Pharmaceutical & Medical Device Regulatory Update
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Jones Day Announcements

Health Care and Life Sciences Practice Expands with Arrival of Edgar Asebey
Jones Day welcomes **Edgar Asebey** to its Health Care and Life Sciences Practice. Mr. Asebey's practice focuses on foods, medical devices, drugs, dietary supplements, and cosmetics, and he advises clients in these industries on regulatory, registration, importation, and enforcement matters. He also counsels clients on premarket approval submissions and on compliance issues associated with the development, manufacture, marketing, and sale of FDA-regulated products. Mr. Asebey has extensive experience with clients in Latin America, and he is an active speaker and writer on FDA and life science matters.

Top News

FDA Approves First Biosimilar
On March 6, 2015, FDA approved Zarxio (filgrastim-sndz), the first biosimilar product to be approved in the United States under the Biologics Price Competition and Innovation Act ("BPCI Act"). The BPCI Act created an abbreviated licensure pathway for biological products shown to be "biosimilar" to a previously licensed biological product, called the "reference product."

To be approved, a biosimilar must be "highly similar" to its reference product, which generally means the two compounds have the same indications for use, mechanisms of action, routes of administration,

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UPCOMING EVENTS

dosage forms, strengths, and safety and effectiveness, and no more than minor differences in inactive ingredients. The biosimilar may be approved only for the same indications and uses as the reference product.

Zarxio, like its reference product Neupogen (filgrastim), is indicated to treat neutropenia, a deficiency of infection-fighting white blood cells caused by cancer and cancer therapies such as bone marrow transplant and chemotherapy. Zarxio is marketed outside of the U.S. in more than 60 countries worldwide and was approved in Europe in 2009, before a regulatory pathway existed to obtain marketing approval for biosimilars in the United States.

While FDA's approval of the first biosimilar is a major step forward in the process of implementing the BPCI Act, significant issues affecting product development and marketing remain uncertain and open for debate, including key scientific policy questions such as naming, labeling, indication extrapolation, and interchangeability. In the meantime, additional biosimilars applications are under consideration by the agency. Noting that it can disclose only applications that the companies have made public, FDA has stated four such applications are currently in the pipeline.

FDA's 2016 Budget Request Focuses on Biosimilars, Food Safety, and Drug Compounding

At the FY2016 Budget Hearing for FDA before a House Appropriations Subcommittee, FDA Commissioner Margaret Hamburg testified regarding the agency's $4.9B request, focused on biosimilars, food safety, and drug compounding. The request is for a 9 percent increase over the FY2015 budget.

March 25–27, 2015: **Laura Laemmle-Weidenfeld** will speak at the AHLA Institute on Medicare and Medicaid Payment Issues program titled *Recent Developments in Fraud and Abuse Prevention and Enforcement*.

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, Issue Spotting: Updates on the Substantive Legal Developments Affecting Life Sciences Companies in 2015 and Beyond*.

April 27, 2015: **Maureen Bennett** will serve as a panelist on the Boston Bar Association's *Health Law Education Committee—Legal and Ethical Implications of Medical Tourism*.

May 3–5, 2015: **Scott Edelstein** and **Alexis Gilroy** will speak at the American Telemedicine Association's Annual Meeting in a program titled *Telehealth Partnering in US & Abroad—A Look at Viable Strategies & Legal Considerations*. **Laurie Clarke**, **Doug Pearson**, and **Bruce Olcott** will speak at a pre-conference session titled *Digital Health in Transition: Regulatory Insight for Product Developers*.

RELATED PRACTICES

FDA Regulatory & Compliance Counseling

Health Care

Life Sciences

Dr. Hamburg, who is resigning this month, testified that the requested budget would support several important agency initiatives including the implementation of key provisions of the FDA Safety and Innovation Act of 2012 (FDASIA) and the Drug Quality and Security Act (DQSA), efforts to fight antibiotic resistance, and further development of biosimilars guidance. Several members of Congress expressed reservations about the request, including Rep. Harold Rogers (R-KY), chairman of the full House Appropriations Committee, who voiced concern about the amount, and Rep. Robert Aderholt (R-AL), chairman of the subcommittee, regarding the shortage of FDA staff to inspect Chinese facilities.

FDA Outlines Plan to Regulate Next Generation Gene Sequencing Tests

At a recent public workshop, FDA's Office of In Vitro Diagnostics and Radiological Health addressed the need for FDA to develop a regulatory system for next generation sequencing ("NGS") tests. Sometimes referred to as "high throughput sequencing," NGS tests sequence large segments of DNA to identify genetic variants that may lead to disease. FDA acknowledged a wide spectrum of options for regulating NGS tests but ultimately pointed to a white paper in which the agency described its marketing authorization for an NGS instrument and its related reagents and assays. In that case, the

company had used representative variants to demonstrate test performance, rather than methods requiring assessment of the enormous number of genetic variants detected by the tests. FDA plans to continue to use this approach in the future, along with other "novel and efficient approaches."

