JONES DAY | **Pharmaceutical & Medical Device Regulatory Update**
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## Top News

**New Congress Brings New Zeal for Drug Innovation and Repealing Medical Device Tax**
President Obama paid special attention to medical innovation during his State of the Union Address last week when he highlighted a "precision medicine initiative" aimed at finding cures for cancer, diabetes, and other diseases. Some have linked this announcement to the 21st Century Cures initiative, legislation under development in the House Energy and Commerce Committee, designed to revamp how medical research and drugs are approved. Lawmakers released a 400-page discussion draft for the "21st Century Cures Act" alongside a more condensed section-by-section analysis and a press release calling for continued feedback.

In addition to new therapies, the President and the Congress continue to address the issue of antibiotic resistance. Four months ago, the Obama administration released its *National Plan for Combating Antibiotic Resistance*, calling for the development of new antibiotics and preventing the spread of drug-resistant bacteria.

This week, the White House announced that the President's proposed FY2016 budget would double the amount of federal funding for combating and preventing antibiotic resistance, increasing to more than $1.2 billion. On the legislative side, two senators recently reintroduced legislation to speed up regulatory approval for new treatments, citing the need for new drugs to fight antibiotic-resistant bacteria. The Promise for Antibiotics and

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## UPCOMING EVENTS

Therapeutics for Health Act (the "PATH Act") would create an accelerated approval process for treatments that address unmet needs for serious or life-threatening conditions. Although there is general support for the President's plan and the PATH Act, consumer advocates want more controls on antibiotic use in food animals to prevent antibiotic resistance.

The medical device tax is another issue that Congress, and likely the President, will revisit this year. As in the previous two Congresses, both houses have introduced legislation to repeal the medical device tax. The House has twice before passed such legislation, but similar measures were defeated in the Democratic-controlled Senate. With Republicans gaining control of the Senate, opponents of the tax are more optimistic, and some have predicted a bill repealing the tax could pass both chambers as soon as late March 2015.

The President, however, has said he would veto the bill because it undermines the Affordable Care Act, his administration's signature law. In an interesting twist, the nonpartisan Congressional Research Service issued a report challenging the medical device industry's claims that the tax would have significant economic impacts, including moving production overseas and costing jobs. However, lawmakers and advocates for repealing the tax remain undeterred.

**February 12, 2015**: **Scott A. Edelstein** will speak at a webinar on *US Cooperative for International Patient Programs: Legal Issues in US/Mexico Cross-Border Telemedicine*.

**February 24, 2015**: **Laura Laemmle-Weidenfeld** will speak as a panelist at the American Conference Institute's program *Professional Responsibility and Legal Ethics in Life Sciences*.

**March 4–7, 2015**: **Michael Carvin** will speak at the American Bar Association's *16th Annual Conference on Emerging Issues in Healthcare Law*.

**April 22–23, 2015**: **Cristiana Spontoni** will speak at the 1st Annual Women Leaders in Life Sciences Law Conference program *Pharmaceutical and Medical Device Regulatory Developments* in the session *Issue Spotting: Updates on the Substantive Legal Developments Affecting Life Sciences Companies in 2015 and Beyond*.

RELATED PRACTICES

FDA Regulatory & Compliance Counseling

Health Care

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**EMA Recommends Suspending 700 Medicines Due to Issues with Approval Process**

The European Medicines Agency ("EMA") has recommended the suspension of approximately 700 medicinal products distributed in Europe due to irregularities in their approval process. The recommendation follows an EMA review of findings of the French medicines agency ("ANSM") that GVK Biosciences, the company that carried out the clinical studies upon which the European Union ("EU") authorizations are based, did not comply with good clinical practices ("GCP") at their Hyderabad site in India. In particular, EMA found electrocardiogram data had been manipulated during some generic medicines' studies, which has cast doubt on the reliability of the bioequivalency data used to support the medicines' licenses. The EMA recommendation will be sent to the European Commission, which will consider whether to issue a legally binding decision in the coming days. This decision would apply to all Member States irrespective of whether the country has taken interim measures to suspend the medicine.

