Top Stories

Senate Confirms Burwell as HHS Secretary
On June 5, the U.S. Senate confirmed Sylvia Mathews Burwell as Secretary of Health and Human Services ("HHS"), a leadership position that oversees FDA and has ultimate authority over most agency actions, although rarely used. The Senate voted 78–17 to confirm Burwell, who previously served as the White House budget director and will replace Kathleen Sebelius as head of the government agency charged with implementing the Affordable Care Act. After the Senate approved her nomination, President Obama credited Burwell's proven management skills and wealth of bipartisan relationships for the strong vote in her favor.

Report on CDRH Device Submissions Highlights Progress, Says Center Should Assess Withdrawn Submissions and Time Gaps
On June 11, FDA's Center for Device and Radiological Health ("CDRH") released an independent auditor's report containing final findings on FDA's medical device submission review process and noting areas for continued improvement. The report examined the Center's process for reviewing premarket approval and 510(k) notification submissions and also evaluated its performance in meeting certain challenges outlined during the enactment of the 2012 Medical Device User Fee Amendments (MDUFA III), such as sponsor communication, reviewer training, submission quality, and IT infrastructure.
- read more below

States Consider "Right-to-Try" Laws to Expand Treatment Options for Terminally Ill
According to an article in *Governing* magazine, some states are beginning to expand treatment options for patients with debilitating conditions through new preapproval programs. Known as "right-to-try" laws, the measures allow terminally ill patients to use pharmaceuticals not yet approved by FDA, such as drugs confirmed by Phase 1 clinical trials but lacking additional studies. Colorado led the nation in enacting the first law of this kind, when its legislature unanimously approved the measure earlier this year. On June 2, Louisiana adopted its own right-to-try law, and there are similar proposals under consideration in Arizona, Minnesota, and Missouri. Popularized by the film *Dallas Buyers Club*,

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Resources

- *Pharmaceutical & Medical Device Regulatory Update* Issue 8 Printable Version
- Jones Day's FDA Regulatory & Compliance Counseling Practice
- Jones Day's Health Care Practice

- Jones Day's Life Sciences Practice

the "right-to-try" movement aims to provide terminally ill patients with additional avenues to promising treatments, especially when they may not be eligible to participate in clinical trials. FDA has its own expanded access program, also known as "compassionate use," that permits certain patients to use investigational drugs outside of the typical clinical trial setting.

Federal, State, and Local Governments Pursue Varied Policies to Address Opioid Abuse
Federal, state, and local governments continue to target the rising abuse of opioid painkillers, albeit often through different approaches. On June 17, Massachusetts Gov. Deval Patrick hosted the governors of four other New England states to discuss collaborative efforts to rein in opioid abuse in the region, such as law enforcement and public information initiatives. Massachusetts recently unveiled its own task force's recommendations, including plans to spend $20 million and develop public health programs to provide greater access to services for individuals prone to drug abuse. Several local governments have also filed suits against opioid drug manufacturers, alleging the companies used deceptive marketing practices to increase usage and seeking damages in amounts equivalent to what the local government has paid in prescription costs for the drugs, plus related treatment costs.
- read more below

Next-Generation Biologics Market May Top $30 Billion by 2024
An article in *Pharma Manufacturing* describes the tremendous growth potential for the next-generation biologics market, whose current value of $1.5 billion could rise to $30 billion over the next 10 years. Analysts for Visiongain forecast that growth would be driven by at least five new blockbuster biologics and the acceleration of seven brands already on the market. However, there continue to be challenges associated with manufacturing complex proteins and developing linker technology for bound molecules. The analysts expect significant investment in these areas and predict that next-generation biologics will address current shortcomings, such as difficult dosing regimens and potential side effects. As the biologics industry grows, the market for generic biological products, known as biosimilars, is also likely to increase.

EMA Tweaks Guidelines for Clinical Trial Data Transparency
On June 12, the European Medicine Agency ("EMA") accepted, in principle, new transparency guidelines regarding the proactive disclosure of clinical trial data. However, against the background of intense pressure from stakeholders pushing for greater transparency, including the ombudsman and European Parliament, EMA was not able to adopt the final guidelines and instead chose to make last-minute changes during its management board meeting. The major changes include easier access to data for research and noncommercial use. EMA is now expected to adopt and release the final version by mid-July.

Latest FDA Regulatory Agenda Describes Upcoming Rules
The White House recently published its Current Regulatory Plan and Unified Agenda of Regulatory and Deregulatory Actions reporting on regulatory priorities for spring 2014. According to the Agenda, some regulations expected this spring and summer will not be issued until later this year. For example, changes to certain procedures for abbreviated new drug applications and related applications to patent certifications were set to be announced this spring, but finalization of the rulemaking is now slated for the end of the year. The Agenda also describes current good manufacturing practice requirements for drug products compounded by outsourcing facilities, which are expected to be formally proposed in November 2014.

