Reilly said. ''There's been a shift towards patients having to bear a higher burden of their costs. We're seeing growing numbers of patients in the commercial markets who are now subject to high deductible plans.''

Reilly said PhRMA has been focusing on the health insurance exchanges because ''often what we're seeing there are real challenges for patients to access the medicines. For example, for HIV/AIDS patients, in the majority of the silver plans, every single medicine is on the highest tier of cost sharing for them. So, focusing on ensuring patients have access to medicines is very high on the list.''

''Ensuring that we continue to have a competitive marketplace and one that encourages innovation is also important for us,'' Reilly said. ''There's been a lot of debate going on over the last several years about potential changes that we think could be harmful to our ability to continue to innovate, so we'll continue to work to ensure that there remains a competitive marketplace and an environment that encourages innovation.''

Reilly also said that as the health-care system moves to a value-based system, PhRMA will be working to address some of the challenges that exist for the pharmaceutical industry, whether it's outcomes based contract agreements or other types of value contracting.

Reilly also said PhRMA will be ''gearing up'' for the reauthorization of PDUFA in 2017.

**Industry Concerned About Quality Metrics Initiative.** Along with these issues, Burgess of Alston & Bird said the FDA's Quality Metrics initiative is likely to be a chief concern for the pharmaceutical industry in 2016.

In July 2015, the FDA issued a draft guidance on quality metrics issues for pharmaceutical companies. The draft guidance requests that companies submit data metrics and considers companies' drugs to be adulterated if the companies don't submit the metrics. Based on public comments submitted to the FDA, Burgess said industry is likely to challenge any final guidance as exceeding the agency's authority under the federal Food Drug and Cosmetic Act (FDCA).

''Commenters have noted that adopting requirements that arguably exceed FDA's statutory authority could cause implementation problems for the Quality Metrics program,'' Burgess said. Some commenters have asserted that, based on the size, scope and mandatory nature of the proposed program, the guidance is more in the nature of a substantive rule which can only be implemented through notice-and-comment rulemaking, she added.

Burgess also noted that there are industry concerns that the draft guidance underestimates the true burden of the program, and, as it's currently structured, it may fail to achieve FDA's stated objectives.

**Biosimilars and Pricing.** AMCP's Rosato said one promising improvement in prescription prices occurred in 2015 when the FDA approved the first biosimilar, and more biosimilars are in the pipeline.

The first biosimilar, Zarxio, was approved by the FDA in March 2015. Zarxio is from Sandoz, part of Novartis AG, and is a biosimilar version of Amgen Inc.'s cancer drug Neupogen.

''Biosimilars are safe and effective alternatives to brand name biologic agents that improve patient access to biologic products by lowering the price,'' Rosato said. ''Outstanding federal and state regulatory issues, including whether biosimilars will share the same name with reference biologics and whether pharmacists in states will be able to automatically substitute interchangeable biologic products without unnecessary en-

cumbrances, could still influence the future market adoption of biosimilars.''

Rosato said, ''Insurers, pharmacists, and some consumer advocacy groups continue to advocate for policies that allow consumers to access biosimilars without unnecessary regulatory barriers and to provide education on the safety, efficacy and benefits of these agents.''

''Biosimilars have the potential to become an answer to some of the antitrust issues presented by big pharma,'' Baker Donelson's Burns said. ''If biosimilars are viewed as acceptable alternates to certain branded drugs, the market power currently wielded by the branded drugs could be reduced, creating greater competition and, with it, consumer benefit.''

Holcombe also said the new biosimilars pathway will benefit consumers.

''We have always believed at BIO that this new pathway will benefit patients by providing them with additional choices of biological products that are helping them and that potentially could be less expensive than the products that they are taking now,'' she said.

But Linda D. Bentley, of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. in Boston, said the savings from biosimilars may not be as great as anticipated.

''The question of how much approved biosimilars will save the health-care system remains to be seen,'' Bentley said, adding that recent analyses suggest that the savings will not be as great as initially expected.

**Companies Looking for Biosimilars Guidance.** As to other biosimilar issues, BIO's Holcombe said that the reauthorization process for the biosimilars user fee law will begin shortly after the first of the year. ''It's very important that we get that program reauthorized,'' she said.