**FDA Releases New Health IT Guidance**

FDA recently issued two draft guidance documents intended to reduce oversight for low-risk medical devices: *Medical Device Accessories: Defining Accessories and Classification Pathway for New Accessory Types* and *General Wellness: Policy for Low Risk Devices*. To encourage innovation in health IT, FDA proposes to regulate medical device accessories based on the risks they present when used as intended with their parent devices, rather than the risk of the parent device itself. The medical device accessories guidance clarifies that FDA considers "accessories" to be devices intended to augment, supplement, or support another device, and it provides some examples of how FDA would evaluate a device under these criteria. In its general wellness guidance, FDA proposes to not evaluate whether low-risk general wellness products are "devices" as defined in the Food, Drug, and Cosmetic Act or if they are devices, whether they comply with the device

requirements. For the purpose of this guidance, the Agency defines "general wellness products" as products that present a very low risk to users' safety and are intended only for "general wellness use." Interestingly, FDA does not state that it is exercising "enforcement discretion," which is the term that the Agency commonly uses to describe its informal decision not to regulate, in whole or in part, a type of product as a device. The guidance clarifies that general wellness use means an intended use that relates to maintaining or encouraging a general state of health or a healthy activity and may reduce the risk or impact of certain diseases or conditions through a healthy lifestyle under certain circumstances. ***Comments on both guidances are due April 20, 2015***.

**Amended Rules on Off-Label Use of Drugs in France**
France has amended its rules on off-label use of drugs by broadening the instances in which such use can be authorized. On December 31, 2014, a decree was published to implement aspects of last summer's social security budget bill, which revised the French Public Health Code. As a result of these changes (as reflected in the revised version of Article L.5121-12-1 of the French Public Code), a medicinal product can now be authorized for "off-label" use under the so-called "temporary recommendation of use" ("RTU" or "*recommandation temporaire d'utilisation*") as long as no product that is already authorized for the indication or in the conditions of use has the same active ingredient, the same dosage, or the same pharmaceutical form. Previously, off-label use could be allowed under an RTU only where no approved product was available, irrespective of whether such approved product had the same active ingredient, the same dosage, or the same pharmaceutical form of the product used off-label.

**Other News**
FDA Removes Pre-2005 Warning Letters from Website

ONC Hires First Chief Health Information Officer

FDA Posts LDT Workshop Presentations and Videos

FDA to Launch New Office on Pharmaceutical Quality

FDA to Evaluate Drug-Impaired Drivers

FDA Issues Med-Watch Alert for Non-Sterile Saline Solution

Report: FDA Advisory Committees Not Influenced by Industry Ties

Colorado Reintroduces Biosimilars Substitution Bill

Washington, D.C. and Maryland to Consider "Death With Dignity" Laws

Second Wholesaler Sentenced for Smuggling Counterfeit Cancer Drugs

Japan Joins Medical Device Safety Coalition

Dr. Robert Califf Named FDA Deputy Commissioner for Medical Products and Tobacco

## Regulatory Notices

**EMA Seeks Comments on Clinical Trial Regulation**
On January 21, 2015, EMA launched a public consultation on the application of the transparency rules for new Clinical Trial Regulation EU No 536/2014, which will apply to the new clinical trial database starting May 28, 2016. ***Comments due February 18, 2015***.

**EMA to Share Generics Assessments with Other National Regulatory Authorities**
EMA announced it will share assessment reports of generic medicines with collaborating regulatory agencies outside of the EU as part of the International Generic Drug Regulators Pilot ("IGDRP"). The first phase of the pilot project will involve the EU, Australia, Canada,

Chinese Taipei, and Switzerland. Other members of the IGDRP may decide to take part in the pilot program at a later stage. These include Brazil, China, Japan, Korea, Mexico, New Zealand, Russia, Singapore, and South Africa.

**European Pharma Groups Launch Clinical Trial Tool to Avoid Duplicate Enrollments**
The European Federation of Pharmaceutical Industries and Associations and Innovative Medicines Initiative announced the launch of NewMeds new tool for avoiding duplicate enrollment of patients in clinical trials.

**FDA Requests Nominations for Science Board**
In the January 23, 2015, *Federal Register*, FDA requested nominations for members to serve on the Science Board to the FDA's Office of the Commissioner, Office of the Chief Scientist. ***Nominations due March 24, 2015***.

