JONES DAY | **Pharmaceutical & Medical Device Regulatory Update**
Vol. II | Issue 12 | July 2015 JONES DAY

Top News

House of Representatives Passes 21st Century Cures Act
On July 10, 2015, the U.S. House of Representatives approved H.R. 6 , the 21st Century Cures Act ("Cures Act"), by a vote of 344–77, setting up the legislation for consideration in the U.S. Senate. The legislation focuses on reducing regulatory obstacles to the review process through FDA for new pharmaceuticals and medical devices. In general, the Cures Act aims to hasten discovery, development, and delivery of medical products by removing barriers to collaboration, incorporating patients' perspectives into the drug development and review process, modernizing clinical trials, addressing regulatory uncertainty surrounding new medical apps, and incentivizing drug development for rare diseases.

While the bill's advance has generally been received with favorable attention, some criticism remains. Earlier in the legislative process, a national association of health care providers sent a letter to lawmakers questioning the viability of the bill's interoperability provisions and the fairness of the enforcement provisions.

FDA Strengthens NSAID Warning
Earlier this month, FDA announced it was requiring heightened warnings about heart attack and stroke risks on the labels of all non-aspirin, nonsteroidal anti-inflammatory drugs ("NSAIDs"), in prescription and over-the-counter form. The warning updates existing label information from a statement that NSAIDs "may cause" increased heart attack and

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UPCOMING EVENTS

September 17–18, 2015: Laura Laemmle-Wiedenfeld will give a presentation on *Damages and Penalties*

stroke to a more conclusive statement that the drugs "cause an increased risk" of serious heart failure. The labeling revision comes from a comprehensive analysis of new safety information, including observational studies, combined analyses of clinical trials, other scientific publications, and the input of the Arthritis and Drug Safety and Risk Management Advisory Committees in early 2014.

FDA Issues Notice of Enforcement Action Against Unapproved Prescription Ear Drop Products

On July 1, 2015, FDA announced it will begin taking enforcement action against companies that manufacture or distribute certain unapproved prescription ear drop products, known as otic products. In a *Federal Register* notice and press release, the agency described general safety concerns about the misbranded products and informed manufacturers that they would face enforcement actions, such as product seizure, injunction, or criminal proceedings, if they continued producing the drugs without premarket approval.

The unapproved ear drops range from single-ingredient forms to combination products and contain active ingredients such as benzocaine and hydrocortisone, which FDA indicated have not been reviewed for safety and effectiveness for labeled uses in treating ear pain, infection, and inflammation, including "swimmer's ear." The notice advises manufacturers to submit a new drug application or abbreviated new drug application ("ANDA") for premarket approval.

EMA Provides Update on the Implementation of Transparency Policy

The European Medicines Agency ("EMA") has published a video and presentations from its June 24, 2015, webinar, which provide an update on the implementation of its Transparency Policy. The policy came into force on January 1, 2015, and applies to clinical reports contained in all marketing-authorization applications submitted on or after this date. The webinar provides an explanation of the principles for the submission of redacted clinical reports, the redaction consultation process, as well as guidance on redacting commercially confidential information in clinical reports and on the anonymization of clinical reports for purposes of publication.

Japan Joins Medical Devices Single Audit Program Pilot

Last month, the Ministry of Health, Labor and Welfare of Japan officially announced it will join the Medical Devices Single Audit Program ("MDSAP") Pilot. The MDSAP initiative is intended to allow a recognized auditing organization to conduct a single audit of a medical device manufacturer that will satisfy the relevant requirements of each regulatory authority participating in the pilot program. Four other regulatory authorities have joined the initiative: the U.S. FDA, Australia's Therapeutic Goods Administration, Brazil's Agencia Nacional de Vigilancia Sanitaria, and Health Canada. With the addition of Japan, the burden for quality management system investigations imposed by each country's regulatory authority is expected to decrease through consolidation into reviews conducted by a recognized MDSAP auditing organization.

Other News

FDA's Acting Commissioner Observes Regulatory Achievements on Third Anniversary of FDASIA

Federal Court Enters Permanent Injunction Against Manufacturer for Marketing

Under the FCA at the CLE International Conference in San Francisco, CA.

October 1–2, 2015: Colleen Heisey will moderate a session titled *Challenging Hypotheticals*, at the Food & Drug Law Institute's program on Advertising and Promotion for the Pharmaceutical, Medical Device, Biological, and Veterinary Medicine Industries, in Washington, D.C.

October 21, 2015: Maureen Bennett will give a presentation on *International Clinical Research Issues* to the Boston Bar Association's Health Law Education Committee.