Other News
FDA to Issue Rules, Guidance for Distributing Off-Label Drug Information

CMS, FDA Expand Open Data Initiatives

Commissioner Hamburg Addresses Global Regulatory Issues at World Health Assembly

HHS Plans to Appeal Court Order Striking 340B Drug Discounts

FDA Issues Guidance on UDI Data Submissions

House Republicans Question ONC's Regulatory Authority Over EHR

CDC Report Says Drug Diversion in Hospitals Exposes Patients to Infection

Veterinary Association Forms Committee to Look at Compounded Drugs

Sales of Leftover Diabetes Strips Coming Under Public Scrutiny

N.C. Senate Approves Legislation to Set "No Fault" Presumption in Cases Where Drug Company Warns About Side Effects

UK Scientific Panel Supports Mitochondrial Replacement IVF.

Regulatory Updates

FDA Issues Final Rule Amending Postmarketing Safety Requirements for Drugs and Biologics
In the June 10 *Federal Register*, FDA amended its postmarketing safety reporting regulations for human and drug biological products to require those subject to mandatory reporting requirements to submit safety reports electronically for FDA to process, review, and archive. The new requirement of electronic submissions will help FDA more quickly review postmarketing safety reports, identify emerging safety problems, and disseminate safety information. The amendments will also be a key part of aligning FDA's postmarketing safety reporting regulations with international standards for electronic submission of such information. In the same *Federal Register*, FDA also released an accompanying draft guidance for industry, *Providing Submissions in Electronic Format—Postmarketing Safety Reports.* ***The rule is effective June 10, 2015; comments on the Draft Guidance are due August 11, 2014****.*

FDA Issues Final Rule Establishing List of Qualifying Pathogens Under FDASIA
In the June 5 *Federal Register*, FDA issued a final rule implementing a provision of the Generating Antibiotic Incentives Now ("GAIN") title of the Food and Drug Administration Safety and Innovation Act ("FDASIA"). GAIN is meant to encourage development of new antibacterial and antifungal drugs for treating serious or life-threatening infections, and it provides incentives such as eligibility for designation as a fast-track product and an additional five years of exclusivity for qualifying products. The final rule lists the pathogens that qualify for GAIN. ***The rule is effective July 7.***

FDA Extends Comment Period for Proposed Rule on Medical Device Classification Procedures
In the June 12 *Federal Register*, FDA extended the comment period to September 22 for the proposed medical device classification rule appearing in the March 25 *Federal Register*. The proposed rule primarily would amend FDA's regulations governing classification and reclassification of medical devices to conform to the applicable provisions in FDASIA and codify the procedures and criteria for classification and reclassification of medical devices. ***Comments are now due September 22.***

FDA Corrects Notice of Independent Assessment of the Process for the Review of Device Submissions
In the June 12 *Federal Register*, FDA corrected a notice, "Independent Assessment of the Process for the Review of Device Submissions; Final Comprehensive Findings and Recommendations and First Implementation Plan," that appeared in the May 29 *Federal Register*. The May 29 notice was issued earlier than intended, and the June 12 correction notes that the documents will instead be available here on June 11.

FDA Withdraws Proposed Effective Date of Requirement for Premarket Approval for Cranial Electrotherapy Stimulator Devices
In the June 12 *Federal Register*, FDA withdrew the August 8, 2011 proposed rule and the April 4, 2013 proposed order that would have required filing a premarket approval application or notice of completion of a product development protocol for the class III preamendment device, cranial electrotherapy stimulator. FDA withdrew the proposed rule and proposed order after reviewing information received in response to the proposals.

FDA Announces Grant Funds Available for Support of CDER's Kidney Health Initiative Program
In the June 10 *Federal Register*, FDA announced the Center for Drug Evaluation and Research (CDER), Office of Medical Policy's intent to accept and consider a single-source application for a grant to the American Society of Nephrology to support the Kidney Health Initiative. ***Applications due June 30.***

FDA Issues Final Order Classifying Nonabsorbable Expandable Hemostatic Sponge into Class II with Special Controls
In the June 16 *Federal Register*, FDA issued a final order classifying the nonabsorbable expandable hemostatic sponge for temporary internal use into class II with special controls. ***The order is effective July 16.***

FDA Issues Final Order Classifying Powered Surgical Instruments for Improvement in the Appearance of Cellulite as Class II with Special Controls
In the June 3 *Federal Register*, FDA issued a final order classifying powered surgical instruments for improvement in the appearance of cellulite into Class II with special controls. ***This order is effective July 3***.

