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FDA Regulatory and Compliance Monthly Recap

JANUARY 2016

KEY FINDINGS

OPDP enforcement reaches record low in 2015 as drugmakers face uncertainty in digital marketing

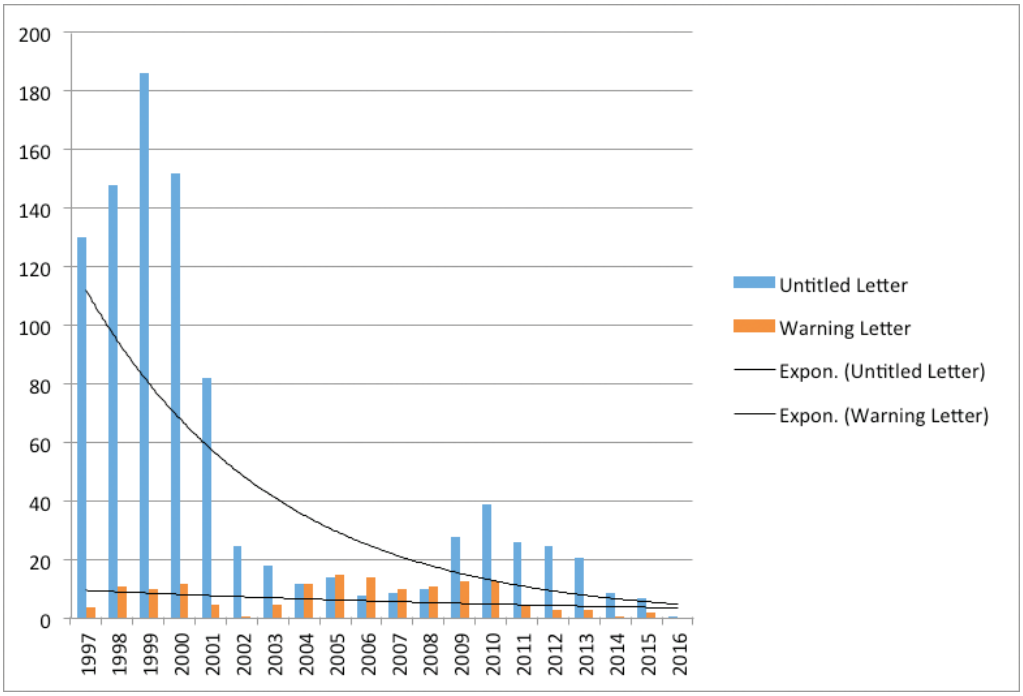
Enforcement by the OPDP has fallen notably since 2010. The decline has been attributed, in part, to the agency's slow adoption of digital marketing guidance, even as drugmakers embrace the new marketing formats afforded them. Expected guidance on Internet, social media and promotional labeling could have an impact on enforcement levels.

In 2015, the FDA's Office of Prescription Drug Promotion (OPDP) issued markedly fewer warning and untitled letters than in previous years, continuing a downward trend.

After hitting a high of 196 in 1999, the number of letters issued by the Division of Drug Manufacturing, Advertising and Communications (DDMAC) began to plummet, dropping to 23 in 2003. There was a slight uptick in 2005 (29), but warning letters continued to fall overall until 2008. In 2008, the number of letters began to climb gradually, back up to 52 in 2010. During an FDA reorganization that year, DDMAC became OPDP, and since then, the number of letters has continued to slide, reaching a record low of nine in 2015.

Only two of the nine letters issued in 2015 were warning letters; the rest were untitled letters. Five of the letters related to issues with risk information, while four related to unsubstantiated claims. Letters also addressed superiority claims (one), overstated efficacy (one), promotion of an unapproved drug (one) and other claims (six).

Communication methods targeted in the letters were primarily digital (four) and traditional media. Three of the letters regarding digital media involved websites, while one related to a post on Instagram and Facebook that included risk information only via a link. To date, the FDA has issued little guidance on digital media, but the Center for Drug Evaluation and Research is planning to publish guidance on Internet,



social media and promotional labeling this year. The lack of guidance to date could play a role in the declining enforcement levels, as the guidance needed to signal which violations could warrant letters has been missing. Significantly, the first letter sent in 2016 involved a YouTube video.

Notably, these letters were primarily sent to smaller, lesser-known pharmaceutical companies. In contrast, the first letter sent in 2016 was to one of the best-known pharmaceutical companies in the world — Pfizer — with regard to an online video for a sedative.

