Top Stories

FDA Continues to Bolster Regulation of Compounding Pharmacies
Armed with new authority granted by the Drug Quality and Security Act ("DQSA"), FDA is increasingly using its regulatory powers to enhance oversight of compounding pharmacies. DSQA amended section 503A of the Food, Drug, and Cosmetic Act ("FDCA") to clarify the scope of approval, labeling, and manufacturing regulations for compounding pharmacies, and it added a new section 503B to exempt certain "outsourcing facilities" from some of these requirements. In an exercise of its expanded authority, FDA recently issued a proposed rule, two guidance documents, and two revised requests for nominations for the bulk drug substances lists.
- read more below

FDA Contemplates Further Revisions to "Off-Label" Drug Marketing Rules and Guidance
According to recent reports, FDA is reevaluating longstanding policies regarding the marketing of pharmaceutical products for "off-label" uses, such as when a manufacturer promotes an otherwise approved product for an indication, age group, or dosage that has not been approved. As described in a recent *Washington Post* article, FDA has begun the process of developing revised guidance, in light of a court decision two years ago reversing the conviction of a pharmaceutical sales representative for discussing certain unapproved uses of a drug with doctors.
- read more below

New 510(k) Draft Guidance Focuses on Assessing Differences Between Device Iterations
On July 14, 2014, FDA issued new draft guidance explaining its current thinking on approaching the premarket clearance process for moderate-risk medical devices. The Agency withdrew its prior guidance on the subject after the FDA Safety and Innovation Act of 2012 called for an overhaul of the 510(k) process. The new draft guidance devotes significant content to helping industry and FDA staff evaluate differences between new devices and predicate devices, particularly when new technological characterizations are involved. The 510(k) process allows companies, in their submissions, to rely heavily on a predicate device's safety

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Resources

- *Pharmaceutical & Medical Device Regulatory Update* Issue 10 Printable Version
- Jones Day's FDA Regulatory & Compliance Practice
- Jones Day's Health Care Practice

- Jones Day's Life Sciences Practice

record and prior clinical evidence by demonstrating substantial equivalence. The new draft guidance elaborates on the substantial equivalence requirement and outlines what data FDA will assess, including the types of benefits; the probability, substantiality, and duration of such benefits; and similar factors associated with the device's risks. The document also provides seven example submissions to help illustrate potential pitfalls of the 510(k) process. ***Interested parties may submit comments through November 18, 2014.***

Payers, Pension Plans, Pharmacies Ask FDA Not to Give Unique Names to Biosimilars
Earlier this month, a group of 32 companies and organizations, including health insurers, pharmacies, labor unions, and pension plans, urged FDA not to require distinct names for biosimilar products, explaining that such a policy would undermine the potential cost savings generated by such generic products—which are predicted to be as much as $100 billion over the first 10 years of biosimilar market formation.

In its letter to Commissioner Margaret Hamburg, the group argues that biologics and biosimilars should be required to have the same International Nonproprietary Name ("INN") in order to reduce provider and patient confusion and to promote swift uptake of biosimilar products when they come to market. Although no such products are currently sold in the United States, the group claims if biosimilars are marketed under unique names, then individuals might fail to recognize them as substitutes for brand-name biologics, which could stifle their use and hence undermine cost savings. The group also argues that using unique INNs would also disconnect biosimilars from existing safety information about their underlying molecules.

The Biologics Price Competition and Innovation Act of 2009 established a regulatory pathway for approving biosimilars, but FDA has yet to specify a naming policy for this category of products.