The user fees are paid by drugmakers and help fund the agency's operations, in addition to congressional appropriations. The agency works with industry on goals for reviews and other actions as part of its user fee discussions.

She also said industry is hoping that the FDA will issue some additional guidance on biosimilar issues.

''We have been pleased that FDA is going forward with the implementation of the new biosimilars pathway, but it has been going, so far, relatively slowly,'' Holcombe said.

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Holcombe said BIO has been urging the FDA to expedite ''its issuing of guidance documents so that sponsors will know what kinds of requirements and what kinds of processes FDA is using and is going to need for the approval of new biosimilar products.'' She said the guidance on biosimilar interchangeability ''is one of the important ones'' that the FDA still needs to issue.

A biosimilar is a biologic product that is approved for market by the FDA based on a showing that it is highly similar to an already approved biologic known as a reference product. An interchangeable biologic product is biosimilar to an FDA-approved reference product and meets additional standards for interchangeability, which would allow it to be substituted for the reference product by a pharmacist without prior permission from the prescribing physician.

Michael Reilly, executive director of the Alliance for Safe Biologic Medicines (ASBM), told Bloomberg BNA said he thinks the FDA will issue more guidance on biosimilars in early 2016. Reilly said FDA's Janet Woodcock has stated that the agency plans to have more transparency regarding biosimilars, and ''that was really saying, We're going to get more guidance out.''

''The lack of guidance is the reason we only have one approval after five years,'' Reilly said. If guidance isn't out in the first quarter of 2016, ''then I think all bets are off.'' The big issue, Reilly said, is interchangeability. The rest of the world ''is trying to deal with interchangeability in a different way, which is almost to create data from use. And that is really kind of a back-door way to get to interchangeability,'' rather than approving it as an interchangeable product and providing the data before approval, he said.

Meanwhile, Arent Fox's Short said the issue of biosimilar naming will likely come to a head in 2016 as the FDA makes decisions on naming conventions for biosimilar products and deals with applications for approval of a growing number of such products.

However, Reilly said the presidential election could have an impact on the FDA's actions on biosimilars. ''The question is, from the agency's perspectives, does that put pressure on them to finalize this administration's view on a lot of things,'' he said. While the FDA isn't a political agency, it can get pressure from the Office of Management and Budget and the health and human services secretary's office, Reilly said.

''Part of what has caused problems with the agency overall is that there's so many bigger fish to fry with the'' larger portions of the Affordable Care Act, Reilly said. ''This has made the BPCIA [Biologics Price Competition and Innovation Act] a smaller player. So the question is who is going to be driving.'' The biologics law is part of the ACA.

Reilly also said the FDA and the ASBM will be focusing on educating prescribers and pharmacists about biosimilars. He said ASBM will be doing a ''significant'' education campaign beginning in the first quarter.

Additionally, Reilly said another issue for biosimilars will be what goes on at the state level. He said last year was a big year for passing state legislation. The substitution of a biosimilar product for the innovator or brand-name biologic product can't be done without a state law in place to authorize the substitution.

**Biosimilars and the Trans-Pacific Partnership.** Another biosimilar issue that many expect to be tackled in the coming year concerns the differences between market exclusivity provisions for biosimilars contained in the BPCIA versus market exclusivity provisions for biosimilars contained in the Trans-Pacific Partnership (TPP) agreement.

The TPP is a trade agreement among 12 Pacific Rim countries concerning a variety of matters of economic policy, which was reached on Oct. 5, 2015.

  PLIR ISSN 1542-9547

BIO's Holcombe said BIO is ''very disappointed'' in the TPP agreement. Specifically, she said BIO is ''very disappointed that the agreement does not include the 12 years of biological product exclusivity that was included in the U.S. legislation that established the biosimilars pathway.''

According to Terry G. Mahn of Fish and Richardson P.C. in Washington, there will now be a lot of international pressure on the U.S. to harmonize with the TPP.

**Litigation Over Biosimilars.** As biosimilars begin to enter the market, experts predict that more litigation is likely to ensue over the implementation of the BPCIA.

According to Kevin Noonan of McDonnell Boehnen Hulbert & Berghoff LLP in Chicago, the big story in biosimilars isn't so much the FDA licensing of the first U.S. biosimilar, Sandoz's Zarzio, but in Sandoz's successful avoidance of the ''patent dance'' provisions of the BPCIA and the consequences of that strategy.