**FDA Releases Study Data Technical Conformance Guide Version 2.0, Updates Catalog**
In the January 12, 2015, *Federal Register*, FDA announced the availability of a Study Data Technical Conformance Guide, Version 2.0 ("Guide"), and an update to the Data Standards Catalog. The Guide supplements *Guidance for Industry: Providing Regulatory Submissions in Electronic Format—Standardized Study Data*.

**FDA Issued the Following Draft and Final Guidance Documents**

- *Draft Guidance for Industry: Evaluating Drug Effects on the Ability to Operate a Motor Vehicle*, January 16, 2015, *Federal Register*. ***Comments due March 17, 2015***.
- *Draft Guidance for Industry and FDA Staff: Current Good Manufacturing Practice Requirements for Combination Products*, January 27, 2015, *Federal Register*. ***Comments due March 27, 2015***.
- *Draft Guidance for Industry and FDA Staff: Medical Device Accessories: Defining Accessories and Classification Pathway for New Accessory Types*, January 20, 2015, *Federal Register*. ***Comments due April 20, 2015***.
- *Draft Guidance for Industry and FDA Staff: Current Good Manufacturing Practice Requirements for Combination Products Information Collections*, January 27, 2015, *Federal Register*. ***Comments due April 20, 2015***.
- *Draft Guidance for Industry and FDA Staff: Mitigating the Risk of Cross-Contamination from Valves and Accessories Used for Irrigation through Flexible Gastrointestinal Endoscopes*, January 20, 2015, *Federal Register*. ***Comments due April 20, 2015***.
- *Draft Guidance for Industry and Food and Drug Administration Staff: General Wellness: Policy for Low Risk Devices*, January 20, 2015, *Federal Register*. ***Comments due April 20, 2015***.

**European Authorities Issue Guidance on Nanomaterials, Pharmacovigilance**
The European Commission and the Scientific Committee on Emerging Newly Identified Health Risks have published guidance on determining potential health effects of using nanomaterials in medical devices. Meanwhile, EMA has published guidance on the implementation of new ISO Standard EN ISO 27953-2:2011 Health Informatics, individual case safety reports ("ICSRs") in pharmacovigilance—Part 2: Human pharmaceutical reporting requirements for ICSR (ISO 27953-2:2011), which will take effect on July 1, 2016. The guidance aims to improve the reporting of suspected side effects of medicines in ICSRs.

**FDA Announced that the Following Collections Have Been Submitted to OMB**

- Extralabel Drug Use in Animals
- Disclosure Regarding Additional Risks in Direct-to-Consumer Prescription Drug Television Advertisements
- Waiver of In Vivo Demonstration of Bioequivalence of Animal Drugs in Soluble Powder Oral Dosage Form Products and Type A Medicated Articles

**FDA Announced the Opportunity to Comment on the Following Proposed Information Collections**

- Extension: Guidance for Industry on Postmarketing Adverse Event Reporting for Nonprescription Human Drug Products Marketed Without an Approved Application
- Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products

## Upcoming Meetings, Workshops, and Conferences

**Drugs and Biologics**
The Seventh Annual Sentinel Initiative Public Workshop, **February 5, 2015**, in Washington, D.C.

Public Meeting on Breast Cancer Patient-Focused Drug Development, **April 2, 2015**, in Silver Spring, MD.

Public Meeting on Chagas Disease Patient-Focused Drug Development, **April 28, 2015**, in Silver Spring, MD.

Public Meeting on Functional GI Disorders Patient-Focused Drug Development, **TBD**, in Silver Spring, MD.

**Medical Devices**
Public Workshop—Optimizing FDA's Regulatory Oversight of Next Generation Sequencing Diagnostic Tests Public Workshop, **February 20, 2015**, in Silver Spring, MD

**Advisory Committees**
February 20, 2015: Orthopaedic and Rehabilitation Devices Panel of the Medical Devices Advisory Committee (to discuss premarket approval of a spine-spacing device)

February 23–24, 2015: Pharmacy Compounding Advisory Committee (to discuss proposed revisions to the list of drug products that may not be compounded under the exemptions provided by the FDCA because the drug products have been withdrawn or removed from the market for reasons of safety or effectiveness)

February 27, 2015: General and Plastic Surgery Devices Panel of the Medical Devices Advisory Committee Meeting (to discuss a panel-track supplement to a premarket approval application to expand the indication for use for an injectable implant device to include subdermal implantation for hand augmentation to correct volume deficit in the hands)