FDA Offers Additional Insights on Social Media and Internet Policies for Drugs and Devices
In a follow up to two social media and internet guidance documents issued last month, FDA hosted a webinar last week to present additional information and answer questions. The two new draft guidance documents outline FDA's thinking on the presentation of risk and benefit information on social media and correction of third-party misinformation on the internet. Jones Day recently reported on these guidance documents in a Jones Day *Alert*. Although the live webinar experienced technical difficulties, a significant portion of the training focused on the importance of conveying risk information, particularly on technology platforms that have character space limitations such as Twitter. Heavy emphasis was placed on the requirement that when presenting drug benefit information, manufacturers generally should disclose all boxed warnings, including fatal and life-threatening conditions, and all contraindications. Linking to the information is insufficient. For more details, the Agency has posted its presentation slides and Q&A from the July webinar online.

Around the same time the new draft guidance documents were released, FDA issued warning letters providing further insight on the Agency's social media and internet policies. In one letter, FDA warned a dietary supplement manufacturer that "liking" a post on Facebook equates to an endorsement of any express or implied claims made in the post. In this context, FDA found that the manufacturer was promoting supplements for unapproved drug uses by "liking" comments that made express or implied therapeutic claims. Though the letter was issued to a dietary supplement company, drug and medical device companies can expect FDA to apply this policy across all categories of FDA-regulated products. In another letter, FDA warned a drug company that its sponsored Google link provided evidence the drug is intended for a new use for which it lacks approval. Specifically, the sponsored link appeared when a user searched for a therapeutic use for which the drug was not approved.

Other News
EU Fines Six Drug Firms $582 Million in Pay-for-Delay Cases

FDA Commissioner: Agency Completes FDASIA Initiatives for First Two Years

India Prime Minister Pledges to Provide Free Vaccines to Curb Child Mortality

FDA Panel Recommends Restrictions for or Outright Ban on Uterine Morcellation

Different Regions of U.S. Sprout New Biotech Hubs

President Nominates Former P&G Executive to be VA Secretary

Scientists Urge More Alzheimer's Research as 99% of Therapy Trials Failed in Last Decade

CDC, NIH Report Shortfalls in Safeguarding of Laboratory Pathogens

Regulatory Updates

FDA Issues Proposed Rule to Expand List of Drugs that May Not Be Compounded Under Exemptions to FDCA
In the July 2, 2014, *Federal Register*, FDA issued a proposed rule to amend its regulations by expanding the number of drug products that may not be compounded under exemptions to the FDCA. FDA noted these revisions are necessary because, since FDA published the original list as a final rule in 1999, some products have been withdrawn or removed from the market because they were found to be unsafe or not effective. The proposed rule would add 25 drug products to the list and modify the description of one drug product already on the list. In the same notice, FDA withdrew a related January 4, 2000, proposed rule. ***Comments are due September 2, 2014***.

FDA Reopens Nominations for Two Lists of Bulk Drug Substances Used to Compound Drug Products
In the July 2, 2014, *Federal Register*, FDA issued two notices with revised requests for nominations of bulk drug substances (active pharmaceutical ingredients or APIs) that may be used to compound drug products pursuant to FDCA sections 503A and 503B (see "Top News" section for more information on these provisions). In December 2013, FDA had issued similar calls for nominations for bulk drug substances that may be used for compounding under 503A and 503B, but many of the responses were insufficient or inadequate. FDA has provided more details in the current call for nominations to assist stakeholders with making appropriate nominations. ***Nominations for both lists are due September 30, 2014***.

FDA Reopens Docket to Collect Information on Innovative Means to Address the Misuse and Abuse of Opioid Analgesics
In the July 8, 2014, *Federal Register*, FDA reopened the docket to receive suggestions, recommendations, and comments on innovative packaging, storage, and disposal systems, technologies, or designs that could be used to prevent or deter misuse and abuse of opioid analgesics by patients and others, originally noticed in the April 9, 2014, *Federal Register*. The initial comment period had just closed on June 9, 2014. ***Comments are due August 7, 2014***.

FDA Reopens Comment Period for Feedback on Improving the OTC Monograph Process
In the July 1, 2014, *Federal Register*, FDA reopened the comment period for the notice of public hearing, originally published in the February 24, 2014, *Federal Register*, requesting comments on how to improve or alter the current Over-the-Counter ("OTC") Monograph Process for reviewing nonprescription drugs marketed under OTC Drug Review. ***Comments are now due July 31, 2014***.