Draft guidance calls on medical device manufacturers to establish processes to monitor, respond to cybersecurity vulnerabilities

The FDA's draft guidance on cybersecurity risks associated with medical devices encourages medical device manufacturers to actively monitor potential issues, and outlines when they must report such issues. It aligns with the agency's efforts to establish a medical device evaluation system.

The FDA published draft guidance with recommendations for addressing medical device cybersecurity issues. The guidance, titled "Postmarket Management of Cybersecurity in Medical Devices," is meant to address the uptick in medical devices designed to be networked, which may make them vulnerable to cybersecurity risks.

The goal of the guidance is to encourage medical device manufacturers to take a proactive approach to dealing with cybersecurity risks. The guidance supplements guidance on premarket submissions for the management of medical device cybersecurity, which provides recommendations to address cybersecurity during the development of devices. The guidance follows the FDA's efforts to use more real-world evidence to monitor the safety of medical devices and its goal of establishing a medical device evaluation system.

It outlines postmarket recommendations, urging medical device makers to incorporate cybersecurity risk monitoring into their postmarket management strategies. It applies to medical devices that contain software or programmable logic, as well as to

software that is designated as a medical device. Risk management programs and documentation should be in line with the Quality System Regulation, and should focus on addressing vulnerabilities that may allow unauthorized access, modification, misuse or denial of use, and the unpermitted use of information shared between medical devices and external sources.

These programs should include methods to evaluate vulnerabilities, coupled with methods to investigate threat sources. The FDA recommends that these programs follow the NIST Framework for Improving Critical Infrastructure Cybersecurity, which defines the steps to an effective program as identify, protect, detect, respond and recover.

For most cases, the FDA defines actions to address cybersecurity issues as "routine updates or patches," which do not require advance notification or reporting. However, there are a small portion of cybersecurity issues that may alter the clinical performance of a device. For these issues, the FDA would require that a manufacturer provide notification. When certain conditions are met and issues are addressed sufficiently in a quick manner, the agency would not enforce urgent reporting.

First OPDP untitled letter of 2016 criticizes Pfizer subsidiary's YouTube video for misbranding Precedex

The untitled letter sent to Hospira takes issue with a video advertisement for Precedex for failing to present risk information and representing the drug in ways that don't align with FDA-approved product labeling and indication. It is the first letter issued by the office in 2016.

The FDA's Office of Prescription Drug Promotion sent an untitled letter to Hospira, a subsidiary of Pfizer, over what it calls a "misleading" YouTube video on the sedative Precedex. The office reviewed that video as part of its monitoring and surveillance program and found that it omitted risk information, misbranding the drug based on the Federal Food, Drug, and Cosmetic Act.

The drug's approved product labeling includes warnings and precautions on its administration and adverse events. The video included multiple claims of efficacy for the drug, but failed to include this risk information and suggested arousability is a benefit, instead of treating that as a warning and precaution. Because of these omissions, the FDA found that the video presents a misleading impression of the drug's safety.

The agency also cites the video's representations about the drug's use for sedation in the intensive care setting, finding that it fails to include material information about the FDA-approved indication for Precedex. Specifically, Precedex is indicated for sedation of initially intubated and mechanically ventilated patients during treatment in an ICU.

