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Inside

Executive Summary....1
Introduction....1
Court Decisions (Drugs)....2
Court Decisions (Devices)....4
Settlements & CIAs....4
FDA Actions (Drugs)....5
FDA Actions (Devices)....6
Agency Reports (Drugs)....6
Agency Reports (Devices)....7
Industry Studies (Drugs)....7
Industry Studies (Devices)....7
Tobacco....8
Marijuana....9
ACA Device Excise Tax....9
Mobile Medical Applications....10
Conclusion....10

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Executive Summary

In the first quarter of 2014 there have been some significant developments in the areas of drugs and medical devices. This White Paper provides a non-exhaustive overview of these developments, including court decisions, significant FDA actions, settlements, agency reports, and industry studies. In addition, there have been important developments in the field of tobacco, marijuana, and the medical device excise tax.

A summary of each of these developments, and many more items of interest, is included below, along with helpful links to full text documents.

Introduction

Three court decisions were particularly significant in the drug arena: (1) the Arkansas Supreme Court's reversal of a $1.2 billion verdict against Johnson & Johnson; (2) the D.C. District Court's finding that a therapy's combination of a patient's own stem cells and antibiotics are a drug, subject to FDA drug regulation; and (3) the Sixth Circuit's reversal of a district court finding that Mylan's fentanyl patch was a drug, remanding to determine if it is a drug, device, or combination product.

One significant medical device decision was a Michigan district court finding that FDA employees that examined a defective oxygen tank could not be compelled to testify in a state court action without FDA permission, and that the FDA's submission of a sample of the oxygen tank's contents to the parties in state action, rather than full return of the actual tank, was sufficient to comply with a *subpoena duces tecum*. Another important decision involved a West Virginia district court judge's reversal of his own prior ruling in the multi-district pelvic mesh litigation, in which, after conducting his own research in preparation for trial, he required the plaintiff to establish the existence of a safer alternative design as an element of her strict liability claim.

Significant FDA drug actions were the agency's launch of its Secure Supply Chain Pilot Program and establishment of a docket for comments on the interoperable exchange of information with respect to prescription drug transactions. Important FDA device actions included: (1) new requirements for pediatric devices; (2) the electronic submission of adverse event reports; (3) clarification for when product modifications require premarket notification (510(k)) submissions; and (4) a proposal to allow reclassification of devices by administrative order, rather than through the traditional notice and comment process.

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A report by the HHS Office of Inspector General found that the FDA device center's computer monitoring of certain employees suspected of disclosing trade secrets or confidential commercial information failed to fully assess beforehand whether the scope of the monitoring was consistent with government limitations and whistleblower protections. In addition, a Government Accountability Office report found that the FDA needs improvement in handling rising drug shortages.

An industry report by *Transparency Market Research* revealed increasing trends in preventive medicine and, in turn, a growing self-care medical device market. Another report, by the *Emergo Group*, analyzed the average time it takes for the FDA to clear a premarket notification (510(k)) submission and the effect the new refuse-to-accept program may have on future clearance time.

Tobacco regulation has been a busy area. In the first quarter, the FDA: (1) ordered the first-ever "stop sale, distribution" order for tobacco products; (2) proposed exclusion of some tobacco products from Environmental Impact Assessments; and (3) introduced "The Real Cost" tobacco education program. In addition, 25 states asked the chief executive officers of five major retail pharmacies to cease the sale of tobacco products, and a bipartisan group of U.S. Senators asked the FDA and Federal Trade Commission to take enforcement action against false advertising by electronic cigarette manufacturers.

The march of states considering some form of marijuana legalization continued with the Florida Supreme Court deciding that a medical marijuana legalization amendment to the November 2014 state ballot would be allowed. In addition, the Drug Enforcement Administration continued its strict enforcement efforts by adding (at least temporarily) four synthetic compounds into Schedule I of the Controlled Substances Act due to their functional similarity to *delta9-tetrahydrocannabinol* (THC), the main active ingredient in marijuana.

The controversy continued with regard to the 2.3 percent Patient Protection and Affordable Care Act (ACA) medical device excise tax. Some studies indicated that the tax is resulting in severe job loss in the device manufacturing industry, while other studies minimized the effects of the tax on job loss and lauded the tax as a revenue producer. In addition, one federal district court made it clear that the device excise tax falls on the manufacturer of the device, not the distributor.

Finally, Congress continued to urge the FDA not to stifle progress and growth in the mobile medical application (MMA) industry by over-regulating MMAs.

