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

FDA Finalizes Three Guidance Documents on Biosimilars
FDA recently finalized three draft guidance documents addressing scientific and regulatory issues associated with the development and licensure of biosimilars:

• *Scientific Considerations in Demonstrating Biosimilarity to a Reference Product* advises sponsors to consider the complexities of protein products when designing programs to demonstrate biosimilarity, discusses a "stepwise" approach sponsors should use in developing the evidence needed to support biosimilarity, and advises sponsors that FDA will use a totality-of-the-evidence approach to assess a demonstration of biosimilarity.
• *Quality Considerations in Demonstrating Biosimilarity of a Therapeutic Protein Product* to a Reference Product focuses on scientific and technical information for the chemistry, manufacturing, and controls section of a biosimilar application. The guidance discusses limitations of current technology in characterizing structural and functional differences between the two protein products and identifies factors to consider in assessing whether products are highly similar, including manufacturing process, physicochemical properties, functional activities, receptor binding, impurities, reference standards, and stability.
• *Biosimilars: Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation Act of 2009* ("BPCIA") provides answers to common questions regarding FDA's

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RELATED PRACTICES

FDA Regulatory & Compliance Counseling

interpretation of the BPCIA, in three categories including permissible differences between biosimilars and reference products, meeting the amended definition of a "biological product" and how "product class" is defined, and orphan exclusivity for biosimilar products.

Health Care

Life Sciences

Second Draft of "21st Century Cures" Legislation Shows Significant Changes from Original Version
On April 28, 2015, the House Energy & Commerce Committee released its second discussion draft of the 21st Century Cures legislation, a bipartisan effort aimed at accelerating the pace of innovative medical therapies in the United States. The second draft retains key sections for modernizing clinical trials and authorizing FDA to perform priority review of certain "breakthrough" medical devices but omits other provisions from the original draft that would have granted increased exclusivity periods to various new drugs, such as 15 years for dormant therapies. Legislators also punted on the issue of telemedicine reimbursement reform, a significant feature of the original draft, by noting the topic is under review by a working group.

FDA Issues Draft Guidance on Use of Medical Device Clinical Data from Foreign Sources
Last month, FDA released a draft guidance document detailing the ways in which data from clinical studies outside the United States can be used in support of medical device premarket submissions. The draft guidance reiterates that medical device applications must be supported by valid scientific evidence, regardless of source, and advises clinical sponsors to consider differences in clinical settings, study populations, and regulatory requirements when developing investigations. FDA has long accepted foreign data for certain medical devices, and its regulations specifically address the use of such data in premarket approval ("PMA") applications.

Federal Circuit Grants Preliminary Injunction Against Marketing of First Licensed Biosimilar
As reported in the last Jones Day Update, in litigation involving the first U.S. biosimilar Zarxio, a federal court in California denied a request to enjoin the marketing of the product based on alleged violations of the patent litigation provisions of the BPCIA, and the biologic reference sponsor subsequently appealed this decision to the Federal Circuit. Since then, the Federal Circuit has granted another motion by the sponsor for preliminary injunction, effectively halting the commercial launch of Zarxio pending outcome of the appeal. Meanwhile, six parties have filed *amicus curia* briefs in the Federal Circuit that request reversal of at least part of the lower court decision.

EMA Publishes Annual Report
The European Medicines Agency ("EMA") has published its 2014 Annual Report. Highlights include the agency's recommendation of 103 new medicines for marketing authorization, adoption of the EMA's policy on publication of clinical data, and the launch of the pilot project on adaptive pathways to accelerate access to new medicines for patients.