FDA Confirms Maximum Civil Penalties Effective June 18
In the June 6 *Federal Register*, FDA confirmed the effective date for the direct final rule revising the regulations on civil penalties to adjust the penalty amounts for inflation and amend the process for initiating certain civil penalty administrative actions issued in February. FDA is required to adjust the CMP at least once every four years under the Federal Civil Penalties Inflation Adjustment Act of 1990. The rule increased the maximum CMP amount anywhere from $1,000 to $25,000 per individual, $10,000 to $25,000 per violation, and $50,000 to $850,000 for multiple violations being adjudicated in a single proceeding.

FDA Issued the Following Guidance Documents
Guidance for Industry: Q4B Evaluation and Recommendation of Pharmacopoeial Texts for Use in the International Conference on Harmonisation Regions; Annex 6: Uniformity of Dosage Units General Chapter. June 16 *Federal Register*.

Draft Guidance for Industry: ANDA Submissions—Content and Format of Abbreviated New Drug Applications. June 12 *Federal Register*. ***Comments due August 11.***

Draft Guidance for Industry: Drug Supply Chain Security Act Implementation: Identification of Suspect Product and Notification. June 11 *Federal Register*. ***Comments due August 11.***

Draft Guidance for Industry: Distributing Scientific and Medical Publications on Risk Information for Approved Prescription Drugs and Biological Products—Recommended Practices. June 11 *Federal Register*. ***Comments due August 11.***

Guidance for Industry: Global Unique Device Identification Database. June 11 *Federal Register*.

Draft Guidance for Industry: Providing Submissions in Electronic Format—Postmarketing Safety Reports. June 10 *Federal Register*. ***Comments due August 11***.

Draft Guidance For Industry: Product Development Under the Animal Rule. June 3 *Federal Register*. ***Comments due August 4***.

FDA Determines Regulatory Review Periods for Drug, Biological Patents
FDA recently published determinations regarding the regulatory review periods for patent extensions of the following drugs: XIAFLEX; STENDRA, Xience Prime LI Everolimus Eluting Coronary Stent System, VANDETANIB; Vandetanib; Arcapta Neohaler; ZUPREVO; Arctic Front Cryocatheter System. FDA did not publish any determinations regarding the regulatory review periods for patent extensions of biologics.

FDA Determines Certain Drugs Not Withdrawn for Safety or Effectiveness
FDA determined that certain AZO GANTANOL (Phenazopyridine Hydrochloride, Sulfamethoxazole) and LEUCOVORIN CALCIUM-PRESERVATIVE FREE Injection products were not withdrawn for reasons of safety or effectiveness.

Information Collection Activities
FDA Announces that OMB has Approved Information Collections for:
Request for Information from U.S. Processors that Export to the European Community

Safety Assurance Case

FDA Announces that the Following Collections have been Submitted to OMB:
General Administrative Procedures: Citizen Petitions; Petition for Reconsideration or Stay of Action (***comments due to OMB July 7***)

Focus Groups as Used by the Food and Drug Administration (***comments due to OMB July 7***)

Prescription Drug Advertisements (***comments due to OMB July 7***)

Testing Communications on Biological Products (***comments due to OMB July 9***)

Guidance for Industry on Specification of the Unique Facility Identifier System for Drug Establishment Registration (***comments due to OMB July 14***)

FDA Announces the Opportunity to Comment on the Following Proposed Information Collections:
Testing Communications on Food and Drug Administration-Regulated Products Used in Animals (***comments due August 15***)

Medical Devices; Humanitarian Use Devices (***comments due August 11***)

Good Laboratory Practice Regulations for Nonclinical Studies (***comments due August 11***).

Upcoming Meetings, Workshops, and Conferences

Drugs and Biologics
Public Hearing Before the Commissioner on Confidentiality of Interim Results in Cardiovascular Outcomes Safety Trials; Part 15, will be held August 11, in Silver Spring, MD.

Public Meeting on Clinical Development of Drugs for the Prevention of Infections Caused by Staphylococcus aureus in the Health Care Setting will be held September 5.

Public Meeting on Methodological Considerations in Evaluation of Cancer as an Adverse Outcome Associated With Use of Non-Oncological Drugs and Biological Products in the Postapproval Setting will be held September 11, in Silver Spring, MD.

Medical Devices
Public Workshop on Hemostatic Medical Devices for Trauma Use will be held September 3–4, in Silver Spring, MD.