Court Decisions (Drugs)

$1.2 billion verdict against Johnson & Johnson reversed. The Supreme Court of Arkansas reversed a $1.2 billion jury verdict against Johnson & Johnson and its subsidiaries for making false statements on the labeling of it antipsychotic drug, Risperdal™ (risperidone), and in a 2003 "Dear Doctor" letter to Arkansas healthcare providers. In this suit, Johnson & Johnson's Janssen subsidiary was accused of making misleading claims about Risperdal's effectiveness and downplaying its diabetes risks on warning labels. The Arkansas high court found that (1) the state erroneously used an inapplicable state Medicaid statute governing healthcare facilities to bring its claim and (2) the admission into evidence of an FDA Warning letter was prohibited hearsay and more prejudicial than probative. As a consequence, the state Medicaid fraud claim was dismissed and a state deceptive practice action was reversed and remanded to the trial court (*Ortho-McNeil-Janssen Pharmaceuticals, Inc. v State of Arkansas*, Ark. Sup. Ct., March 20, 2014).

In a separate action brought by the U.S. Department of Justice, in November 2013, Johnson & Johnson and its subsidiaries agreed to pay more than $2.2 billion to resolve criminal and civil liability arising from allegations relating to the prescription drugs Risperdal, Invega and Natrecor, including promotion for uses not approved as safe and effective by the FDA and payment of kickbacks to physicians and to the nation's largest long-term care pharmacy provider. This was one of the largest health care fraud settlements in U.S. history, with criminal fines and forfeiture totaling $485 million and civil settlements with the federal government and states totaling $1.72 billion.

Johnson & Johnson and Janssen are also awaiting a ruling by the South Carolina Supreme Court, where the companies have an appeal pending of a $327 million judgment in a similar case. A $330 million verdict against both companies in Louisiana was overturned in January.

Mixture of stem cells and antibiotics violated FDA regulations. The D.C. Circuit has found that a medical therapy, developed by Regenerative Sciences, LLC, using a mixture produced by combining patient stem cells and antibiotics to treat orthopedic conditions is subject to, and in violation of, FDA regulations. Back in July 2008, the FDA sent a warning letter notifying Regenerative that the re-injected stem cell product used in the procedure constituted a drug under the Federal Food Drug & Cosmetic Act (FDC Act) (21 U.S.C. sec. 321(g)) and a biological product under the Public Health Services Act (42 U.S.C. sec. 262). And because Regenerative had not obtained the necessary FDA drug

and biologic approvals for the stem cell product, its actions were possibly unlawful.

Regenerative filed suit in federal court challenging the FDA's determination that Regenerative is a drug manufacturer. The FDA contended that Regenerative is subject to FDA enforcement because an antibiotic, doxycycline, is combined with the stem cell product and the doxycycline is shipped from out of state to the Colorado facilities. Therefore, according to the FDA, because a small component of the cell product was shipped through interstate commerce, the agency had jurisdiction to regulate the product as an adulterated or misbranded drug due to Regenerative's failure to apply for and gain prior FDA approval. The U.S. District Court for the District of Columbia granted the FDA summary judgment and entered a permanent injunction against Regenerative's use of its Regenexx™ Procedure.

Before the D.C. Circuit, Regenerative argued that the product and process of using this product to treat orthopedic issues were exempt from federal regulations because: (1) the regulations may not be used to infringe on states' rights to regulate medical practice; (2) the process is not subject to the Commerce Clause; and (3) the mixture is minimally manipulated and thus exempt from regulation. The D.C. Circuit rejected each of these arguments finding that is within the purview of the FDA and the Commerce Clause to regulate the mixture, that the creators' own concessions indicate it is more than minimally manipulated, and under the federal FDC Act the mixture was *per se* misbranded and adulterated (*USA v Regenerative Sciences, LLC*, D.C. Cir., February 4, 2014).

Sixth Circuit questions ruling that fentanyl patch is a drug. The Sixth Circuit sent a products liability suit involving a fentanyl-medicated patch, manufactured by Mylan, Inc., back to the lower court to determine whether the patch is a drug, a medical device, or a combination product. Beth Ann Kelly died after receiving a fatal dose of fentanyl. Her estate subsequently brought a lawsuit alleging that Mylan's fentanyl patch caused Kelly's death. Mylan pleaded immunity under a Michigan statute that immunizes manufacturers of "drugs" from suit. The district court determined that the fentanyl patch was a "drug" and consequently granted Mylan's motion to dismiss the complaint. The Sixth Circuit concluded that the district court's analysis was incomplete and that a factual question remains as to whether the fentanyl patch was a "combination product," the manufacturers of which do not enjoy immunity under Michigan law. The Sixth Circuit reversed the judgment of the district court and remanded for further proceedings. In its decision, the court noted ambiguity in the Michigan law called upon by the defendant manufacturer for immunity (*Miller v Mylan Inc.*, 6th Cir., January 21, 2014).

PLIVA USA, Inc. escapes additional Reglan product liability claims. Maryland state law tort claims against PLIVA, Inc. were found to be preempted by the Federal, Food, Drug, and Cosmetics Act (FDCA), in a case where a patient took and suffered injuries from the generic drug Reglan. The Fourth Circuit determined that it was proper to dismiss the state law claims against the generic drug manufacturer, since the company would have been required to either change the drug's warning or formulation, in violation of the FDCA; or would be required to exit the market or accept state tort liability, in violation of recent Supreme Court decisions (*Drager v PLIVA USA, Inc.,* 4th Cir., January 28, 2014).

