This year marks the 40th anniversary of the Medical Device Amendments (MDA). Some might think that the MDA’s ruby anniversary would be celebrated by stability, predictability, and a general easing of regulatory developments and challenges. Thanks to technological developments in digital health, laboratory testing (e.g., genetic tests), combination products, however, there is no shortage of new ways to analyze and interpret the 40-year-old MDA and its implementing regulations. The FDLI Annual Conference highlighted all of these areas and more. Discussed below are some of the issues that appear to be most in flux with respect to FDA’s regulatory oversight and therefore, where industry can expect to see the most movement over the next few years.

**Digital Health**

Bradley Merrill Thompson (Epstein Becker & Green, PC) led a session with Vernessa Pollard (McDermott Will & Emery LLP) and Linda Ricci (FDA CDRH) discussing developments in digital health, including wearables, mobile medical applications, and clinical decision support software. The key issue with which the group wrestled was how to determine when standalone software and consumer-wearable products become

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**Devices May Be Over-the-Hill, but Regulatory Developments and Challenges Show No Signs of Slowing Down**

By Allyson B. Mullen

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regulated medical devices. The answer: it depends on their claims.

The session focused on a hypothetical company that makes a wearable product, like many in the market today, that tracks various biometric data, including sleep patterns, gait, and other physiological changes. The company makes no medical claims about its product. A university develops a software algorithm that analyzes data from the wearable to track biometric data of a patient with multiple sclerosis. The university tells physicians to buy the wearable and upload the data for its analysis. The data analysis can help physicians understand how a patient’s disease is presenting and potentially identify a change in a patient that would necessitate bringing the patient into the physician’s office sooner than the next scheduled visit.

This hypothetical raises a plethora of potential regulatory issues. For example, there is the question of whether the use of the software with the wearable changes the regulatory status of the wearable itself, or if only the software would be regulated as a medical device. The key question, of course, turns on the claims being made both about the wearable and the software. The speakers indicated that if the wearable or software manufacturers claimed that immediate clinical action was necessary based on the information obtained from the wearable or the results of the data analysis, it could suggest active patient monitoring, which would likely be an FDA-regulated use. On the other hand, if the wearable manufacturer makes no medical claims and the software developer claims only that the data analysis can aid physicians in developing a treatment strategy, the speakers said it is possible that the wearable would not be regulated and the software would be subject to FDA’s current enforcement discretion as clinical decision support software. As with all devices, the regulatory status of digital health products hinges primarily on what a company says about the product.

The group also highlighted FDA’s two recent guidances regarding interoperability and postmarket cybersecurity. These guidances are particularly relevant in the digital health space to ensure that devices such as wearables that collect data are interoperable with the software and systems analyzing the data, and that all aspects of digital health from collection to analysis and storage have appropriate cybersecurity controls. Digital health is constantly developing and the lines separating what is and is not a device are not clear. FDA has indicated that it will take a risk-based approach to digital health products, and does not plan to regulate every device or mobile application that meets the definition of a device so long as the risks associated with them are low. Nonetheless, before jumping into a new and exciting medical use, manufacturers should carefully consider the potential regulatory implications and think through their marketing and regulatory strategy.

**Laboratory Developed Tests**

For decades, FDA and the laboratory world have argued over whether the statutory definition of a device includes laboratory testing services when there is no physical “device” being distributed in commerce. FDA issued draft guidances in October 2014 describing a plan to regulate laboratory developed tests (LDTs). Jeff Gibbs (Hyman, Phelps & McNamara, PC) was joined by Katherine Serrano (FDA CDRH) and Shelia Walcoff (Goldbug Strategies LLC) to discuss the current status of LDTs.

FDA plans to promote greater patient interaction with specific goals of creating new mechanisms for patient participation in both the pre- and postmarket settings in both 2016 and 2017. FDA, as part of an interagency task force, which included FDA, CMS, CDC, and NIH, met with lab test accrediting agencies and the states to better understand the current regulatory requirements for LDTs. Ms. Serrano stated that, as a result of task force meetings and other outreach with the lab community, FDA has heavily revised the draft guidances.

FDA agreed that the draft guidance required clarity, specifically around the exclusions and carve outs to the general rule that all LDTs will be regulated under the new framework. Concerns regarding the timing for implementation of the final framework were taken to heart by FDA as it considered the final guidance. Ms. Serrano also noted that FDA understood the challenges of implementing the quality system regulation (QSR) in a laboratory. FDA visits to labs provided some important insights. To this end, FDA will help to educate the laboratory community by providing supplementary materials, in draft format, regarding compliance with the regulatory requirements. Such materials may include guidance addressing how Clinical Laboratory Improvement Amendments (CLIA) compliance can aid in QSR compliance, and a list of the LDTs FDA considers to be Class III, thereby requiring approval of a premarket approval application (PMA).

While there was (and continues to be) much speculation about what will be in FDA’s final LDT guidance, no one knows if or when it will ever be issued. The group speculated that there is a high probability of litigation if FDA releases a
final LDT guidance. Ralph Hall (Leavitt Partners and University of Minnesota Law School), a member of the Diagnostic Test Working Group, provided a brief update on the House Energy & Commerce Committee’s counter-proposal to FDA’s draft LDT guidance. He indicated that the proposal removes LDTs from the device regulatory scheme and draws clear jurisdictional lines between LDTs and devices.