EU Rare Disease Day
On February 28, 2015, the European Organisation for Rare Diseases ("Eurordis") coordinated a Rare Disease Day to raise awareness of rare diseases across Europe. Terkel Andersen, the president of Eurordis, stressed the differences in access to therapies for patients with rare diseases across the Member States. Speaking ahead of the event, the European Heath Commissioner, Vytenis Andriukaitis, called for Member States to devise national actions plans on rare diseases. The event was supported by the European Medicines Agency.

European Court Hands Down Judgment in Medical Device Case
In proceedings involving pacemakers that had been replaced based on manufacturer recommendations, the *Bundesgerichtshof* (Federal Court, Germany) asked the Court of Justice ("ECJ") whether the device may be classified as defective based solely on evidence that quality control checks on devices of the same model disclosed a potential defect. The ECJ held that when a medical device has a potential defect, it is possible to classify all products of the same model as defective, without showing the product is defective in each individual case.

FDA Launches First Drug Shortage Mobile App
FDA launched its first mobile app to speed public access to information about drug shortages. Users can search by name, active ingredient, or therapeutic category, and the app will identify current drug shortages, resolved shortages, and discontinuations of drug products. App users can also report suspected shortages. FDA developed the app as part of its Strategic Plan for Preventing and Mitigating Drug Shortages.

Other News
FDA Issues Revised Draft Guidance on Use of Imaging Endpoints to Support Approval of Drugs and Biologics

UK Funds $85M Cell Manufacturing Facility to Boost Biotech

GAO: HHS Needs Better Dissemination of Comparative Effectiveness Research

HHS OIG Reports Medicare's Drug Substitution Policy Saved $13M in 2013–2014

Presidential Bioethics Commission Issues Recommendations on Ebola Response

Federal Court Invalidates Maine Law Allowing Imported Prescription Medicines

Consumer Group Seeks FDA Ban on Antifungal Drug Linked to Liver Damage

Regulatory Updates

FDA Releases Product-Specific Bioequivalence Recommendations for ANDAs
In the March 9, 2015, *Federal Register*, FDA announced the availability of additional draft and revised draft product-specific bioequivalence ("BE") recommendations on the design of BE studies to support abbreviated new drug applications ("ANDAs"). FDA produced the recommendations in accordance with the process outline in a 2010 guidance document. The new BE recommendations for specific products are available on FDA's website.

FDA Opens Docket for General Comments on Drug Compounding Policies
In the March 9, 2015, *Federal Register*, FDA announced a public docket to receive information, recommendations, and comments on matters related to the agency's regulation of compounding of human drug products under Sections 503A and 503B of the FD&C Act. Docket No. FDA-2015-N-0030 is intended for general comments related to human drug compounding that are not specific to documents or issues that are the

subject of other dockets.

FDA Extends Comment Period for Proposed Rule on Electronic Distribution of Prescribing Information for Drugs and Biologics
In the March 9, 2015, *Federal Register*, FDA announced it is extending the comment period for the proposed rule, announced December 18, 2014, to amend labeling regulations for human prescription drugs and biological products to require that the prescribing information intended for health care professionals provided on or within the dispensed package be distributed electronically and not in paper form, except as provided by the proposed rule. ***Comments now due May 18, 2015***.

FDA Solicits Information on Research Efforts to Address Public Health Concerns for Racial/Ethnic Demographic Subgroups
In the February 25, 2015, *Federal Register*, FDA announced it has opened a public docket to obtain information and comments on specific areas of public health concern for racial/ethnic demographic subgroup populations, focusing on certain disease areas where significant outcome differences may be anticipated. FDA is seeking public input on disease areas that can be addressed through regulatory science research. ***Comments due April 27, 2015***.

FDA Releases Report on National Medical Device Surveillance System
In the February 25, 2015, *Federal Register*, FDA announced the availability of the report titled *Strengthening Patient Care: Building an Effective National Medical Device Surveillance System*, developed by the National Medical Device Postmarket Surveillance System Planning Board. The report reflects recent studies by FDA examining the effectiveness of its postmarket oversight systems. FDA is soliciting comments from stakeholders. ***Comments due April 27, 2015***.

FDA Classifies Powered Exoskeleton as Class II Medical Device
In the February 24, 2015, *Federal Register*, FDA issued an order classifying the powered exoskeleton into class II for medical devices. A powered exoskeleton is identified as "a prescription device that is composed of an external, powered, motorized orthosis used for medical purposes that is placed over a person's paralyzed or weakened limbs for the purpose of providing ambulation." The order identifies the special controls for this type of medical device, which will be included in its classification regulation.