Public Workshop on Additive Manufacturing of Medical Devices: An Interactive Discussion on the Technical Considerations of 3D Printing will be held October 8–9, in Silver Spring, MD.

Advisory Committees
June 17: Gastroenterology and Urology Devices Panel of the Medical Devices Advisory Committee Meeting

June 25: Oncologic Drugs Advisory Committee Meeting

July 10–11: Obstetrics and Gynecology Devices Panel of the Medical Devices Advisory Committee

July 30–31: Gastroenterology and Urology Devices Panel of the Medical Devices Advisory Committee

October 16: Joint Meeting of the Psychopharmacologic Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee Meeting

For more comprehensive listings of FDA meetings, please visit these FDA webpages:
Meetings, Conferences, and Workshops (Drugs)

Workshops, Meetings, and Conferences (Biologics)

Workshops and Conferences (Medical Devices)

FDA Advisory Committee Calendar

Enforcement Updates

Recent Product Recalls
There have been no new drug recalls or biologic recalls since the last Jones Day *Pharmaceutical & Medical Device Regulatory Update*.

Since the last Update, FDA posted a recall of blood glucose test strips due to a labeling error.

Click here for a complete listing of FDA Recalls.

Recent Warning Letters
In recent weeks, the majority of warning letters posted by FDA were issued to medical device manufacturers and clinical investigators.

Five foreign medical device manufacturers and one in Oklahoma were cited primarily for violations of the Quality Systems Regulation and Medical Device Reporting regulations. The foreign firms included two German manufacturers and one each from Spain, Italy, and India. The agency additionally warned one of the manufacturers for failing to obtain 510(k) clearance before marketing its products. All letters to foreign manufacturers were sent directly from CDRH headquarters, while the Dallas District Office issued the letter to the Oklahoma firm.

FDA also warned three clinical investigators for objectionable conditions at a clinical site. All three investigators were cited for failing to ensure that their investigation was conducted according to the investigational plan. One investigator was also cited for failing to maintain adequate and current case histories and for failing to maintain adequate records of the disposition of the drug. Another investigator was cited for failing to submit an investigational new drug ("IND") application for conducting clinical investigations with an IND and for failing to maintain adequate records for receipt, shipment, or other disposition of the investigational drug.

Finally, FDA also warned a pharmaceutical compounding company for not having valid prescriptions for its drug products and for producing drug products in a nonsterile environment.

Click here for FDA's Warning Letters Home page (scroll down for listing of recently posted Warning Letters).

The Office of Prescription Drug Promotion ("OPDP") issued one untitled letter to a drug manufacturer for omitting risk information or material facts.

Click here for a complete listing of 2014 OPDP Warning Letters.

Recent Drug and Device Approvals
FDA approves Lymphoseek to help determine the extent of head and neck cancer in the body (June 13).

FDA approves the first antihemophilic factor, Fc fusion protein for patients with Hemophilia A (June 6).

For additional information on drug and device approvals and clearances, please visit FDA's webpages on Drug Approvals and Databases (includes biologics) and Device Approvals, Denials, and Clearances.

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In a blog post, CDRH Director Jeffrey Shuren said the final report confirms the Center is on track to improve these processes, noting recent successes in bringing down total review times. However, the report highlights several areas for continued improvement, including a need to focus on the causes of withdrawn applications and time gaps in the review process. Most withdrawn submissions were pulled during the MDUFA review phase, including a large portion withdrawn within the final 10 days, usually because of inadequate data to support substantial equivalence. As for review times, the Office of Device Evaluation often takes longer to reach a decision than the Office of In Vitro Diagnostics. Review times were shortest when the reviewers and device sponsors engaged in substantial communications. CDRH plans to reform its internal policies and staff training in response to these reports.

The final report follows an initial assessment released in December 2013. Both studies were commissioned as part of MDUFA III, and the findings, as well as CDRH's plans for improvement based on those findings, will play a big role in the next medical device user fee negotiations.

Top Stories

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Meanwhile, federal policymakers appear to lack a unified front on the opioid abuse issue, according to a *Boston Globe* article detailing position statements of various agencies and leaders. The Centers for Disease Control and Prevention and the Drug Enforcement Administration have asked providers to significantly reduce the use of prescription opioids. While FDA Commissioner Margaret Hamburg acknowledges the need to exercise caution with opioid prescriptions, she remains committed to keeping these drugs accessible to patients suffering from chronic pain. House leaders have pressured FDA to take a more active role against opioid abuse by threatening to withhold $20 million in appropriations until the agency finalizes guidance on abuse-deterrent formulations of opioids. We continue to monitor federal and state developments regarding opioids in our Jones Day *Updates*.