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# OUTLOOK 2016: Lab Tests, Cybersecurity, Off-Label Use Among Top Device Issues

How to regulate laboratory-developed tests (LDTs), concerns over cybersecurity, a new FDA user fees law and possible guidance for clinical decision support software are among the top issues that will affect the medical devices industry in 2016.

Bloomberg BNA talked with attorneys, other policy experts and stakeholders in late 2015 and early 2016 about device-related issues for the new year. They said they expect to see a flurry of activity in 2016 centered on the regulation of LDTs, which are tests that are designed, manufactured and used in a single laboratory.

''I think a major issue for 2016 will be what action occurs on LDTs,'' Peter Kazon of Alston & Bird LLP in Washington said.

The new year ''will almost certainly see some major activity on LDTs that could have ramifications for years to come,'' he added.

**Debate Over Regulation of LDTs.** Historically, the regulation of diagnostic procedures such as LDTs has been under the aegis of the Centers for Medicare & Medicaid Services (CMS) under the Clinical Laboratory Improvement Amendments (CLIA).

But the Food and Drug Administration has said it wants to increase its oversight of LDTs and plans to issue a final guidance on LDTs in 2016, following up on a draft guidance it issued in the fall of 2014. In that guidance, the agency said it intended to phase out its general policy of exercising enforcement discretion over LDTs and start actively overseeing at least some of these tests. The agency recently said the LDT guidance is on its high priority list of 2016 guidances.

And Jeffrey Shuren, director of the FDA's Center for Devices and Radiological Health (CDRH), said at a congressional hearing in 2015 that CDRH intends to move forward with implementing a lab test framework in 2016.

''FDA seems determined to tackle lab-developed tests,'' said Bradley Merrill Thompson of Epstein Becker & Green in Washington. ''Equally significant, CMS has chimed in to say that FDA is indeed the right regulatory agency to take the lead.''

According to John Manthei of Latham & Watkins LLP in Washington, ''FDA's proposal to implement a regulatory framework for LDTs represents a major change for this segment of the medical device industry.''

And, despite the CMS's support for the FDA's plan for increased oversight of LDTs, there is opposition to the agency's proposal both in Congress and in the clinical laboratory community.

''There are some in Congress who would like to take steps to limit or at least more carefully define the FDA's role in regulating LDTs,'' Kazon said. And clinical labs generally have opposed the FDA's plan, while the device industry has supported the FDA plans for stricter lab test oversight.

**Potential for Legislation on Lab Tests.** Theodore M. Sullivan, a Washington-based attorney at Buchanan Ingersoll & Rooney PC, told Bloomberg BNA in an early January phone interview he's watching Congress to see if someone will introduce legislation that would explicitly give the FDA the authority to regulate LDTs. Alternatively, someone may sponsor a bill that would prohibit the agency from regulating the tests, Sullivan said, adding there's also a possibility that someone could introduce legislation that would be a middle-of-the-road approach to the issue.

William Garvin, also a Washington-based attorney at Buchanan Ingersoll, said, ''I expect there to be major fights in the LDT space in 2016.'' Industry needs to pay attention to what Congress and/or what the FDA does on the matter because ''there's so much uncertainty'' surrounding the issue, he told Bloomberg BNA.

Colleen M. Heisey, of Jones Day in Washington, said the debate regarding FDA oversight of LDTs will continue in 2016.

**A potential legal challenge by a trade group for clinical labs is looming as the FDA prepares its final plan for regulating laboratory-developed tests.**

''If FDA takes any action on LDTs in 2016, regardless of what direction, we could expect one or more parties to take issue,'' Heisey said. For example, she said, ''in anticipation of greater regulation of LDTs, the American Clinical Laboratory Association is preparing to make a legal argument against FDA's statutory authority, tapping heavyweights Paul D. Clement and Lawrence Tribe to lead the charge.''

''Given the money involved, no one should expect clinical laboratories to back down quietly,'' Thompson said.

Gregory H. Levine, of Ropes & Gray LLP in Washington, predicted that the ''FDA will seek to continue to ad-

vance its proposed framework on LDTs, while lab groups will continue to threaten litigation and various groups will be pursuing legislative proposals.''

While the issue of LDT regulation remains in flux, the FDA is likely to continue its enforcement against direct-to-consumer laboratory testing but otherwise not pursue regulation of LDTs, Levine said.

**What Will FDA's Plan Look Like?** In any event, given how LDTs have evolved over the decades, ''the FDA has acknowledged that its general enforcement discretion policy no longer reflects the complexity of LDTs,'' Michael Gaba, of Holland & Knight in Washington, said.