Other News
Generic Pharmaceutical Association Asks FDA to Adopt Alternative to Proposed Rule on Generic Drug Labeling

Republican Senators Respond to Recent Biosimilars Guidance, Urge FDA to Provide More Certainty for Approval Process

EMA Advises Against Using Codeine as Cough, Cold Treatment for Children Under 12

FDA Proposed Rule Would Address Data Gaps for Certain Active Ingredients in Antiseptics

EMA Recommends Avoiding the Combined Use of Certain Hepatitis C Medicines and Amiodarone

MIT Reports Declining Investment in Basic Research as Threat to U.S. Innovation

Regulatory Updates

FDA Issues Proposed Rule on Antiseptic Drug Products
In the May 1, 2015, *Federal Register*, FDA issued a proposed rule to amend the 1994 tentative final monograph for over-the-counter ("OTC") antiseptic drug products. The proposed rule would establish conditions under which OTC antiseptic products intended for use by health care professionals are generally recognized as safe and effective, and it would institute additional measures, such as in vitro data characterizing the antimicrobial properties of active ingredients and in vivo clinical simulation studies showing that specified log reductions in the amount of certain bacteria are achieved using the ingredient. The notice includes proposed classifications for active ingredients used in OTC antiseptics. ***Comments are due October 28, 2015***.

CDRH Announces Progress Report on 2014–2015 Strategic Priority
In the April 29, 2015, *Federal Register*, FDA's Centers for Devices and Radiological Health ("CDRH") issued a progress update on its 2014–2015 Strategic Priority titled "Strike the Right Balance Between Premarket and Postmarket Data Collection." To achieve this Strategic Priority, CDRH has been conducting a retrospective review of active PMA applications approved prior to 2010, in order to determine the appropriate level of premarket review for certain Class III medical devices. As of the end of 2014, CDRH had reviewed 69 percent of the product codes slated for retrospective review. The agency's updated report provides recommendations for product codes that are candidates for reclassification, a reduction in premarket data collection through reliance on postmarket controls, or a shift in premarket data collection to postmarket collection. ***Comments are due June 29, 2015***.

FDA Issues Correction to Final Rule on Administrative Detention of Drugs
In the April 22, 2015, *Federal Register*, FDA announced corrections to the final rule entitled "Administrative Detention of Drugs Intended for Human or Animal Use," which sets forth the procedures for detention of drugs believed to be adulterated or misbranded. The corrections clarify the impact of the final rule on small entities.

FDA Determines that Oxytocin in Dextrose Injection Products Were Not Withdrawn for Safety or Effectiveness Reasons
In the April 22, 2015, *Federal Register*, FDA determined, in response to a citizen petition, that oxytocin in dextrose 5% injection products were not withdrawn from sale for reasons of safety or effectiveness. This determination allows FDA to approve an abbreviated new drug application ("ANDA") for these oxytocin drug products, if all other legal and regulatory requirements are met.

FDA Requests Nominations for Participation on the Allergenic Products Advisory Committee
In the April 21, 2015, *Federal Register*, FDA announced it is seeking nominations for nonvoting industry representatives to serve on the Allergenic Products Advisory Committee for the Center for Biologics Evaluation and Research. Industry organizations interested in participating in the selection of the nonvoting representatives should notify the FDA. ***Interest letters and nominations are due May 21, 2015***.

FDA Extends Comment Period for MMA Proposed Rule on Approval of ANDAs
In the April 24, 2015, *Federal Register*, FDA announced it has extended the comment period for the proposed rule to implement Title XI of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 ("MMA"). This provision of the MMA governs the approval of 505(b)(2) applications and ANDAs. ***Comments are now due June 8, 2015***.

FDA Publishes List of Approved PMAs
In the April 22, 2015, *Federal Register*, FDA published a list of 11 PMAs approved by the agency from October 1, 2014, through December 31, 2014. FDA is required to report on

PMA approvals and denials every quarter.

FDA Issued the Following Draft and Final Guidance Documents
Guidance for Industry: Scientific Considerations in Demonstrating Biosimilarity to a Reference Product, April 30, 2015, *Federal Register*.

Guidance for Industry: Quality Considerations in Demonstrating Biosimilarity of a Therapeutic Protein Product to a Reference Product, April 30, 2015, *Federal Register*.

Guidance for Industry: Biosimilars: Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation Act of 2009, April 30, 2015, *Federal Register*.

Guidance for Industry: Clinical Trial Endpoints for the Approval of Non-Small Cell Lung Cancer Drugs and Biologics, April 22, 2015, *Federal Register*.