The D.C. Circuit has found that a medical therapy, developed by Regenerative Sciences, LLC, using a mixture produced by combining patient stem cells and antibiotics to treat orthopedic conditions is subject to, and in violation of, FDA regulations.

According to the Fourth Circuit, the Supreme Court's *PLIVA, Inc. v Mensing* and *Mutual Pharmaceutical Co., Inc. v Bartlett* decisions establish that under the FDCA and the Hatch-Waxman amendments thereto, a generic drug company "may not unilaterally change its labeling or change its design or formulation, and cannot be required to exit the market or accept state tort liability." Consequently, a state law is preempted in the event a generic drug manufacturer must take one of the aforementioned actions in order to comply with a state law duty.

Novartis fails to provide adequate warnings. The Eight Circuit confirmed a decision by a district court that Novartis Pharmaceuticals Corporation's failure to provide adequate warnings about its product's tendency to cause osteonecrosis of the jaw (ONJ) was the proximate cause of a patient's injury. Ruth Baldwin

developed ONJ after two of her teeth were extracted. She sued, alleging Novartis Pharmaceuticals Corporation negligently failed to provide adequate warnings for two drugs she took, Aredia and Zometa. After a jury trial, Baldwin, by her executor, received $225,000 in compensatory damages, plus certain costs. Novartis appealed, arguing that the district court: (1) improperly found that inadequate warnings proximately caused Baldwin's injuries; (2) erred in applying Missouri law to the punitive damages claim; (3) abused its discretion in admitting hearsay evidence; and (4) abused its discretion in awarding the costs for depositions conducted as part of multi-district litigation. The Eighth Circuit confirmed that the lower court correctly applied Missouri law, which allowed for the showing of a punitive damages claim at the trial level. The appeal, filed by the patient's estate, was only granted to the extent costs were incorrectly awarded (*Winter v Novartis Pharmaceuticals Corp.*, 8th Cir., January 9, 2014).

Wellness Support Network Inc. liable for false advertising of diabetes products. A federal district court held that the owners of Wellness Support Network, Inc., that sold the Diabetic Pack and the Insulin Resistance Pack, engaged in false advertising and deceptive practices in violation of the Federal Trade Commission (FTC) Act. The owners claimed that the FTC's causes of action should have failed because their products are medical foods and as such, the standard the FTC sought to apply is inapplicable. The court found the owners were liable for the claims made on the company's website and the advertising of the products; and those claims were material and misleading to consumers who purchased the products. The court granted the FTC's request for summary judgment (*FTC v Wellness Support Network Inc.*, N.D. Calif., February 19, 2014).

Court Decisions (Devices)

FDA employees could not be compelled to testify in state products liability action. A federal district court held that the FDA did not act arbitrarily or capriciously in failing to return a defective oxygen tank it had examined to an injured patient and by not allowing its employees to testify in a state court action against the manufacturer and filler of the oxygen tank. According to the court, the FDA employees who examined the tank could not testify in the state court action without agency authorization, which the FDA determined was inappropriate because their testimony would not promote the interests of the FDA or the public. In making its decision to recognize the need for federal agencies to conserve resources and avoid involvement in private lawsuits, the court also found that the FDA's submission of a sample of the tank's contents and a report on its investigation was sufficient (*Frank v FDA*, E.D. Mich., February 26, 2014).

Safer alternative design required to establish design defect claim in bellwether transvaginal mesh case. In a reversal of his own ruling, a federal district court judge presiding over the multi-district litigation (MDL) relating to claims arising out of patient injuries allegedly resulting from the manufacturer's pelvic mesh device that had been implanted in the patients held that the plaintiff in one of the MDL's bellwether cases is required to establish a safer alternative design as part of a strict liability claim. The judge reversed his earlier decision that a safer alternative design was not required after conducting his own research in preparation for trial in the case (*In re Ethicon Inc., Pelvic Repair System Products Liability Litigation*, S.D. W.V., February 3, 2014).

Settlements & CIAs

New York AG reaches settlement with generic pharmaceutical companies. On February 19, 2014, New York Attorney General Eric T. Schneiderman announced a settlement with two generic pharmaceutical manufacturers, Ranbaxy Pharmaceuticals, Inc. and Teva Pharmaceuticals USA, Inc., resolving concerns that an agreement between the companies unlawfully restricted competition**.** Ranbaxy and Teva had agreed that each would not challenge the other party's "first to file" exclusivities for a large number of drugs, for a several year period. The settlement with the Attorney General requires the parties to terminate the "no challenge" agreement, refrain from entering into similar agreements in the future, and make monetary payments to New York State totaling $300,000.