FDA Releases Modifications to FDA-Recognized Consensus Standards
In the July 9, 2014, *Federal Register*, FDA announced modifications to the list of recognized standards the Agency uses in premarket reviews (FDA Recognized Consensus Standards). The publication, *Modifications to the List of Recognized Standards, Recognition List Number: 036*, will assist manufacturers that declare conformity with consensus standards to meet certain requirements for medical devices.

FDA Seeks Public Comments on FY 2014–2018 Strategic Priorities
In the July 1, 2014, *Federal Register*, FDA requested comments on its draft Strategic Priorities Fiscal Year (FY) 2014–2018 document, which outlines the strategic priorities and core mission goals that will guide the Agency's efforts over the coming years. ***Comments are due July 31, 2014***.

FDA Confirms Effective Date for Final Rule on Confidentiality of NADA File Data
In the July 1, 2014, *Federal Register*, FDA confirmed the July 30, 2014, effective date of the final rule appearing in the March 17, 2014, *Federal Register*, which amended the regulation regarding the confidentiality of data and information in and about new animal drug application ("NADA") files. The

final rule changes the timing of when certain approval-related information will be disclosed by the Agency.

FDA Calls for Nonvoting Industry Representatives to Serve on CBER's Cellular, Tissue, and Gene Therapies Advisory Committee
In the July 9, 2014, *Federal Register*, FDA requested that any industry organizations interested in participating in the selection of a nonvoting industry representative to serve on the Center for Biologics Evaluation and Research's ("CBER") Cellular, Tissue, and Gene Therapies Advisory Committee notify FDA in writing. The chosen representative would represent industry interests on the committee. FDA also requested nominations for nonvoting industry representatives to serve on the committee. Nominees may be either self-nominated or nominated by an organization. ***Industry representatives must notify FDA of interest in participating in selection of nonvoting committee members by August 8, 2014; nomination materials are also due August 8, 2014***.

FDA Announces Grant Funds Available for Strengthening Medical Product Regulatory Systems in the Americas
In the July 8, 2014, *Federal Register*, FDA's Office of International Programs ("OIP") announced the availability of grant funds for the support of a single source cooperative agreement to the Pan America Health Organization ("PAHO") for fostering cooperation and strengthening medical product regulatory systems in the Americas. The goal of the cooperative agreement is to build upon existing cooperation between OIP/FDA and PAHO to foster regulatory collaboration and strengthen regulatory capacity throughout the Americas. ***Applications are due August 1, 2014***.

FDA Announces Meetings and Opportunities for Comments on Patient-Focused Drug Development for Idiopathic Pulmonary Fibrosis and Heritable Bleeding Disorders
In the July 8, 2014, *Federal Register*, FDA announced a public meeting and opportunity for public comment on Patient-Focused Drug Development for idiopathic pulmonary fibrosis. In the July 9, 2014, *Federal Register*, FDA announced a public meeting and opportunity for public comment on Patient-Focused Drug Development for Hemophilia A, Hemophilia B, von Willebrand Disease, and other heritable bleeding disorders. Patient-Focused Drug Development is one of the Agency's performance commitments as provided by the fifth authorization of the Prescription Drug User Fee Act. The meetings are intended to allow FDA to collect patient perspectives on the impact of and treatment approaches for these disorders. ***The public meeting on Idiopathic Pulmonary Fibrosis will be held on September 26, 2014; comments are due November 26, 2014. The public meeting on heritable bleeding disorders will be held on September 22, 2014; comments are due November 28, 2014***.