In light of this uncertainty, the group discussed how best to counsel clients before the guidance is finalized. Assuming there will be some “grandfathering” of LDTs that are already on the market when the final LDT guidance is issued, labs will have a great advantage if they are on the market sooner rather than later, even if what it means to be “on the market” is not entirely clear.

Laboratories are also well advised to be aware that FDA’s definition of a “direct-to-consumer” (DTC) LDT is evolving. The term, which once appeared to encompass only tests marketed directly to consumers with no involvement from a physician, is now expanding to include tests marketed directly to consumers that may be ordered by a physician and/or tests for which the results must be reviewed by a physician. Ms. Serrano explained that FDA’s oversight of LDTs is currently subject to enforcement discretion. However, DTC LDTs, do not get the benefit of enforcement discretion (i.e., they are regulated). FDA has expanded the definition of DTC LDTs to include tests for which a physician’s role may not appear to be adequate to protect a patient who is receiving a test (e.g., the physician is not sufficiently independent from the lab).

If FDA does not issue a final LDT guidance, the group expects FDA will continue to try to regulate LDTs through other means, including regulation of collection devices, research use only products used in LDTs, and enforcing the limits of the LDT definition (e.g., licensing of technology, transfer of tests developed in one lab to another). Even with all of the uncertainty in this area, one thing is certain: the LDT debate is far from over, and all of the panelists agreed that they expect LDTs to be on the agenda again at FDLI’s 2017 Annual Conference.

Combination Products
Nancy Stade (Sidley & Austin) moderated a combination product panel with Philip Desjardins (Johnson & Johnson), Suzanne O’Shea (Navigant Consulting), Rachel Turow (Novo Nordisk) and John (Barr) Weiner (FDA Office of Combination Products). After an introduction and brief regulatory history from Ms. Stade, the group focused the discussion on challenges facing companies integrating the regulatory process for novel device technology with drugs and biologics. The panel generally agreed that there must be a better way than the current combination products regulatory process, although there was no consensus on what that way might be. For example, embedding device experts in the drug center to help with drug delivery issues might work, but then the device experts in the drug center might begin doing things differently from the device center and they would not have the benefit of the device center’s extensive knowledge. Conversely, the idea of completely reorganizing FDA to focus on disease states rather than drugs/devices/biologics was discussed, but this carries with it significant financial, operational, and logistical issues, and would also create challenges for products that are used across multiple specialties.

Ms. Stade highlighted a few recent developments, suggesting that FDA is thinking about ways to improve combination product review and approval particularly in light of rapidly changing device technology leading to greater integration of devices with drug and biologic products. For example, in March 2016, FDA launched its “lean management process mapping approach” to improve efficiency, consistency, and predictability in the combination product review.
process. Additionally, in April 2016, FDA announced the creation of the Combination Products Policy Council, a senior-level, agency-wide forum intended to address combination product issues. It is too soon to tell whether or how these activities will aid the current combination product review process. There are also several legislative activities that could affect the review of combination products.

**CDRH Priorities**

All of the above issues present a number of challenges for FDA. During the CDRH update, Center Director Dr. Jeffrey Shuren highlighted CDRH’s priorities: (1) establish a National Medical Device Evaluation System (NMDES); (2) partner with patients; and (3) promote a culture of quality and organizational excellence.

Dr. Shuren explained that the NMDES is intended to aggregate significant amounts of both pre- and postmarket information into a single system, including information from claims and administrative systems, patient-generated data, EHRs, and device-specific and clinical care registries. The goal of the NMDES is to allow for the collection of safety data in a timely and efficient manner. If effective, the system could permit FDA to shift some premarket data requirements to the postmarket setting, thereby potentially allowing for faster clearances and approvals. Of course, in April 2015 CDRH issued a guidance document addressing this very issue: the shifting of some premarket data requirements to the postmarket setting. Over a year later, it is not clear that FDA has taken steps to effectuate this shift in data requirements, so there is some doubt as to whether NMDES will achieve its stated outcome, and other FDA and congressional initiatives have also tried to promote this same goal. Dr. Shuren indicated that FDA has committed some initial funding for the program with the plan to obtain additional funding through access fees to the data.
collected in the new system.

Dr. Shuren highlighted that CDRH’s goal is to ensure that U.S. patients are the first in the world to have access to high-quality, innovative, safe and effective medical devices. Accordingly, FDA plans to promote greater patient interaction with specific goals of creating new mechanisms for patient participation in both the pre- and postmarket settings in both 2016 and 2017. As with the postmarket data shift, CDRH has previously issued guidance—as far back as March 2012—that proposes greater patient involvement in the device review and approval process. Given the lack of traction resulting from prior statements on this matter, some in industry may be skeptical as to whether the new plans for patient involvement are likely to bear fruit.

Finally, CDRH is developing a culture of quality by, among other things, working towards various quality standards, including ISO 9001, and training CDRH employees regarding quality systems.

In sum, no matter the age of the MDA, the issues surrounding device regulation are showing no signs of simplifying and in fact, seem to be getting more complicated. With the current rate of technological developments, the next forty years of device regulatory developments will undoubtedly be as exciting as the last forty.