Endo Pharmaceuticals enters into settlement and CIA for illegal marketing of Lidoderm. On February 21, 2014, Endo Health Solutions Inc. and its subsidiary Endo Pharmaceuticals Inc. (Endo) agreed to pay $192.7 million to resolve criminal and civil liability arising from Endo's marketing of the prescription drug Lidoderm for uses not approved as safe and effective by the FDA. The settlement includes a deferred prosecution agreement, a forfeiture totaling $20.8 million, and civil false claims settlements with the federal government, states, and the District of Columbia totaling $171.9 million. As part of a criminal and civil settlement with the Justice Department, Endo agreed to enter into a Corporate Integrity Agreement (CIA) with the HHS Inspector General. Among other things, the CIA requires Endo to implement an internal risk assessment and mitigation

program and requires numerous internal and external reviews of promotional and other practices. The CIA also requires key executives and individual board members to sign certifications about compliance, and it requires the company to publicly report information about its financial arrangements with physicians (*CIA Between the Office of Inspector General of the DHHS and Endo Pharmaceuticals Inc.,* February 21, 2014).

EndoGastric Solutions agrees to pay up to $5.25 million to settle false billing allegations. Medical device manufacturer EndoGastric Solutions Inc. agreed to pay the government up to $5.25 million to resolve allegations that it violated the False Claims Act by misleading health care providers about how to bill federal health care programs for a procedure using a device manufactured by the company and by paying kickbacks. As part of the settlement, EndoGastric Solutions entered into a corporate integrity agreement (CIA) with the HHS Office of Inspector General to promote the corporation's compliance with Medicaid, Medicare, and other federal health care program statutes, regulations, and requirements (*Integrity Agreement between the Office of Inspector General of the Department of Health and Human Services and EndoGastric Solutions, Inc.*, February 21, 2014).

Teva Pharmaceuticals pays $27.6 Million to settle false claims. Teva Pharmaceuticals USA, Inc., and its subsidiary IVAX, LLC (collectively Teva) agreed to pay a total of $27.6 million to the federal government and the State of Illinois in a settlement regarding allegations of false billing practices. Illinois Attorney General Lisa Madigan announced the settlement, which required Teva to pay almost $15.5 million to the federal government and over $12.1 million plus interest to the State of Illinois within 10 days. The government claimed that Teva paid and provided other remuneration to a physician, Dr. Michael J. Reinstein, to prescribe generic clozapine, an anti-psychotic drug, to thousands of Medicare and Medicaid beneficiaries in nursing homes and hospitals.

FDA Actions (Drugs)

FDA launches Secure Supply Chain Pilot Program, prequalifies 13 companies. The FDA announced the launch of the Secure Supply Chain Pilot Program (SSCPP) and the names of 13 drug companies that have been prequalified for participation in the program, which provides for expedited entry for up to five selected drugs imported into the United States. The SSCPP was created by the FDA in an effort to identify best practices for supply chain integrity for participating importers so that the agency may focus on imported drugs that are more likely to be adulterated, misbranded, or unapproved from other sources. A notice in the *Federal Register* in August of 2013 outlined the requirements for participation in the program and requested applications for companies requesting prequalification prior to the launch date. The 13 pre-qualified drug companies: Abbvie, Inc., Allergan, Inc., Astellas U.S. Technologies, Inc., Bristol-Myers Squibb Company, Celgene Corporation, GE Healthcare, Inc., GlaxoSmithKline, LLC, Merck Sharpe & Dohme Corporation, Mylan Pharmaceuticals, Inc., Novartis Pharmaceuticals Corporation, Pfizer, Inc., Teva Pharmaceuticals USA, Inc., and Watson Laboratories, Inc.

Effective August 14, 2015, device manufacturers and importers will be required to submit mandatory reports of individual medical device adverse events, also known as medical device reports (MDRs), to the FDA in an electronic format that the agency can process, review, and archive.

FDA requests comments on interoperable exchange of information for drug security reform. The FDA has established a public docket to receive comments on standards for the interoperable exchange of information with respect to prescription drug transactions. The information will be used to comply with requirements of the Drug Supply Chain Security Act (DSCSA), enacted November 27, 2013. The DSCSA, Title II of the Drug Quality and Security Act (DQSA), outlines critical steps to build an electronic, interoperable system to identify and trace certain prescription drugs as they are distributed in the United States. The FDA notice requests comments and answers to specific questions from drug manufacturers, re-packagers, wholesale distributors, dispensers, supply chain stakeholders, and other interested parties including standards organizations, state and federal agencies, and solution providers (*Notice*, 79 FR 9745, February 20, 2014).

FDA Actions (Devices)

Requirements set for approval of pediatric devices. The FDA has published a final rule implementing the FDA Amendments Act of 2007 provisions that imposed new requirements for applications for approvals related to medical devices to be used by pediatric patients. The final rule, which is effective April 10, 2014, applies to all applications for premarket approval (PMA), product development protocol (PDP), and humanitarian device exceptions (HDE), and to PMA supplements, except for certain 30-day notices (*FDA Order*, 79 FR 1735, January 10, 2014).