Indeed, Sonali Gunawardhana of Wiley Rein LLP in Washington said, although the FDA historically has exercised ''enforcement discretion'' over LDTs (generally not enforced applicable regulatory requirements), ''Today, many of these tests may compete with FDA-approved tests without clinical studies to support their use.''

''FDA has made it clear, as has CMS, that they have the ability and the experience to establish an LDT oversight framework, including pre-market review for higher-risk LDTs, such as those that have the same intended use as FDA-approved or cleared companion diagnostics currently on the market,'' Gunawardhana said.

But so far, it's unclear what the FDA's final LDT guidance will look like and how it will differ from the draft guidance, Kazon said.

This will be an important issue for the device industry to continue to watch closely, Levine said, because ''the proverbial devil will be in the details.''

According to James N. Czaban of Wiley Rein LLP in Washington, how the regulatory framework on LDTs develops is likely to have long-lasting effects that reach beyond the tests themselves to the world of precision medicine.

Precision medicine uses an individual's genetic information to determine whether that person might respond to a targeted drug treatment. Because diagnostic tests may be used to determine whether a patient will benefit from a particular therapy, Czaban said, the regulation of LDTs ''will impact precision medicine as it goes forward.''

In any event, regardless of what specific actions occur on LDTs in 2016, there is consensus that LDTs will continue to be a hot topic.

''I do not foresee the regulatory momentum that has been building at FDA slowing down at all in this area,'' Stephanie Philbin, of Goodwin Procter in Washington, said.

**Cybersecurity Issues.** Cybersecurity is another issue that experts agree will be a hot topic in 2016.

With cybersecurity threats to the health-care and public health sectors expected to increase, including an increase in threats directed at lifesaving medical devices, cybersecurity will continue to be a focus in 2016, Heisey of Jones Day said.

Indeed, increasingly complex and networked medical devices mean new and significant privacy and security concerns and challenges, Jake Holdreith of Robins Kaplan LLP in Minneapolis said, citing ''digital health convergence, especially the regulatory, privacy, security and IP [intellectual property] challenges arising from the marriage of consumer interaction with hardware and software into the device space.''

''The culture of consumer-facing software development is so different from the culture of the regulated device industry that there are significant challenges in putting the two together,'' he said.

There will be an increased focus on data privacy and security with regard to data stored in devices, Mike Bell of consulting firm R-Squared Services & Solutions Inc. in Princeton, N.J., predicted. And, he said, European Union laws and regulations on these issues that are expected soon also ''will bring a renewed focus on privacy/security compliance.''

The FDA is working proactively in the cybersecurity space, Gunawardhana said, noting that the agency, in collaboration with the National Health Information Sharing Analysis Center (NH-ISAC), the Department of Health and Human Services and the Department of Homeland Security, is kicking off 2016 with a two-day public meeting to discuss complex challenges in medical device cybersecurity.

Gunawardhana also said that the FDA is planning to issue a guidance document to address post-market medical device cybersecurity issues, having previously issued one on pre-market issues.

Heisey said that 2016 also may bring an evaluation of the FDA's oversight of networked devices.

According to the Department of Health and Human Services' Office of Inspector General's FY 2016 Work Plan, the OIG plans to initiate a review of ''whether FDA's oversight of hospitals' networked medical devices is sufficient to effectively protect associated electronic protected health information (ePHI) and ensure beneficiary safety,'' Heisey said.

Following and participating in the FDA's cybersecurity efforts will be important for the medical device industry, Gaba of Holland & Knight said.

**Mobile Apps.** Experts also predicted that 2016 will bring FDA action on the burgeoning area of health care-related mobile applications and data systems.

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—JOHN MANTHEI, LATHAM & WATKINS

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''FDA's attempt to regulate this growing and evolving area [of mobile apps] will likely continue to develop and face new challenges over the coming year,'' Manthei of Latham & Watkins said.

''Pharmaceutical companies seem poised to dive in at an accelerated rate into digital health,'' Thompson observed. ''This means that pharmaceutical companies will continue to partner with Silicon Valley tech companies to develop software and wearables that will supplement drug therapy.''

''These technologies can help optimize the timing and dosage of pharmaceutical products, as well as enhance compliance with drug regimens,'' he said.

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Nonetheless, Thompson said, many issues are swirling around whether these products are medical devices, and, if so, how they should be regulated.