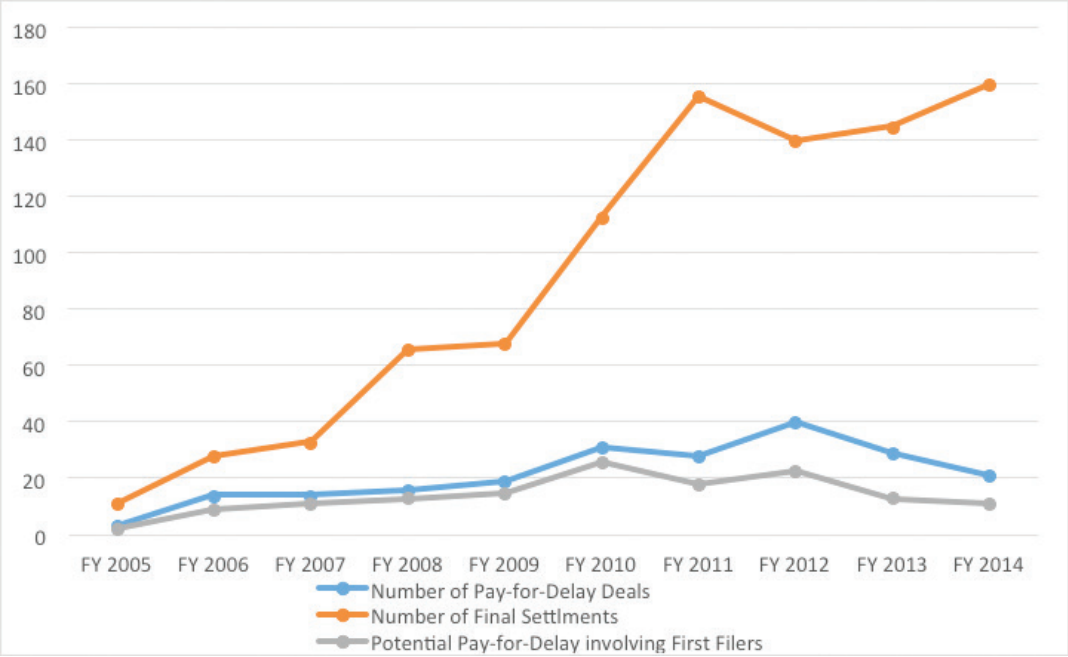
The regulatory authority also criticized Hospira for failing to submit a copy of the video to the OPDP, as required at the time of initial publication of an advertisement for a prescription drug. The drugmaker should have submitted a transmittal Form FDA-2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use).

The letter is the first to be issued by the OPDP in 2016 and comes in advance of expected guidance on Internet, social media and promotional labeling.

FTC FY2014 statistics highlight impact of *FTC v. Actavis* dispute as number of potential pay-for-delays falls

The Federal Trade Commission (FTC) found that pharmaceutical companies filed a total of 160 agreements to resolve patent disputes in fiscal year 2014 — the first full year since the Supreme Court ruled in FTC v. Actavis that brand makers' reverse payments to generic competitors may violate antitrust laws.

In FY2014, the FTC found that the number of overall settlements was consistent with previous years, but the number of potential pay-for-delay deals dropped markedly. The overall number of deals increased slightly from 140 in the previous year, while the



number of potential pay-for-delay deals slid from 29 in FY2013 to 21, continuing a fall from the record high of 40 such deals in FY2012.

During the year, 21 settlements constituted potential pay-for-delays because they contained clear compensation from a branded drugmaker to a generic drugmaker, along with a restriction on the latter's ability to produce its competitor product. These deals involved 20 branded products with combined annual sales of nearly $6.2 billion, the FTC said.

Nearly half (10) involved a cash payment, which ranged from $35,000 to $5 million, while six included compensation in the form of a side business deal between the parties. The remaining deals involved compensation in the form of a branded maker's promise not to market an authorized generic in competition with the generic maker's product for an established period of time.

Fifty-three of the 160 deals in FY2014 involved first-filer generics — producers who were the first to file abbreviated new drug applications. Of these, 11 contained compensations — the lowest number since 2007. In FY2013, 13 potential pay-for-delay deals involved first filers, down from 23 in FY2012.

The FTC identified another eight deals that contained "possible compensation" because it was not obvious whether provisions in the deals served as compensation. A majority of the overall deals (111) restricted the generic maker's ability to market its product, but did not include compensation. Twenty contained no restrictions on generic entry.

The FTC also found that approximately 81 percent of the patent disputes were resolved without compensation — a trend that's been on the rise in recent years.

For more information on any of these FDA regulatory and compliance updates, please contact Scott S. Liebman at sliebman@loeb.com.

Loeb & Loeb LLP's FDA Regulatory and Compliance Practice

Loeb & Loeb's FDA Regulatory and Compliance Practice comprises an interdisciplinary team of regulatory, corporate, capital markets, patent and litigation attorneys who advise clients on the full spectrum of legal and business issues related to the distribution and commercialization, including marketing and promotion, of FDA-regulated products. Focusing on the health and life sciences industries, including pharmaceuticals, biologics, medical devices, wellness products, dietary supplements and organics, the practice counsels clients on regulatory issues, compliance-related matters and risk management strategies; advises on laws and regulations related to product advertising and labeling; counsels on FDA exclusivity policies and related Hatch-Waxman issues; and provides representation in licensing transactions and regulatory enforcement actions.