Adverse event reports must now be electronically submitted. Effective August 14, 2015, device manufacturers and importers will be required to submit mandatory reports of individual medical device adverse events, also known as medical device reports (MDRs), to the FDA in an electronic format that the agency can process, review, and archive. Electronic reporting is also available to user facilities, but this rule permits user facilities to continue to submit written reports to the FDA. The final rule changes to reporting includes reports of deaths, serious injuries, and malfunctions that must be submitted to the FDA in initial 5-day, 10-day, or 30-day individual MDRs as well as information that must be reported to the FDA in supplemental or follow-up reports. It does not change the underlying reporting requirements, only the manner in which they are submitted to the FDA (*FDA Order*, 79 FR 8832, February 14, 2014).

FDA issues report clarifying when modifications require 510(k) premarket notification. The FDA and HHS have complied with the FDA Safety and Innovation Act's (FDASIA) (P.L. 112-144) adjustment to the Federal Food, Drug, and Cosmetic Act (FDC Act) (21 USC 360(n)(2)), by issuing its "Report to Congress; Report on the Food and Drug Administration's Policy to be Proposed Regarding Premarket Notification Requirements for Modifications to Legally Marketed Devices." The report sets forth the agency's policy on when an FDC Act 510(k) premarket notification should be submitted for a modification to a legally marketed 510(k) device (*Notice*, 79 FR 12695, March 6, 2014).

FDA enhances CDRH Export Certification Tracking System. The FDA's Center for Devices and Radiological Health (CDRH) has updated the CDRH Export Certification and Tracking System (CECATS). An electronic system that allows manufacturers and initial importers to utilize online documents rather than paper submissions, the benefits of CECATS include reductions in processing time, cost savings on materials and mailing, real-time validation of data, and status updates. The second phase of CECATS implementation allowed for the submission of requests for certificates of exportability. Enhancements implemented in February 2014 permit users to make changes to applications prior to review, to upload additional documents, and to copy export certificates, according to FDA FAQs. Changes in early 2015 will allow manufacturers and initial importers to submit requests having to do with permit letters, simple notification, and non-clinical research-use-only certificates. Following nearly a year after the second phase of the system's launch in March 2013, the updates incorporated enhancements to CECATS stemming from user feedback.

Reclassification of medical devices by administrative order proposed. The FDA is proposing revision of its medical device classification regulations to conform to recent changes made by the FDA Safety and Innovation Act (FDASIA) (P.L. 112-144) to the Food Drug & Cosmetic Act. These changes, which became effective July 9, 2012, established processes for reclassification of medical devices by administrative order instead of by regulation. The FDA also proposes to update other reclassification provisions and to clarify the meaning of certain terms. The FDA is taking this action to codify these procedures and to provide for classification of devices in the lowest regulatory class consistent with the public health and the statutory scheme for device regulation (*Proposed rule,* 79 FR 16252, March 25, 2014).

Agency Reports (Drugs)

Rogue internet pharmacies pose challenges to prosecution and education efforts. A report by the Government Accountability Office (GAO) stated that rogue internet pharmacies are, for the most part, operated abroad. The GAO report acknowledged that many of these pharmacies sell drugs that are not approved by the FDA or are counterfeit or substandard and sell prescription drugs without the necessary prescription. Since the rogue internet pharmacies are often complex, global organizations that employ sophisticated marketing techniques to appear legitimate and in compliance with federal laws, investigation and prosecution efforts as well as consumer education on the topic face many challenges. The GAO asserted that according to a recent FDA survey, one in every four adult internet consumers in the U.S. reports purchasing prescription drugs online. In addition, 30 percent of the respondents claimed to lack confidence in purchasing drugs online. The GAO also related the results of a National

Association of Boards of Pharmacy's (NABP) survey, which revealed that 97 percent of over 10,000 online pharmacies investigated were in violation of laws and industry standards (*GAO Report*, No. GAO-14-386T, February 27, 2014).

FDA needs improvement in handling rising drug shortages. In its report, "Threat to Public Health Persists, Despite Actions to Help Maintain Product Availability," the GAO reviewed and commented on: (1) recent drug shortage trends; (2) causes of drug shortages; and (3) FDA progress in addressing such shortages. According to the report, although new drug shortages decreased from 255 drugs in 2011 to 195 drugs in 2012, the total number of active shortages increased. While there were 439 active drug shortages in 2011, there were 456 active shortages in 2012. In addition, ongoing shortages increased from 261 in 2012 to 288 in 2013. The GAO noted that active drug shortages have actually been on the rise since 2007, when there were only 40 ongoing shortages and 114 new shortages. The GAO recommends that the FDA: (1) create policies and procedures to ensure information is consistently and accurately recorded in the drug shortages database and the future drug shortages information system; and (2) routinely analyze the data to identify risk factors for potential shortages, recognize trends, clarify causes, and solve issues before drugs are in short supply (*GAO Report*, GAO-14-339T, February 10, 2014).