RELATED PRACTICES

FDA Regulatory & Compliance Counseling

Health Care

Life Sciences

Unapproved Prescription Drugs for Treatment of Inflamed Hemorrhoids

Following Investigation by FDA and HHS, Company CEO Sentenced to Two Years in Prison for Distributing Adulterated Medical Devices

EMA Adopt Revised Guideline on Core Summary of Product Characteristics for Plasma-Derived Fibrin Sealant/Haemostatic Products

European Commission Publishes the Final Opinion on the Safety of Medical Devices Containing DEHP (phthalates)

European Commission Adopts Series of Communications Updating Lists of Harmonized Standards for Medical Devices

Regulatory Updates

FDA Announces Intent to Review Study Data Reviewer's Guide Template
In the July 23, 2015, *Federal Register*, FDA and the Center for Drug Evaluation and Research announced the establishment of a public docket to collect comments related to a proposed Study Data Reviewer's Guide template. The purpose of the review is to determine whether FDA will recommend its use either as is, or in a modified form, for regulatory submissions of data. ***Comments are due September 21, 2015.***

FDA Requests Stakeholder Participation in Meetings on Prescription Drug User Fee Act Reauthorization
In the July 20, 2015, *Federal Register*, FDA requested that public stakeholders, including patient and consumer advocacy groups, health care professionals, and scientific and academic experts, notify FDA of their intent to participate in periodic consultation meetings on the reauthorization of the Prescription Drug User Fee Act ("PDUFA") for which the statutory authority expires in September 2017. FDA is required, under the Federal Food, Drug & Cosmetic Act ("FDCA") to consult with a range of stakeholders in developing recommendations for the next PDUFA program. ***Notifications of Intent are due August 28, 2015.***

FDA Extends Nomination Period for List of Bulk Drugs Used by Outsourcing Facilities
In the July 20, 2015, *Federal Register*, FDA announced it was extending the nomination period for bulk drug substances that may be used by facilities registered as outsourcing facilities to compound animal drugs from bulk substances. ***Nominations are due November 16, 2015.***

FDA Authorizes Emergency Use of In Vitro Diagnostic Device for Enterovirus D68
In the July 1, 2015, *Federal Register*, FDA announced the issuance of an Emergency Use Authorization ("EUA") for an in vitro diagnostic device to detect Enterovirus D68 strains observed in North America in 2014. The EUA was issued pursuant to the FDCA at the request of the Centers for Disease Control and Preventions.

FDA to Take Enforcement Action on Unapproved and Misbranded Otic Prescription Drug Products
In the July 2, 2015, *Federal Register*, FDA announced its intention to take enforcement action against unapproved and misbranded otic drug products labeled for prescription use. These unapproved and misbranded otic drug products are marketed and labeled for temporary relief of pain associated with ear infection or inflammation, among others.

FDA Amends Biologics Regulations
In the July 2, 2015, *Federal Register*, FDA announced it is amending the biologics regulations by removing the general safety test ("GST") requirements for biological products. The existing codified GST regulation are duplicative of requirements specified in

biologics license applications and are no longer necessary or appropriate to ensure the safety, purity, and potency of licensed biological products. ***Effective August 3, 2015.***

FDA Proposes to Remove Two Regulations on Biological Products
In the July 2, 2015, *Federal Register*, FDA proposed to remove two regulations dictating procedures for FDA's review and classification of biological products licensed before July 1, 1972. The two regulations are no longer necessary due to other statutory and regulatory authorities established since 1972 that allow FDA to evaluate and monitor the safety and effectiveness of all biological products.

FDA Announces Disease Areas to be Discussed for Drug Development in Fiscal Years 2016–2017
In the July 2, 2015, *Federal Register,* FDA announced the selection of disease areas to be addressed during fiscal years 2016–2017 of its Patient-Focused Drug Development Initiative. The diseases, which vary greatly in severity and size of the affected population, include alopecia areata, autism, hereditary angioedema, non-tuberculous mycobacterial infections, patients who have received an organ transplant, psoriasis, neuropathic pain associated with peripheral neuropathy, and sarcopenia.

FDA Revokes Company's Biologics License for Murine Monoclonal
In the July 7, 2015, *Federal Register,* FDA announced the revocation of a company's biologics license for the manufacture of Anti-A (Murine Monoclonal), Anti-B (Murine Monoclonal), Anti-Lea (Murine Monoclonal), and Anti-Leb (Murine Monoclonal).

FDA Implements Drug Shortage Provisions
In the July 8, 2015, *Federal Register,* FDA announced it is amending its regulations to implement certain drug shortages provisions of the FDCA. The rule requires all applicants of covered approved drugs or biological products to notify FDA electronically of a permanent discontinuance or an interruption in manufacturing of the product that is likely to lead to a meaningful disruption in supply (or a significant disruption in supply for blood or blood components) of the product in the United States.