**Hands-Off Approach for Low-Risk Devices.** But at least where low-risk wireless medical devices and mobile apps are concerned, in 2016, the FDA will likely continue to apply a hands-off, deregulatory approach, Keith A. Barritt, of Fish & Richardson P.C. in Washington, said.

In 2015, the FDA released a draft guidance titled ''General Wellness: Policy for Low Risk Devices'' that proposed to deregulate low-risk products that are intended to (1) help maintain or encourage a general state of health or healthy activity such as weight management or physical fitness or (2) promote, track and/or encourage choices that may help to reduce the risk of, or the ability to live well with, certain chronic diseases or conditions.

''The proposal represents a potentially exciting new development in the regulation (or lack thereof) of medical devices, particularly mobile apps that are designed to provide people with real time information to make well-informed choices that may affect their health,'' Barritt said.

**Guidance on Clinical Decision Software?** While the FDA has published guidances on health-care-related mobile apps and data systems, it has explicitly said that the mobile apps guidance didn't apply to Clinical Decision Software (CDS).

CDS refers to stand-alone software that provides clinical decision support to help physicians make decisions about patient diagnoses.

And the CDS industry is eager for guidance. The FDA promised to publish a guidance for industry for clinical decision software in 2015, but didn't do so.

''There are many people in the stand-alone software industry who are waiting to see what happens, [and who are] struggling to develop clinical decision support software in the present void,'' Thompson said.

''Right now, if raising venture capital or otherwise trying to get funding for a project, companies struggle to explain whether their product will be regulated by FDA, and therefore struggle to predict the time-to-market and cost,'' Thompson said. ''That means a bunch of projects are simply stymied right now due to the uncertainty.''

The health-care software industry is keen to see some guidance in the CDS area, concurred Edgar J. Asebey, of Jones Day in Miami.

''With the continuing launch of Clinical Decision Software for varying medical functions, industry is looking for guidance from the FDA on this fast-emerging area of medical technology,'' Asebey said.

''This draft guidance is important to developers of software tools that help guide clinical decision-making,'' Ropes & Gray's Levine said.

While the ''FDA is expected to continue to take a relatively hands-off approach to software regulation, as suggested in the FDASIA [the FDA Safety and Innovation Act of 2012] Health IT report issued in 2014,'' the details of this draft guidance could be important, Levine said.

The FDA's promised draft guidance on CDS ''will hopefully assist medical device manufacturers to better navigate the regulatory environment and keep patients safe with promising technology and advanced medical devices,'' Wiley Rein's Gunawardhana said.

**''Either Congress will pass legislation limiting the scope of FDA review of health information technology, or FDA will publish a guidance document on clinical decision support software.''**

—Bradley Merrill Thompson, Epstein Becker & Green

Thompson of Epstein Becker & Green predicted that, in 2016, ''Either Congress will pass legislation limiting the scope of FDA review of health information technology, or FDA will publish a guidance document on clinical decision support software.''

''Either way, the dividing line between FDA regulation and unregulated should get clarified,'' he said.

''Depending on how complex the legislation or guidance is, it will answer questions, raise new ones or both,'' Thompson said.

**Genetic Test Kit Marketing.** The FDA also will continue to keep a watchful eye on the marketing of genetic test kits, Barritt said.

In 2013, the FDA issued a warning letter directing Mountain View, Calif.-based 23andMe Inc. to stop selling its Saliva Collection Kit and Personal Genome Service because it lacked marketing clearance or approval to assure that its tests were accurate, reliable and clinically meaningful. In late 2015, the FDA sent similar letters (that weren't designated as warning letters) to several other companies questioning the legality of their genetic test kits.

While 23andMe since has secured FDA approval for its genetic test kit and relaunched it, the kit is only approved for Bloom Syndrome, which is associated with short stature, sun sensitivity and higher cancer risk.

''Thus, while genetic testing is clearly a part of the future of health care,'' Barritt said, ''the FDA is keeping a close eye on the market.''

The ECRI Institute's president and chief executive officer, Jeffrey C. Lerner, said the patient safety organization intends to focus on the claims made by genetic test makers in 2016.

Genetic tests and precision medicine ''have exploded'' in popularity, Lerner told Bloomberg BNA in an early January interview. He said the public is being told precision medicine is ''terribly important'' by politicians and corporate interests.

According to Lerner, the problem is that the promise of precision medicine is being oversold. ''When ordering these tests, patients don't know what they're asking for and/or payers don't know what they're paying for.''