March 4, 2015: Vaccines and Related Biological Products Advisory Committee Meeting (to discuss and make recommendations on the selection of strains to be included in the influenza virus vaccines for the 2015–2016 influenza season)

For more comprehensive listings of FDA meetings, please visit these FDA web pages:
Meetings, Conferences, and Workshops (Drugs)
Workshops, Meetings, and Conferences (Biologics)
Workshops & Conferences (Medical Devices)
FDA Advisory Committee Calendar

## Enforcement Updates

**Recent Product Recalls**
In recent weeks, a drug manufacturer recalled one lot of sodium chloride injections due to particulate matter, and another drug manufacturer recalled sodium chloride IV bags because the products may have been used outside their intended use. A ribavirin powder for solution was recalled due to microbial contamination, and another drug was recalled due to confirmed subpotency and elevated impurity levels. A combination omeprazole

paste product was recalled because it was not approved for use as an animal drug.

A sporting goods store recalled an inversion table (which is a medical device) after discovering that users have the potential to fall from the table and suffer injuries.

View a complete listing of FDA Recalls.

**Recent Warning Letters**
Since we last reported on enforcement actions in December 2014, FDA posted warning letters to drug and device manufacturers, as well as one fertility center, for violations related to CGMP ("Current Good Manufacturing Practices"), QSR ("Quality Systems Regulations"), MDR ("Medical Device Reporting"), selling unapproved animal drugs, clinical investigations, and deviations from the regulations for human cells, tissues, and cellular and tissue-based products.

FDA continues to cite medical device manufacturers for CGMP and QSR violations, including those related to design change procedures, complaints handling, process controls, corrective and preventative action procedures, and maintaining device master records. Recipients of these warning letters, three of which are located overseas, included manufacturers of coronary bypass cannulas, endoscopes, portable oxygen generators, gas flow regulators, peripheral vascular testing devices, therapeutic infrared heating lamps, neuromuscular stimulators, acupuncture needs, slings, incontinence mesh, and dental devices. Six medical device manufacturers, three of which are located abroad, were also warned for failure to follow the MDR regulations. Two medical device manufacturers, one located abroad, were cited for marketing medical devices without the necessary marketing clearance or approval. One of the firms had obtained clearance for its device but was promoting the device beyond the scope of its intended use without submitting a new premarket notification.

Drug manufacturers continue to receive warning letters for CGMP violations, as well as misbranded or unapproved drugs. CGMP violations include those related to preventing contamination and maintaining a sterile environment. FDA additionally warned an active pharmaceutical ingredient manufacturer in China for CGMP violations. A Mexican drug manufacturer was also warned for failing to pay required Generic Drug User Fee Amendments fees.

FDA continues to monitor compounding pharmacies. One such pharmacy was warned after FDA received reports of adverse events in patients who used the pharmacy's products. The compounding pharmacy was cited for practices that render the pharmacy ineligible for statutory exemptions from the laws that generally apply to drug manufacturers. The compounding pharmacy was additionally cited for violations relating to insanitary conditions and CGMP.

FDA cited a clinical investigator for failing to properly maintain case histories and for failing to ensure the investigation adhered to the investigational plan. A fertility center received a warning letter for deviations from the relevant regulations for human cells and tissues, including failure to collect and screen donor specimens for relevant communicable diseases.

Finally, FDA posted one warning letter to a veterinary company that sells animal drugs online for marketing an unapproved new animal drug, and another warning letter to a dairy operation for using a veterinary drug beyond what was directed by the drug's approved labeling.

View FDA's Warning Letters homepage (scroll down for listing of recently posted Warning Letters).

The Office of Prescription Drug Promotion ("OPDP") has issued no new warning letters since the last *Update*.

View a complete listing of 2014 OPDP Warning Letters.

## Recent Notable Drug and Device Approvals/Clearances

FDA approves first generic esomeprazole (January 26, 2015)

FDA permits marketing of first system of mobile medical apps for continuous glucose monitoring (January 23, 2015)

FDA approves a second vaccine to prevent serogroup B meningococcal disease (January 23, 2015)

FDA approves new psoriasis drug Cosentyx (January 21, 2015)

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

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