FDA Determines that Tessalon (Benzonatate) Capsules and Other Drug Products Were Not Withdrawn from Sale for Reasons of Safety or Effectiveness
In the July 20, 2015, *Federal Register,* FDA announced its determination that the drug products listed in the notice were not withdrawn from sale for reasons of safety or effectiveness. This determination means FDA will not begin procedures to withdraw approval of ANDAs that refer to these drug products, and it will allow FDA to continue to approve ANDAs that refer to the products as long as they meet relevant legal and regulatory requirements.

FDA Issued the Following Draft and Final Guidance Documents

Guidance for Industry: Analytical Procedures and Methods Validation, July 27, 2015, *Federal Register.*

Guidance for Industry and Food and Drug Administration Staff: Intent to Exempt Certain Unclassified, Class II, and Class I Reserved Medical Devices from Premarket Notification Requirements, July 1, 2015, *Federal Register.*

Guidance for Industry, Researchers, Patient Groups, and Food and Drug Administration Staff: Meetings with the Office of Orphan Products Development, July 9, 2015, *Federal Register.*

Draft Guidance for Industry and Food and Drug Administration Staff: Submission of Premarket Notifications for Magnetic Resonance Diagnostic Devices, July 14, 2015, *Federal Register*. ***Comments are due October 13, 2015.***

Draft Guidance for Industry: Testicular Toxicity: Evaluation During Drug Development,

July 17, 2015, *Federal Register*. ***Comments are due October 13, 2015.***

Revised Draft Guidance for Industry: Bioequivalence Recommendations for Lubiprostone, July 20, 2015, *Federal Register*. ***Comments are due September 18, 2015.***

Draft Guidance for Industry: Gastroparesis: Clinical Evaluation of Drugs for Treatment, July 23, 2015, *Federal Register.* ***Comments are due September 21, 2015.***

Draft and Revised Draft Guidances for Industry: Bioequivalence Recommendations for Specific Products, June 30, 2015, *Federal Register.* ***Comments are due August 31, 2015.***

Draft Guidance for Industry and Food and Drug Administration Staff: Premarket Notification Requirements Concerning Gowns Intended for Use in Health Care Settings , June 30, 2015, *Federal Register.* ***Comments are due August 31, 2015.***

Draft Guidance for Industry: Qualification of Biomarker—Plasma Fibrinogen in Studies Examining Exacerbations and/or All-Cause Mortality in Patients with Chronic Obstructive Pulmonary Disease, July 7, 2015, *Federal Register.* ***Comments are due September 8, 2015.***

Draft Guidance for Industry and Food and Drug Administration Staff: Heparin-Containing Medical Devices and Combination Products: Recommendations for Labeling and Safety Testing, July 9, 2015, *Federal Register*. ***Comments are due October 7, 2015.***

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

- Evaluation of the Food and Drug Administration's Campaign to Reduce Tobacco Use Among Lesbian, Gay, Bisexual, and Transgender Young Adults
- Guidance for Industry on Oversight of Clinical Investigations: A Risk-Based Approach to Monitoring
- Guidance for Industry on Questions and Answers Regarding the Labeling of Nonprescription Human Drug Products Marketed Without an Approved Application as Required by the Dietary Supplement and Nonprescription Drug Consumer Protection Act
- Market Claims in Direct-to-Consumer Prescription Drug Print Ads

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

- General Licensing Provisions, Section 351(k) Biosimilar Applications
- Registration of Producers of Drugs and Listing of Drugs in Commercial Distribution
- Guidance for Industry on Controlled Correspondence Related to Generic Drug Development
- Guidance for Industry and Food and Drug Administration Staff, Section 905(j) Reports: Demonstrating Substantial Equivalence of a New Tobacco Product: Responses to Frequently Asked Questions
- Reclassification Petitions for Medical Devices, Correction
- Sun Protection Factor Labeling and Testing Requirements and Drug Facts Labeling for Over-the-Counter Sunscreen Drug Products

FDA Announced that the Following Collections Have Been Approved by OMB:

- Export Certificates for Food and Drug Administration Regulated Products
- Record Retention Requirements for the Soy Protein and Risk of Coronary Heart Disease Health Claim
- Generic Clearance for the Collection of Qualitative Data on Tobacco Products and Communications

EU Regulatory Notices

Mandatory Use of Centralized Repository for EU Centralized Procedure Kicks In
As of July 1 2015, it is mandatory to submit centralized procedure applications for human medicines to the EMA via eSubmission Gateway/Web Client. These applications will automatically be made available to all national competent authorities via a common online repository. Companies should therefore no longer send centralized procedure applications for human medicines to individual Member States on CDs/DVDs or via the Common European Submission Platform. The common repository, available since February 2014, is aimed at accelerating the validation of incoming applications.