Moreover, precision medicine is being advertised as being here, but that's pretty misleading, the ECRI leader said. There aren't that many aspects of precision medicine that have demonstrated proven results, Lerner told Bloomberg BNA.

As part of its focus on precision medicine, Lerner said ECRI will be examining manufacturer claims for diagnostic tests. Specifically, the group will be looking to

see if test makers have evidence about the claims they're making for their products, he noted. In addition, Lerner added that the group will be looking at advertising claims made by hospitals that make tests.

The ECRI Institute is based in Plymouth Meeting, Pa.

**Combination Products to Get Attention.** Reviews of combination products at the FDA also are expected to garner legislative and agency attention in 2016.

''Combination product reform seems likely in 2016,'' Thompson said. Thompson, with Epstein Becker & Green PC in Washington, is also the general counsel of the Combination Product Coalition (CPC), an industry group.

Combination products are made up of combinations of a drug, device and/or biological product. They don't fit into the traditional categories of drugs, devices or biological products. Combination products pose unique challenges for the agency because they may involve new, complex technologies and their review often involves the expertise of more than one of the FDA's centers.

The CDRH's Office of Combination Products designates which of the FDA's centers will be the lead reviewer for a product based on the product's ''primary mode of action'' or PMOA.

How a combination device is designated has huge financial ramifications for companies because products with a device rather than a drug PMOA means a $5,000 user fee is paid by the manufacturer whereas a drug determination carries with it a $260,000 user fee. Accordingly, many companies are eager to have their product designated as a product with a device PMOA so the review will be assigned to the CDRH rather than to the FDA's Center for Drug Evaluation and Research.

Thompson said Robert Califf, currently the deputy commissioner of medical products and tobacco at the FDA, and President Barack Obama's nominee to head the agency, has made combination product reform a major initiative, which is unusual. Califf has said a new pathway is needed and the FDA could come up with a proposal on this for Congress in 2016.

Levine said the FDA is likely to issue a draft guidance in 2016 clarifying and describing the review process for combination products to address the concern of combination product developers and manufacturers about ambiguous and inconsistent intercenter coordination, consultation and review times for such products.

In addition, there are legislative proposals in Congress that would dramatically revise the review of combination products, with an emphasis on eliminating unnecessarily burdensome requirements and generally improving efficiency of the review processes.

**Cures Legislation.** The House version of the 21st Century Cures bill (H.R. 6), an effort to speed the discovery, development and delivery of lifesaving and life-improving therapies, includes a mandate for the FDA to issue guidance delineating the roles and responsibilities of each center during the review of combination products.

''This may not be sufficient, however, to dissuade stakeholders from continuing to push for legislative changes seeking to make the process more efficient,'' Levine said.

''The review process itself has many bumps in the road,'' which can delay bringing combination products to market, Thompson noted.

The FDA seems to be focused on one particular scenario involving combination products whose ''primary mode of action'' (PMOA) is considered a device but that also have drug type issues, Thompson said. However, he said, ''industry in many ways is more concerned'' about combination products that have a drug lead [or drug PMOA].''

When the House approved its Cures bill in 2015, Stephen J. Ubl, who then served as the president and chief executive officer of the Advanced Medical Technology Association (AdvaMed), a device industry trade group, said the bill ''includes a number of proposals designed to strengthen the innovation ecosystem and support the development of life-saving, life-enhancing medical technology.'' Ubl said the legislation ''includes key improvements to FDA's premarket program for medical devices—most significantly the establishment of an expedited pathway for breakthrough, innovative technologies—which will increase the efficiency, predictability and transparency of the agency's review process and improve patient access to the best in medical progress.''

Ubl has since left AdvaMed and is now the president and CEO of the Pharmaceutical Research and Manufacturers of America (PhRMA), a drug industry trade group.

Garvin of Buchanan Ingersoll told Bloomberg BNA the Senate may be moving more slowly than normal on companion legislation to the Cures bill in 2016. Some parts of the bill may be rolled in to drug and device user fee agreements that Congress will consider, Garvin said.

''It's hard to handicap legislation,'' Garvin added, saying ''It's hard to see how fast'' companion legislation will move through the Senate.

**Unique Device Identifiers.** Experts also expect 2016 to bring action on other FDA regulatory initiatives such as implementing the unique device identification system (UDI)—labels and bar codes that allow manufacturers and regulators to track and trace devices—as well as device quality pilot initiatives and the leveraging of big data analytics.

September 2016 will bring the implementation of requirements regarding the UDI marking of labels and packages for moderate-risk (Class II) devices, as well as requirements regarding the direct UDI marking of certain Class III (high-risk) devices, Manthei said.