The BPCIA's patent dance provision requiring exchange of patent information allows the biologic reference product sponsor (RPS) and the biosimilar applicant to deal with the possibility of an infringement action sooner rather than later to avoid unnecessarily putting the applicant's launch of the biosimilar at risk.

In Sandoz's case, it refused to share its biologics license application (BLA)—a request for permission to introduce, or deliver for introduction, a biologic product into interstate commerce—and manufacturing and patent information with Amgen for its biosimilar Zarxio. Amgen sued Sandoz in the U.S. District Court for the Northern District of California, alleging violations of the BPCIA. The Northern District ruled for Sandoz judgment on the pleadings, and Amgen appealed to the U.S. Court of Appeals for the Federal Circuit.

But in July 2015, a panel of the Federal Circuit agreed with Sandoz that the sharing of the BLA and the manufacturing and patent information exchanges are optional, not mandatory. An applicant's refusal to share the necessary information with the RPS allows the RPS to immediately sue for infringement and for a preliminary injunction delaying release of the biosimilar, the panel said.

As a consequence of the Federal Circuit affirmance, ''It's hard to see how any biosimilar applicant would ever disclose, if a lawsuit, which the biosimilar applicant is anticipating, is the only penalty,'' Noonan said.

In the absence of any required patent dance, Gaby L. Longsworth, with Sterne Kessler Goldstein Fox in Washington, predicted that more biosimilars will likely enter the market.

In addition, because the Federal Circuit also decided that the ''Notice of Commercial Marketing'' required by the BPCIA can only be given 180 days before commercial marketing when the biosimilar has FDA approval, there is another perhaps unanticipated consequence to the Federal Circuit panel's decision, Noonan said.

''This would give the RPS time to go to court to seek an injunction and preserve the status quo ante while litigation, which was envisioned to begin well before the end of the 12-year regulatory exclusivity period, ensues,'' he said.

**Off-Label Promotion.** Another hot-button topic for the pharmaceutical industry in 2016 will be the continued apparent collision between the FDA's policy of restricting what drug manufacturers can tell health-care professionals about the off-label unapproved uses of their products and the First Amendment.

Attorneys tell Bloomberg BNA that this year could be a seminal one for pharmaceutical advertising and promotion as the FDA grapples with how to approach the promotion of products for unapproved uses in the wake of several recent court defeats for the agency.

Under long-standing policy at the FDA, companies can be subject to criminal prosecution and civil liability if they promote their products for uses the FDA hasn't specifically approved. But drugmakers have alleged the FDA's off-label regulations unconstitutionally prohibit them from making completely truthful and nonmisleading statements to health-care providers about the unapproved uses of their products.

PhRMA's Reilly said one of the industry group's challenges is ensuring ''our ability to communicate about outcomes that aren't included in the label.''

Because recent rulings in court cases involving promotional issues have gone against the FDA, there is increased pressure on the agency to clarify its position on what is permissible and prohibited speech under the federal FDCA.

Drug manufacturers say the restrictions violate their free speech rights under the First Amendment.

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**Manufacturers say restrictions on drug promotion violate their free speech rights under the First Amendment.**

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The agency suffered multiple setbacks to its off-label promotion policy in 2015, most recently in cases involving the drug companies Amarin Pharma Inc. and Pacira Pharmaceuticals Inc.

Amarin sued the FDA in May 2015, challenging the constitutionality of FDA regulations that prohibit Amarin from making completely truthful and nonmisleading statements about its high-triglyceride treatment Vascepa, a pure omega-3 fatty acid. It won preliminary relief in August 2015 when Judge Paul A. Engelmayer of the U.S. District Court for the Southern District of New York found that Amarin had established a likelihood of success on the merits. The agency subsequently told Amarin in a letter that it didn't object to many of the off-label statements the company wants to make about Vascepa. The parties are currently discussing settlement.

Meanwhile, Pacira, which also challenged the FDA limits on off-label promotion, scored a victory in December 2015 when the FDA agreed to let it market its pain drug Exparel for broader uses than it originally had allowed. Pacira, which sued the FDA in September, has since dropped the suit.