EMA Consults on Viral Safety of Plasma-derived Medicinal Products and Hepatitis E
On June 25, 2015, EMA published a draft reflection paper on viral safety of plasma-derived medicinal products with respect to hepatitis E virus. The draft document analyzes the transfusion-associated infections and clinical experience with HEV-infections, HEV detection and epidemiology of HEV in blood/plasma donations, serum antibodies against HEV, inactivation/removal of HEV during manufacture of plasma-derived products, and risk assessments for plasma-derived medical products. ***Comments are due August 30, 2015.***

EMA Publishes a Draft Guideline on Manufacture of the Finished Dosage Form
On July 9, 2015, EMA published a draft guideline on manufacture of finished dosage form. The objective of the guideline, which will replace the note for guidance on the manufacture of the finished dosage form (CPMP/QWP/486/95), is to provide clarification on the type and level of information that should be included in the Common Technical Document Module 3 of the marketing-authorization application dossier with respect to the manufacturing process description. ***Comments are due January 9, 2016***.

Upcoming Meetings, Workshops, and Conferences

Drugs and Biologics
New Methods to Predict the Immunogenicity of Therapeutic Coagulation Proteins, **September 17–18, 2015**, in Bethesda, MD.

Public Meeting on Patient-Focused Drug Development for Huntingdon's and Parkinson's Diseases, **September 22, 2015**, in Silver Spring, MD.

FDA/PDA Conference titled *Mission Possible: Patient-Focused Manufacturing, Quality, and Regulatory Solutions,* **September 28–30, 2015**, in Washington, D.C.

Public Meeting on Patient-Focused Drug Development for Alpha-1 Antitrypsin Deficiency, **September 29, 2015**, in Silver Spring, MD.

International Cooperation on Cosmetics Regulations (ICCR) – Preparation for ICCR-9 Meeting, **November 4–6, 2015**, in College Park, MD.

Public Meeting on Risk Evaluation and Mitigation Strategies (REMS): Understanding and Evaluating Their Impact on the Health Care Delivery System and Patient Access, **October 5–6, 2015**, in Silver Spring, MD.

Medical Devices
Acute Ischemic Stroke Medical Device Trials Workshop, **October 6, 2015**, in Silver Spring, MD.

Public Workshop: Non-Microbial Biomarkers of Infection for In Vitro Diagnostic Device Use, **October 16, 2015**, in Silver Spring, MD.

Public Workshop on Medical Device Patient Labeling, **September 29, 2015**, in Silver Spring, MD.

Advisory Committees
July 29, 2015: Science Board (to provide advice to the Commissioner of Food and Drugs and other appropriate officials on specific, complex scientific and technical issues important to FDA and its mission, including emerging issues within the scientific community).

September 15, 2015: Vaccines and Related Biological Products Advisory Committee (to discuss and make recommendations on the safety and immunogenicity of Seasonal Trivalent Influenza Vaccine, Surface Antigen, Inactivates, Adjuvanted with MF59 (FLUAD) manufactured by Novartis.

September 24, 2015: Obstetrics and Gynecology Devices Panel of the Medical Devices Advisory Committee (to discuss the risks and benefits of Bayer HealthCare's Essure System for permanent female sterilization).

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

Recent Notable Drug and Device Approvals/Clearances

FDA approves new treatment for chronic hepatitis C genotype 3 infections (July 24, 2015)

FDA approves Praluent to treat certain patients with high cholesterol (July 24, 2015)

FDA approves new treatment for most common form of advanced skin cancer (July 24, 2015)

FDA approves Technivie for treatment of chronic hepatitis C genotype 4 (July 24, 2015)

FDA approves diagnostic test to differentiate between types of HIV infection (July 24, 2015)

FDA authorizes use of prosthesis for rehabilitation of above-the-knee amputations (July 16, 2015)

FDA approves targeted therapy for first-line treatment of patients with a type of metastatic lung cancer (July 13, 2015)

FDA approves new drug to treat schizophrenia and as an add on to an antidepressant to treat major depressive disorder (July 13, 2015)

FDA approves new drug to treat heart failure (July 7, 2015)

FDA approves new treatment for cystic fibrosis (July 2, 2015)

FDA approves new antiplatelet drug used during heart procedure (June 22, 2015)

FDA allows marketing of new device to help the blind process visual signals via their tongues (June 18, 2015)

FDA approves SAPIEN 3 THV artificial heart valve (June 17, 2015)

FDA approves brain implant to help reduce Parkinson's disease and essential tremor symptoms (June 12, 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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