''These constitute significant next steps in the implementation of FDA's UDI rule,'' he added.

And Levine predicted that the CDRH will continue to move ahead with pilot projects on device quality metrics—a set of performance goals and measures to assess device quality—similar to what the FDA already proposed for the pharmaceutical industry in July 2015.

''In 2016, the FDA is expected to begin releasing 'Critical to Quality' guidance documents on specific device types, complete the Medical Device Single Audit Program in cooperation with several foreign governments, and support continued work on device quality metrics through a program run by Xavier Health,'' Levine said.

''Although these are early days for these efforts, device manufacturers should pay close attention because these initiatives have the potential to change the way in which FDA applies its resources to regulate device quality,'' Levine said.

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**FDA Using Its Own Data.** Using big data analytics to aid regulatory decision making is another area that the FDA's Center for Devices and Radiological Health has identified as one of its top 10 regulatory science priorities for FY 2016.

The FDA plans to digitize its inspection and testing processes to improve its use of its own data. In 2016, the agency will connect its testing laboratories and field offices to allow inspectors and researchers to communicate freely and make use of agency data, including data it collects about medical devices.

But, Manthei said, ''Just how CDRH will make use of big data analytics, and the ultimate impact this will have on the center's operations, remains to be seen.''

**Device Evaluation.** Ben Moscovitch, who studies medical device issues at the Pew Charitable Trusts, a nonprofit public policy organization, told Bloomberg BNA in an early January interview that the group will be focusing on an effort that may help facilitate device innovation.

In 2016, Pew will be monitoring the design and implementation of a national medical device evaluation system, Moscovitch said. Under the system, if implemented, manufacturers, health plans, the FDA, researchers and other stakeholders would be able to more quickly evaluate device safety. In turn, he said this system would ''facilitate innovation and more quickly identify safety concerns.''

The Medical Device Epidemiology Network's Medical Device Registry Task Force in August 2015 released a draft report titled ''Recommendations for a National Medical Device Evaluation System: Strategically Coordinated Registry Networks to Bridge Clinical Care and Research.'' The recommendations could help define immediate next steps needed to develop and launch a system, the report said. Created as part of the Medical Device Epidemiology Network public-public partnership, the task force was convened by Duke University under a cooperative agreement with the Food and Drug Administration, an August Federal Register notice (80 Fed. Reg. 51,567) announcing the report said.

In comments on the report made upon its release, Josh Rising, the director of health-care programs at the Pew Charitable Trusts, told Bloomberg BNA, ''This report joins a body of research that shows we need multistakeholder leadership to surmount the technical challenges inherent to creating a 21st-century registry network.'' Currently, registries aren't able to obtain data in a standard way, which hinders the development of a national network that could improve data collection throughout a device's lifecycle, he said.

Registries are a mechanism to document and collect information about patient populations being treated, the provider's quality and processes of care, device performance and the clinical outcomes.

**FDA Leadership Changes.** In addition to the FDA's regulatory initiatives, personnel changes—including new leadership at the top—will be an issue in 2016.

Califf's nomination as FDA commissioner is awaiting a vote by the Senate. The Health, Education, Labor and Pensions Committee held a confirmation hearing in November 2015 and a vote in early January. In addition to the expected change at the top, there also has been a lot of change within the FDA's device center recently.

''There was a fair amount of turnover at the top of CDRH in 2015,'' Gaba said. ''Most notably, there is a new Deputy Center Director for Policy [Lauren Silvis, formerly an attorney with Sidley Austin LLP], and the Center still needs someone to lead ODE [the Office of Device Evaluation] and the Office of Compliance (beyond those currently acting).''

There are lots of new people at the CDRH and industry has noticed inconsistencies among reviewers within the FDA, Judith K. Meritz, of Meritz & Muenz LLP in Quogue, N.Y., said.

**The devices industry should be interested in monitoring new leadership at the FDA devices office ''for any 'course adjustments,' particularly in the compliance arena.''**

—Michael Gaba, Holland & Knight

And Gaba said, while Shuren is still in charge of the CDRH, ''industry should be interested in monitoring the new leadership for any 'course adjustments,' particularly in the compliance arena.''

**MDUFA Reauthorization.** On the legislative front, issues that are expected to arise include medical device user fee reauthorization and the fight to repeal the medical device tax.