Agency Reports (Devices)

Recommendations protect the rights of federal whistleblowers from unlimited agency surveillance. The HHS Office of Inspector General (OIG) has found that the FDA's Center for Devices and Radiological Health (CDRH) computer monitoring of certain employees suspected of disclosing trade secrets or confidential commercial information (CCI) outside the agency failed to fully assess beforehand whether the scope of the monitoring was consistent with constitutional and statutory limitations on government searches and whistleblower protections. The OIG made this finding despite the reasonableness of CDRH's concerns and the explicit language contained in the FDA's network log-on banner that employees had no right to privacy and that all data on the network may be monitored. The OIG recommends that HHS ensure that it's operating divisions draft and implement policies and related procedural internal controls that provide reasonable assurance of compliance with laws and regulations, particularly those governing current and prospective employee monitoring (*OIG Report*, OIG-12-14-01, February 27, 2014).

Industry Studies (Drugs)

Biosimilars to creep slowly into U.S. market. Internationally, the development of biosimilars has been rapid. However, according to a report from Moody's Investors Service, titled Biosimilars: Parsing the Industry's Pipelines, there may be a considerable delay in the entry of biosimilars into U.S. markets. Despite the Patient Protection and Affordable Care Act's abbreviated licensure pathway for these products, applications for biosimilar or "interchangeable" products have yet to be filed with the FDA. Based on the progress of clinical trials, Moody's reports it is likely that applications will begin to be filed this year, with FDA review and approval of applications estimated to take a year or longer. Commercialization, however, may be delayed by the patent protection of current biotechnology. Another delay may be caused by the FDA's determinations of whether certain biosimilars are interchangeable with the original products—a determination which will decide whether biosimilar companies will be able to rely on automatic conversion to their products or whether new marketing (and, thus, increased competition with original drug products) will be required.

On April 7, a bipartisan group of senators urged the FDA and Federal Trade Commission (FTC) to take action against electronic cigarette (e-cigarette) manufacturers who are making unfounded and false claims in their advertising, including claims that the devices can help conventional cigarette smokers quit.

Industry Studies (Devices)

Report predicts the future of the self-care market. A recent report released by Transparency Market Research

(TMR), entitled, "Self-Care Medical Devices Market – Global Industry Analysis, Size, Share, Growth, Trends and Forecast (Value and Volume) 2013-2019," analyzed the future of the self-care medical device industry by breaking it into segments based on types of devices and, also geographically. The report segmented the industry devices into categories as follows: blood glucose monitors, blood pressure monitors, temperature monitors, holter monitors, pregnancy/fertility test kits, sleep apnea monitors, nebulizers, and pedometers. The report also identified several key players in the self-care device industry, including 3M Healthcare, Abbott Laboratories, GE Healthcare, Medtronic, Inc., Johnson and Johnson, and Philips Healthcare. According to TMR, the analysis of self-care medical device industry in a global perspective reveals increasing trends of preventative medicine and, in turn, a larger self-care medical device market. In particular, devices that may potentially reduce health care issues such as blood glucose monitors, heart rate monitors, sleep apnea monitors, and blood pressure monitors are also expected to grow within the industry for that reason.

FDA 510(k) clearance averages five months, according to report. A new report found that on average it takes the FDA five months to clear a medical device 510(k) submission. The Emergo Group released these findings after a review of 24,000 510(k) submissions to the FDA between January 1, 2006, and December 31, 2013. The Emergo Group found that over that period the average review time frame grew from three to five months. The report also revealed the 510(k) review time is significantly reduced when using a third-party to conduct the review in place of the FDA. Finally, the report mentioned the new refuse-to-accept (RTA) program enacted last year by the FDA and noted it's potential to effect the review and clearance time for 510(k) submissions in the future.

Tobacco

State Attorneys General ask national pharmacy chains to stop selling tobacco products. On March 14, 2014, led by New York Attorney General Eric Schneiderman and Ohio Attorney General Mike DeWine, the Attorneys General (AGs) of 25 states, Guam, Puerto Rico, and the District of Columbia wrote to the chief executive officers of Wal-Mart, Walgreens (which also operates Duane Reade stores), Rite-Aid, Safeway and Kroger, asking them to follow the lead of CVS Caremark and cease selling tobacco products in their stores throughout the United States. The AGs also sent a letter to CVS Caremark commending it for its voluntary action. According to AG DeWine, "My fellow Attorneys General and I are asking these national retailers to take an additional step forward in keeping tobacco products away from youth by voluntarily not selling them in their stores with pharmacies. The health of our kids is just too important."