''Recent court decisions suggest that FDA restrictions on off-label advertising may abridge the First Amendment,'' Fish & Richardson's Mahn said. ''The Supreme Court is likely to weigh in and, if it does, FDA rules may need to be revised or eliminated,'' he said.

''I think the FDA's going to bite the bullet on off-label issues and issue guidance,'' John Kamp, consulting counsel to Wiley Rein LLP in Washington and executive director of the Coalition for Healthcare Communica-

tion, an industry group that promotes the free exchange of scientific and medical information, told Bloomberg BNA.

''I think the FDA's Chief Counsel's office 'gets' it and the staff at CDER 'gets' it and they will do something,'' Kamp added.

''I don't expect huge leaps forward from them,'' he said, ''but maybe baby steps forward, and maybe even a few significant steps.''

Indeed, Woodcock has stated that taking a new look at drug advertising and promotion in light of current jurisprudence around the First Amendment is one of the agency's priorities for 2016.

Kamp said, ''I'm most optimistic that they will do something on FDAMA [the Food and Drug Administration Modernization Act] Section 114 so there can be more discussions with payers and more substantive discussions.'' Section 114 of FDAMA required the FDA to give more guidance on discussion with payers, Kamp said.

''I'm hoping for a clean definition of the parameters of scientific exchange,'' he said.

''I'd like to see them begin to discuss some additional off-label information, including information about post-clinical marketing in addition to clinical trials to come under the ambit of 'truthful and nonmisleading' speech,'' Kamp added.

Meanwhile, the suits against the agency and the losses for FDA in the off-label promotion realm are expected to continue.

''I think we'll see more small companies with a lot at stake in their off-label communications challenge the FDA in court or at FDA on some of their restrictions,'' Kamp said. And he said, ''I wouldn't be surprised to see FDA continue to lose in court'' on off-label issues.

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—John Kamp, Coalition for Healthcare Communication

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''The past year has shown again that the FDA still needs to refine its view of what constitutes violative off-label promotion and how long it will continue to bet on a losing horse,'' Mintz Levin's Bentley said.

If the FDA doesn't change what it's doing, that will invite more litigation, Wiley Rein LLP's Czaban said. But he said, ''the off-label issue is going to come to a head eventually,'' forcing the agency to confront its multiple defeats on the issue.

But Richard A. Samp, chief counsel for the Washington Legal Foundation, a pro-business group based in Washington, isn't so sure that the FDA is going to change its approach.

''Despite FDA's repeated losses in the courts, I have seen no evidence that FDA has learned its lesson,'' Samp said.

Instead, Samp said, the agency ''keeps repeating the same pattern: it declines to appeal its losses and then insists that the losses don't inhibit its right to continue with business as usual.''

''I suspect that it's only a matter of time before we see another lawsuit similar to Amarin, but it will probably take several more FDA losses before FDA begins to give serious consideration to First Amendment values,'' Samp said. ''That won't happen during 2016.''

**Off-Label Prosecutions to Continue?** And, even though changes to FDA off-label policy could open up new opportunities for drug manufacturers and patients, there will be still be some off-label speech that will increase the risk of liability for drug manufacturers, Fish & Richardson's Mahn said.

Although government prosecution of companies for off-label speech via the False Claims Act has become more difficult in the wake of the recent jurisprudence, Kamp said such cases will continue.

''I don't think the off-label prosecutions are dead,'' Kamp said, ''but they're going to be much harder for the [government] to bring. I do think they're going to change what they go after.''

**Drug Stores Weigh In.** Carol Kelly, senior vice president of government affairs and public policy for the National Association of Chain Drug Stores (NACDS), told Bloomberg BNA that the NACDS will continue to work with the Pharmaceutical Distribution Security Alliance on the implementation of the Drug Quality and Security Act (DQSA).

''As part of that coalition, we maintain an ongoing interest in working with FDA and other supply chain stakeholders to ensure appropriate implementation of the statute,'' Kelly said.

Kelly also said the NACDS is ''very excited'' about the pilot project that the Centers for Medicare & Medicaid Services announced in September 2015 on medication therapy management (MTM) in Part D.