The FDA's authority to collect user fees from the device industry under the Medical Device User Fee Amendments (MDUFA) ends September 2017, so parties are gearing up for a reauthorization of MDUFA. As part of MDUFA, in exchange for collecting user fees from industry, the FDA agrees to meet performance metrics, including expedited review times.

As MDUFA reauthorization discussions begin, ''expect a good amount of activity on the legislative front,'' Philbin said.

And Manthei said that the MDUFA reauthorization process may have significant effects across the industry, and could affect user fee amounts as well as the timelines for FDA reviews.

**Push to Repeal Device Tax Not Over.** Meanwhile, the 2.3 percent medical device tax, which has caused great consternation for the device industry since it was passed as part of the Affordable Care Act, has been suspended for two years. Obama Dec. 18, 2015, signed a massive year-end spending package (H.R. 2029) that funds the government through 2016 and delays key ACA taxes, including the controversial device tax.

The tax has been targeted for repeal by many stakeholders who have complained about confusion as to what devices the tax applies to and its negative financial impact on device companies.

The fight to repeal the tax for good will move forward during the suspension. For example, AdvaMed in a statement said, ''Congress and the administration have demonstrated that they recognize the negative effects of this tax. We urge policy makers to continue their work to eliminate the device tax and address other factors that are threatening the health care innovation ecosystem.''

And Bloomington, Ind.-based Cook Medical said that it would continue to work with Congress to repeal the medical device tax altogether.

**Off-Label Promotion Questions Remain.** With regard to litigation issues affecting devices, the issue of the FDA's authority to regulate off-label promotion is expected to continue to be a central one. 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.

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

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 discussing a 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, since has dropped the suit.

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**Even after the FDA's recent losses or settlements in off-label cases involving drugs, "off-label marketing continues to be a significant issue not just for pharma manufacturers but also for medical device manufacturers."**

—Laura F. Laemmle-Weidenfeld, Jones Day

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But, even after the FDA's recent losses or settlements in off-label cases such as Amarin and Pacira, ''off-label marketing continues to be a significant issue not just for pharma manufacturers but also for medical device manufacturers,'' Laura F. Laemmle-Weidenfeld, of Jones Day in Washington, said.

Thompson agreed. Off-label promotion will continue to be a major issue, he said, both because the legal consequences are so significant and because companies' need to communicate with physicians also is growing.

''The tension here makes for very high stakes as companies try to figure out how to legitimately promote their products and legitimately collaborate with physicians to identify innovative new uses for products, while avoiding legal violations,'' he said.

But Meritz pointed out that, in the device area, the question of what is considered ''off-label'' often has a different answer than in the pharmaceutical area. In the device arena, how a device is used is a large part of the claims that are made, she said.

''Still, the [problem] of questions posed to a sales representative while in the operating suite as to the 'cleared' use of a product remains an issue,'' she said.

And Laemmle-Weidenfeld said that the FDA and the Justice Department are continuing ''to take an aggressive position as to the prohibitions against off-label promotion, even in the face of judicial holdings that truthful, nonmisleading promotion of uses of the product beyond its approved indications can be protected under the First Amendment.''

''We will certainly be watching for instances of additional manufacturers seeking declaratory judgment from the courts in advance of government enforcement actions,'' she said.

But, she said, despite the aggressive rhetoric from the government on off-label promotion issues, it may be that the government will adopt more moderate positions in enforcement actions or that it will decline to pursue some enforcement actions in this area.

In addition, she said, watch for whether more manufacturers attempt to negotiate their marketing approach with the FDA, pre-enforcement and pre-litigation, and if so, to what extent the FDA will be willing to work with them.

Laemmle-Weidenfeld said, ''It will be interesting to see how these issues play out in the device context, where the question of whether certain uses fall within a particular device's approved indications may be unclear.''

''These instances will be played out within the context of FDA's stated 2016 priority of re-evaluating its regulation of drug advertising in light of evolved First Amendment jurisprudence,'' she added.

**International Issues.** On the international front, Garvin of Buchanan Ingersoll warned that there could be increased oversight of foreign device manufacturing by the FDA in 2016. The agency has ramped up oversight of foreign drugmakers in past years and the FDA could decide to start targeting device makers that assemble products abroad, according to Garvin.

Sullivan agreed. He added the FDA has quite a significant ''compliance footprint'' for drug oversight in China and India. ''This could be easily translated to devices,'' Sullivan told Bloomberg BNA. ''I can't predict what will happen, but if I were a company depending on foreign manufacturing of devices, I'd be concerned, especially if I had Chinese or Indian manufacturing operations,'' he said.

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