Lawmakers urge FDA and FTC to regulate false e-cigarette advertising. On April 7, a bipartisan group of senators urged the FDA and Federal Trade Commission (FTC) to take action against electronic cigarette (e-cigarette) manufacturers who are making unfounded and false claims in their advertising, including claims that the devices can help conventional cigarette smokers quit. "The FTC has not stepped in to protect consumers from the health risks posed by nicotine and other chemicals contained in electronic cigarettes," the senators wrote to the FTC. "We believe that you can and should act immediately to crack down on these false and deceptive claims by e-cigarette manufacturers."

FDA orders first ever "stop sale, distribution order" for tobacco products. For the first time, the FDA exercised its authority under the Family Prevention Smoking and Tobacco Control Act (Tobacco Control Act) to issue an order stopping the sale and distribution for four tobacco products that are currently on the market. The FDA issued the order because the products were found to be not substantially equivalent to tobacco products commercially marketed as of February 15, 2007, or predicate products. Because the FDA's order was issued after the four products were on the market, the FDA did not take enforcement action against the sale of these products by retailers for 30 days, unless the products were purchased by retailers after the issuance of the stop sale order.

The four products at issue are: Sutra Bidis Red, Sutra Bidis Menthol, Sutra Bidis Red Cone, and Sutra Bidis Menthol Cone, all were manufactured by Jash International. Bidis are hand-rolled cigarettes made with leaves from a tendu tree, filled with tobacco, and tied with a string. The FDA denied the application for the Bidis because Jash International failed to identify: 1) an existing predicate product that the Bidis were substantially equivalent to 2) how these new products had similar characteristics to existing predicate products; or 3) how the new products had different characteristics but did not raise public health issues.

FDA introduces "The Real Cost" tobacco education campaign aimed at American youth. On February 2, 2014, the FDA launched "The Real Cost" tobacco education campaign. The campaign is designed to let young Americans know that tobacco use in any form is detrimental to their health and that they should strive to

remain tobacco-free. Through the use of advertisements and social media, the FDA hopes to encourage young Americans to discuss this issue and encourage each other to abstain from using any tobacco products. The campaign is the FDA's first of several planned tobacco education campaigns using its authority granted under the Family Smoking Prevention and Tobacco Control Act (P.L. 111-31). "The Real Cost" campaign will focus on graphic depictions of the health issues caused by tobacco use including the loss of teeth and skin damage. The campaign will also demonstrate that addiction to cigarettes is a loss of self-control because many youth believe they cannot become addicted or that they can quit at any time. Another approach will highlight the fact that menthol cigarettes cause the same health consequences as regular cigarettes.

FDA proposal would exclude some tobacco product actions from environmental impact assessments. The National Environmental Policy Act of 1969 (NEPA) implementing regulations would be revised by the FDA to provide categorical exclusions for actions related to substantial equivalence (SE) reports, SE exemption requests, and tobacco product applications, as well as the rescission or suspension of orders regarding the marketing of tobacco products under the Family Smoking Prevention and Tobacco Control Act (Tobacco Control Act). The FDA would also amend NEPA regulations at 21 CFR part 25 to include tobacco products, where appropriate, in light of its new authority under the Tobacco Control Act (*Proposed rule*, 79 FR 3742, January 23, 2014).

Marijuana

Florida Supreme Court allows medical marijuana initiative on November 2014 ballot. According to the Florida Supreme Court, Floridians will be afforded the opportunity to vote on whether to adopt an amendment legalizing the medical use of marijuana within the state. In its 4-3 decision approving the placement of the initiative on the state's November 2014 ballot, the Florida Supreme Court shot down opponents' arguments that the amendment would be misleading to voters. The court concluded in its January 27, 2014 advisory opinion that in reading the ballot as a whole, "the voters will not be affirmatively misled regarding the purpose of the proposed amendment because the ballot title and summary accurately convey the limited use of marijuana, as determined by a licensed Florida physician." Further, the court found that proponents' interpretation that "the intent is to allow [marijuana] use for a serious medical condition or disease," as opposed to "any medical condition for which a physician personally believes that the benefits outweigh the health risks," is reasonable and supported by the "accepted principles of constitutional interpretation."

On March 18, 2014, a bipartisan group of U.S. Senators ... sent a letter to FDA Commissioner Dr. Margaret Hamburg, urging the FDA to provide further clarity in its policies regarding medical mobile applications (MMAs). In 2013, the FDA issued final guidance for oversight of MMAs.

DEA to temporarily list four synthetic cannabinoids on Schedule I. The Drug Enforcement Administration (DEA) intends to temporarily add certain synthetic cannabinoids to Schedule I pursuant to the Controlled Substances Act (CSA). The four synthetic compounds, which are referred to as PB-22;QUPIC, 5-fluoro-PB-22;5F-PB-22, AB-FUBINACA, and ADB-PINACA, were created in laboratories and are functionally similar to delta9-tetrahyrdocannabinol (THC), the main active ingredient in marijuana. The DEA has determined to list these synthetics on Schedule I in an effort to avoid hazards to public safety (*FDA Proposal*, 79 FR 1776, January 10, 2014).