In September 2015, the CMS announced it will test a new model intended to encourage innovation by Part D prescription drug plans in designing their MTM programs in which enrollees are targeted for consultations and management strategies on their prescriptions. The program, called the Part D Enhanced Medication Therapy Management model, will offer prescription drug plans in 11 states the chance to design and implement innovative strategies to improve medication use and care coordination. The five-year model will begin Jan. 1, 2017, in Virginia, Florida, Louisiana, Iowa, Minnesota, Montana, Nebraska, North Dakota, South Dakota, Wyoming and Arizona.

''Basically, CMS is trying to test better financial alignment, innovation and medication therapy management intervention and better target Part D beneficiaries in the Medicare program,'' Kelly said. ''We really welcome the opportunity to work over the next three to five years'' with the Part D plan and the CMS program ''to get to the next generation of medication therapy management in Part D.''

''It will be incredibly important for our members and for beneficiaries that the Part D plan works with community pharmacy to ensure that retail community pharmacies are involved in the provision of medication therapy management. We take great pride in the work that we've done with the Congress and with the agency to improve the benefit over time. So that is a critical focus area for next year and moving forward.,'' Kelly said.

''At the same time, the fact that there's a pilot ongoing, does not mean we won't be talking to members of Congress and seeing if there are other legislative opportunities,'' Kelly said. For instance, she said the NACDS is looking at the Medication Therapy Management Em-

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powerment Act of 2015 (S. 776), which was introduced in March. The legislation would allow seniors participating in Medicare Part D with any one chronic disease to thoroughly review all of their medications with a pharmacist or other health-care provider in a one-on-one session.

Kelly said ''another piece of legislation that's going to be critically important for our members for next year'' is the Pharmacy and Medically Underserved Areas Enhancement Act (S. 34, H.R. 592). The bill would provide Medicare coverage of pharmacist services.

''That's something we want to move through the legislative process at the federal level as quickly as possible,'' Kelly said.

**Controlled Substances.** Also, Kelly said there is a piece of legislation that passed the House and that's pending in the Senate, called the Ensuring Patient Access and Effective Drug Enforcement Act of 2015 (H.R. 471, S. 483) that her group supports.

The bill would require the Department of Health and Human Services, the Drug Enforcement Administration and the Office of National Drug Control Policy to submit a report to Congress one year after the bill's enactment identifying:

- obstacles to legitimate patient access to controlled substances;
- issues with diversion of controlled substances; and
- how collaboration between federal, state, local and tribal law enforcement agencies and the pharmaceutical industry can benefit patients and prevent diversion and abuse of controlled substances.

''That piece of legislation passed the House in April 2015 by voice vote, and it has been put on the calendar of the Senate Judiciary Committee probably for markup in January,'' Kelly said. ''We will be pursuing that.''

**Medicaid.** Kelly also said that when the CMS releases the final Medicaid outpatient drug rule, the NACDS will be examining the rule ''to make sure we think it's reasonable.'' The rule (RIN 0938-AQ41) would use the average manufacturer price (AMP) model to determine Medicaid reimbursements for prescription drugs. The rule also would implement the ACA by increasing transparency in drug pricing and ensure that taxpayers and states aren't overpaying.

''As we look at that rule and move into 2016, there are 24 jurisdictions throughout the country that either need to change their laws or regulations or both in order to implement the new federal upper limit (FUL),'' Kelly said. The FUL is the maximum Medicaid reimbursement rate for multiple-source drugs, meaning that there are multiple manufacturers for the drug and not just a single brand manufacturer.

''So, this will be a critical area of focus both here in Washington and through the states,'' Kelly said.

**GAO Report.** Members of the House Energy and Commerce Committee also have asked the Government Accountability Office to conduct a study to assess the FDA's regulatory pathway for reviewing generic versions of nonbiologic complex drugs (NBCDs).

NBCDs are drugs of nonbiological origin with an active ingredient that has molecular diversity, according to a December 2015 letter to GAO requesting the study. Examples of NBCDs include sodium ferric gluconate, which treats iron deficiency anemia in kidney dialysis patients, and liposomal doxorubicin hydrochloride, which treats several types of cancer.

The House members said the FDA is using the current regulatory pathway for approval of small-molecule generic drugs to evaluate NBCDs. ''Given the complex natures of these large molecule drugs, we seek GAO's input on whether the current statutory pathway for generic NBCDs is adequate to guarantee patient safety,'' the letter said.

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