FDA Makes Tentative Determinations that Ecamsule and Enzacamene Are Not GRASE for Use in OTC Sunscreen Products
Through dual notices in the February 25, 2015, *Federal Register*, FDA issued proposed sunscreen orders under the FD&C Act, as amended by the Sunscreen Innovation Act, announcing the agency's tentative determinations that ecamsule (at concentrations up to 10 percent) and enzacamene are not generally recognized as safe and effective ("GRASE") and are misbranded when used in over-the-counter ("OTC") sunscreen products. According to the proposed orders, currently available data are insufficient to classify these ingredients as GRASE, and additional information is needed to allow for their approval. ***Comments due April 13, 2015***.

FDA Classifies Assisted Reproduction Embryo Image Assessment System as Class II Medical Device
In the February 26, 2015, *Federal Register*, FDA classified the Assisted Reproduction Embryo Image Assessment System into class II (special controls). An Assisted Reproduction Embryo Image Assessment System is identified as a "prescription device that is designed to obtain and analyze light microscopy images of developing embryos. This device provides information to aid in the selection of embryo(s) for transfer when there are multiple embryos deemed suitable for transfer or freezing." The order provides special controls that will apply to the medical device and be part of the codified language for its classification.

FDA Issues Technical Amendment to eMDR Regulations
In the February 27, 2015, *Federal Register*, FDA amended its postmarket electronic Medical Device Reporting ("eMDR") regulations. The technical amendment addresses the

unintentional removal of certain provisions of the Unique Device Identification System regulations and the updating of contact information listed in the regulations.

FDA Issued the Following Draft and Final Guidance Documents
Draft Guidance for Industry, Clinical Investigators, and Institutional Review Boards: Use of an Electronic Informed Consent in Clinical Investigations: Questions and Answers, March 9, 2015, *Federal Register*. ***Comments due May 8, 2015***.

Draft Guidance for Industry: Clinical Trial Imaging Endpoint Process Standards, March 3, 2015, *Federal Register*. ***Comments due May 4, 2015***.

Draft Guidance for Industry and FDA Staff: Technical Performance Assessment of Digital Pathology Whole Slide Imaging Devices, February 25, 2015, *Federal Register*. ***Comments due May 26, 2015***.

FDA Announced the Opportunity to Comment on the Following Proposed Information Collections
• Reclassification Petitions for Medical Devices

FDA Announced that the Following Collections Have Been Submitted to OMB
• 513(g) Request for Information
• Notification of a Health Claim or Nutrient Content Claim Based on an Authoritative Statement of a Scientific Body
• Investigational New Drug Applications
• Current Good Manufacturing Practice Regulations for Finished Pharmaceuticals

EU Regulatory Notices

Adjusted Fees for Applications to EMA Apply from April 1, 2015
Every year, the European Medicines Agency ("EMA") adjusts its fees on April 1, in line with the European Union ("EU") inflation rate for the previous year. All applications received by March 31 will be charged at the current fee and reduction rates. Applications received after that date will be charged the adjusted fees and be subject to the revised reduction rates, where applicable. For scientific advice and protocol assistance, the cut-off date will be the date of validation of the request for advice.

EMA Recommends Jinarc for Approval in Rare Kidney Disease
The EMA has recommended granting a marketing authorization to Jinarc (tolvaptan), which is indicated to slow the progression of cyst development and failing kidney function in adult patients with autosomal dominant polycystic kidney disease. The opinion adopted by the EMA's Committee for Medicinal Products for Human Use ("CHMP") will now be sent to the European Commission for the adoption of a decision on EU-wide marketing authorization.

Zykadia Recommended for Approval in Advanced Non Small Cell Lung Cancer
The EMA has recommended granting a conditional marketing authorization for Zykadia (ceritinib) for the treatment of adult patients with a type of lung cancer called anaplastic lymphoma kinase positive non-small cell lung cancer, when the disease is advanced and has already been treated with crizotinib. The CHMP opinion will now be sent to the European Commission for the adoption of a decision on EU-wide marketing authorization.

Ambroxol and Bromhexine Expectorants: Safety Information To Be Updated
Europe's Coordination Group for Mutual Recognition and Decentralised Procedures – Human has endorsed recommendations by the EMA Pharmacovigilence Risk Assessment Committee to update the product information for ambroxol- and bromhexine-containing medicines with information about the small risk of severe allergic reactions and severe cutaneous adverse reactions. The medicines are widely available in the EU for use as expectorants (to help clear mucus from the airways).

Upcoming Meetings, Workshops, and Conferences

Drugs and Biologics
Public Meeting on Conditional Approval of New Animal Drugs, **March 16, 2015**, in Rockville, MD.

CBER Regulatory Site Visit Training Program, **March 19, 2015**, in Silver Spring, MD.