Draft Guidance for Industry: Environmental Assessment: Questions and Answers Regarding Drugs with Estrogenic, Androgenic, or Thyroid Activity, April 29, 2015, *Federal Register*.

Draft Guidance: M8 Electronic Common Technical Document ("eCTD") v4.0 Draft Implementation Guide v2.0 and eCTD v4.0 Implementation Package Draft Specification for Submission Formats v2.0, April 27, 2014, *Federal Register*.

Draft Guidance for Industry: Providing Regulatory Submissions in Electronic and Non-Electronic Format—Promotional Labeling and Advertising Materials for Human Prescription Drugs, April 22, 2015, *Federal Register*.

Draft Guidance for Industry and FDA Staff: Acceptance of Medical Device Clinical Data from Studies Conducted Outside the United States, April 21, 2015, *Federal Register*.

FDA Announced the Opportunity to Comment on the Following Proposed Information Collections
• Registration and Product Listing for Owners and Operators of Domestic Tobacco Product Establishments and Listing of Ingredients in Tobacco Products
• Financial Disclosure by Clinical Investigators

EU Regulatory Notices

Eleven Medicines Recommended for Approval by EU's CHMP
During the meeting of the Committee for Medicinal Products for Human Use ("CHMP"), 11 new medicines were recommended for approval. The CHMP's recommendations included marketing authorizations for: **Opdivo**, for the treatment of adults with advanced (unresectable or metastatic) melanoma; **Hetlioz**, for treatment of non-24-hour sleep–wake disorder in totally blind adults; **Lixiana**, for the prevention of stroke and systemic embolism in atrial fibrillation and the prevention and treatment of venous thromboembolism; and **LuMark** for the radio-labeling of carrier molecules. The agency also granted a positive opinion for seven generic medicines and adopted a negative opinion for Lympreva, which was intended for the treatment of patients with follicular non-Hodgkin lymphoma.

EMA Invites Comments on Draft Good Practice Guides
EMA recently issued two draft Good Practice Guides, which are aimed at improving the reporting, evaluation, and prevention of medication errors by regulatory authorities and pharmaceutical industry throughout the EU. The agency invites stakeholders to submit comments by June 14, 2015.

Upcoming Meetings, Workshops, and Conferences

Drugs and Biologics

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

Public Conference on Food and Drug Administration Clinical Trial Requirements, Regulations, Compliance, and Good Clinical Practice, **May 13–14, 2015**, in Cincinnati, OH.

FDA Public Workshop titled *Preparation for ICH Steering Committee and Expert Working Group Meetings in Fukuoka, Japan*, **May 15, 2015**, in Silver Spring, MD.

Public Meeting on the Interim Assessment of the Program for Enhanced Review Transparency and Communication for New Molecular Entity New Drug Applications and Original Biologics License Applications, **May 20, 2015**, in Silver Spring, MD.

FDA Science Forum 2015, **May 27–28, 2015**, in Silver Spring, MD.

Public Meeting on the Generic User Fee Amendments of 2012, **June 15, 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.

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

Medical Devices

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

FDA/Biomedical Engineering Society Public Conference on Frontiers in Medical Devices: Innovations in Modeling and Simulations, **May 18–20, 2015**, in Hyattsville, MD.

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.

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

Advisory Committees

May 12, 2015: Pulmonary-Allergy Drugs Advisory Committee

May 12, 2105: Vaccines and Related Biological Products Advisory Committee

May 13, 2015: Blood Products Advisory Committee

May 14–15, 2015: Gastroenterology and Urology Devices Panel of the Medical Devices Advisory Committee

June 1, 2015: Transmissible Spongiform Encephalopathies Advisory Committee

June 8, 2015: Risk Communications Advisory Committee

June 9, 2015: Endocrinologic and Metabolic Drugs Advisory Committee

June 10, 2015: Endocrinologic and Metabolic Drugs Advisory Committee

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 Raplixa to help control bleeding during surgery (April 30, 2015)

FDA approves treatment for fat below the chin (April 29, 2015)

FDA approves first generic Abilify to treat mental illnesses (April 28, 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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