ACA Device Excise Tax

Medical device excise tax leads to substantial loss of jobs. Approximately 165,000 jobs have been lost as a result of the 2.3 percent medical device tax that went into effect January 1, 2013, according to an AdvaMed® survey measuring the impact of the medical device excise tax. The survey also found that an astounding 75 percent of respondents disclosed negative impacts of the tax, which was implemented by the Patient Protection and Affordable Care Act (ACA) (P.L. 111-148). Other negative impacts included relocating manufacturing outside

of the U.S., with 10 percent of survey respondents acknowledging they had moved jobs abroad because of the tax. In addition, over 30 percent of respondents disclosed a reduction of research and development, as a result of the tax. For every direct job that was terminated or not filled due to the tax, four indirect jobs were consequently terminated or forgone as well.

Excise tax expected to raise $29 billion, have small negative effect on industry. In contrast to the AdvaMed® survey**,** a report released by the Congressional Research Service concluded that the excise tax on medical devices is expected to raise net revenues of $29 billion, which will be used to offset the costs of implementation of the ACA. The report, titled "The Medical Device Excise Tax: Economic Analysis," found that despite what critics of the tax have argued, the excise tax will have a relatively small negative effect on the profits of the medical device industry, with most of the tax being passed on to the consumer in the form of higher prices.

Court finds the medical device tax did not fall on distributor. A federal district court declined to grant Chemence Medical Products, Inc. (Chemence), a manufacturer of medical adhesives, a declaratory judgment that the ACA medical device excise tax should be assessed against Medline Industries, Inc. (Medline), a product distributor. The court granted Medline's motion for partial judgment on the pleadings, reasoning that absent any further agreements found within Chemence and Medline's written contract, the ACA implies that the manufacturer, Chemence in this case, is liable for the medical device tax under the ACA (*Chemence Medical Products, Inc. v Medline Industries, Inc.*, N.D. Ga., December 5, 2013).

Half of small to mid-size companies make no changes in first year of medical device excise tax. In a survey of senior management within the medical devices industry, the impact of the 2.3 percent medical device excise tax seems to be less severe than that depicted by media and industry organizations, with half or more of all small to mid-size companies making no changes in response to the tax. The survey, conducted and reported by the Emergo Group, compared the findings with a survey the previous year asking respondents to predict what impact the excise tax would have on their company. In the recent survey, 45 percent of senior management indicated that the excise tax had a "very negative" (11.5 percent) or "somewhat negative" (33.5 percent) impact on their business in 2013. This was down from the 53 percent of the firms that predicted the previous year that the excise tax would have a "very negative" or "somewhat negative" impact. However, 34.3 percent of senior management reported "no impact" on business operations in 2013, up from 27 percent that had predicted the same.

Mobile Medical Applications

Senators urge FDA not to stifle mobile medical apps through over-regulation. On March 18, 2014, a bipartisan group of U.S. Senators, including Michael Bennet (D-Colo.), Orrin Hatch (R-Utah), Tom Harkin (D-Iowa), Lamar Alexander (R-Tenn.), Mark Warner (D-Va.), and Richard Burr (R-N.C.) sent a letter to FDA Commissioner Dr. Margaret Hamburg, urging the FDA to provide further clarity in its policies regarding medical mobile applications (MMAs). In 2013, the FDA issued final guidance for oversight of MMAs. The final guidance, entitled "Mobile Medical Applications: Guidance for Industry and FDA Staff," uses a risk-based approach to define what the FDA considers to be a MMA, with the agency's efforts concentrated on high-risk medical software. While the senators indicated their appreciation of the FDA's decision to use a risk-based approach to regulation, they are still concerned about possible over-regulation. And they are not the only members of Congress to indicate their concern. In fact, the Sensible Oversight for Technology which Advances Regulatory Efficiency (SOFTWARE) Act of 2013, H.R. 3303, proposed October 22, 2013 in the House of Representatives by U.S. Rep. Marsha Blackburn (R-Tenn.), seeks to curb the FDA's regulatory powers by deregulating less risky medical software. And on February 10, 2014, Sens. Deb Fischer (R-Neb.) and Angus King (I-Maine) introduced the Preventing Regulatory Overreach to Enhance Care Technology (PROTECT) Act of 2014, S. 2007, which seeks to clarify the extent to which the FDA can regulate clinical and health software.

Conclusion

The second quarter (Q2) of 2014 will undoubtedly prove to be just as interesting as this past quarter. In early July, Wolters Kluwer will provide another White Paper detailing Q2 drug and device developments, including our review of significant court decisions, FDA actions, settlements and CIAs, agency reports, industry studies, and other areas of industry interest.