Public Workshop on Measuring Dystrophin in Dystrophinopathy Patients and Interpreting the Data, **March 20, 2015**, in Silver Spring, MD.

FDA/AACR/ASCO Public Workshop on Complexities in Personalized Medicine: Harmonizing Companion Diagnostics Across a Class of Targeted Therapies, **March 24, 2015**, in Washington, D.C.

FDA Pediatric Stakeholder Meeting, **March 25, 2015**, in Silver Spring, MD.

FDA/Xavier University PharmaLink Conference on Leadership in a Global Supply Chain, **March 25–27, 2015**, in Cincinnati, OH.

Public Meeting on Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products, **March 27, 2015**, in Silver Spring, MD.

Public Workshop on Clinical Outcomes Assessment Development and Implementation: Opportunities and Challenges, **April 1, 2015**, in Silver Spring, MD.

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

Public Workshop on Advancing the Development of Pediatric Therapeutics, **April 16–17, 2015**, in Silver Spring, MD.

2015 Office of Regulatory Science and Innovation Science Symposium, **April 17, 2015**, in Silver Spring, MD.

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

Public Workshop: Gastroenterology Regulatory Endpoints and the Advancement of Therapeutics (GREAT III), **March 30–31, 2015**, in Silver Spring, MD.

Public Meeting on Functional GI Disorders Patient-Focused Drug Development, **May 11, 2015**, in Silver Spring, MD.

FDA/AFDO Conference titled *In Motion: Science Transforming Policy in Food, Drug, and Medical Device Regulation*, **June 20–24, 2015**, in Indianapolis, IN.

Medical Devices
FDA Public Workshop titled Robotically-Assisted Surgical Devices: Challenges and Opportunities, **July 27–28, 2015**, in Silver Spring, MD.

FDA/Xavier University Global Medical Device Conference (MedCon), **May 6–8, 2015**, in Cincinnati, OH.

Public Hearing on Generic Drug User Fee Amendments of 2012—Regulatory Science Initiatives, **June 5, 2015**, in Silver Spring, MD.

FDA/AFDO Conference titled *In Motion: Science Transforming Policy in Food, Drug, and Medical Device Regulation*, **June 20–24, 2015**, in Indianapolis, IN.

Advisory Committees
March 17, 2015: Arthritis Advisory Committee Meeting (to discuss biologics license

application for a proposed biosimilar for treatment of moderately to severely active Crohn's disease in patients who have had an inadequate response to conventional therapy)

March 18, 2015: Anesthetic and Analgesic Drug Products Advisory Committee Meeting (to discuss an NDA for treatment to reverse moderate or deep neuromuscular blockade induced by rocuronium or vecuronium)

March 19, 2015: Joint Meeting of the Pulmonary-Allergy Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee (to discuss a supplemental NDA for daily maintenance treatments for asthma)

March 23, 2015: Pediatric Ethics Subcommittee of the Pediatric Advisory Committee (to discuss how procedural sedation for nontherapeutic (research) interventions or procedures in the pediatric population should be considered under the Additional Safeguards for Children in Clinical Investigations)

March 24, 2015: Pediatric Advisory Committee (to discuss pediatric-focused safety reviews for certain products, as mandated by the Best Pharmaceuticals for Children Act and the Pediatric Research Equity Act)

April 14, 2015: Endocrinologic and Metabolic Drugs Advisory Committee (to discuss the results of the cardiovascular outcomes trial for certain new drug applications for anti-diabetic therapies)

April 15, 2015: Cardiovascular and Renal Drugs Advisory Committee (to discuss a new drug application for the proposed indication of reduction of thrombotic cardiovascular events including stent thrombosis in patients with coronary artery disease undergoing percutaneous coronary intervention)

April 17, 2015: Neurological Devices Panel of the Medical Devices Advisory Committee (to discuss the current knowledge regarding the conduct of clinical studies and evaluation of clinical study data for flow diverter technology)

April 29, 2015: Joint Meeting of the Cellular, Tissue and Gene Therapies Advisory Committee and the Oncologic Drug Advisory Committee (to discuss a biologics license application for an oncolytic immunotherapy for the treatment of patients with injectable regionally or distantly metastatic melanoma)

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 CPR devices that may increase chance of surviving cardiac arrest (March 6, 2015)

FDA approves new antifungal drug Cresemba (March 6, 2015)

FDA authorizes use of first device to treat patients with dialysis-related amyloidosis (March 6, 2015)

FDA approves first biosimilar product Zarxio (March 6, 2015) (*see* "Top News" above)

FDA expands approved use of Opdivo to treat lung cancer (March 4, 2015)

FDA approves new antibacterial drug Avycaz (February 25, 2015)

FDA approves Farydak for treatment of multiple myeloma (February 23, 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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