FDA Classifies Two Devices to Treat Headache into Class II
In the July 3, 2014, *Federal Register*, FDA issued a final order classifying the transcutaneous electrical nerve stimulator to treat headache into Class II with special controls, effective August 4, 2014. In the July 8, 2014, *Federal Register*, FDA issued a final order classifying the transcranial magnetic stimulator for headache into Class II with special controls, effective August 7, 2014. The special controls applicable to the device will be part of the codified language for the transcranial magnetic stimulator for headache classification.

FDA Classifies Nonpowered Lower Extremity Pressure Wrap Into Class I
In the July 3, 2014, *Federal Register*, FDA issued a final order classifying the nonpowered lower extremity pressure wrap into Class I. ***The order is effective August 4, 2014***.

FDA Issues the Following Guidance Documents
Draft Guidance for Industry On Benefit-Risk Factors to Consider When Determining Substantial Equivalence in Premarket Notifications [510(k)] with Different Technological Characteristics. July 15, 2014, Federal Register. ***Comments due November 18, 2014***.

Draft Guidance for Industry on ANDA Submissions—Prior Approval Supplements Under GDUFA. July 11, 2014, *Federal Register*. ***Comments due September 9, 2014***.

Draft Guidance for Industry on ANDA Submissions—Amendments and Easily Correctable Deficiencies Under GDUFA. July 11, 2014, *Federal Register*. ***Comments due September 9, 2014***.

Draft Guidance for Industry on Current Good Manufacturing Practice-Interim Guidance for Human Drug Compounding Outsourcing Facilities Under the Federal Food, Drug, and Cosmetic Act. July 2, 2014, *Federal Register*. ***Comments due September 2, 2014***.

Final Guidance for Industry on Pharmacy Compounding of Human Drug Products Under Section 503A of the Federal Food, Drug, and Cosmetic Act. July 2, 2014, *Federal Register*.

Guidance for Industry on Neglected Tropical Diseases of the Developing World: Developing Drugs for Treatment or Prevention. July 7, 2014, *Federal Register*.

Draft Guidance for Industry on Design and Analysis of Shedding Studies for Virus or Bacteria-Based Gene Therapy and Oncolytic Products. July 9, 2014, *Federal Register*. ***Comments due November 19, 2014***.

Draft Guidance for Industry on Reporting Drug Sample Information Under Section 6004 of the Affordable Care Act. July 11, 2014, *Federal Register*. ***Comments due October 9, 2014***.

FDA Determines Regulatory Review Periods for Drug, Biological Patents
FDA recently published a determination regarding the regulatory review period for patent extension for HORIZANT. FDA did not publish any determinations regarding the regulatory review periods for patent extensions of biologics.

INFORMATION COLLECTION ACTIVITIES

FDA Announces that the Following Collections Have Been Submitted to OMB
Antiparasitic Drug Use and Antiparasitic Resistance Survey (***comments due to OMB August 4, 2014***)

FDA Announces the Opportunity to Comment on the Following Proposed Information Collections
Notification and Recordkeeping Requirements (***comments due September 2, 2014***)

Guidance for Industry: Cooperative Manufacturing Arrangements for Licensed Biologics (***comments due September 5, 2014***)

Certification to Accompany Drug, Biological Product, and Device Applications or Submissions (***comments due September 8, 2014***)

Upcoming Meetings, Workshops, and Conferences

Drugs and Biologics
Public Workshop on the Development of New Antibacterial Products: Charting a Course for the Future will be held **July 30, 2014**, in Bethesda, MD.

Public Hearing Before the Commissioner on Confidentiality of Interim Results in Cardiovascular Outcomes Safety Trials; Part 15 will be held **August 11, 2014**, in Silver Spring, MD.

Public Meeting on 2014 Scientific Meeting of the National Antimicrobial Resistance Monitoring System will be held on **August 12–13, 2014**, in Silver Spring, MD.

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, 2014**, in Silver Spring, MD.

Public Meeting on Patient-Focused Drug Development for Hemophilia A, Hemophilia B, von Willebrand Disease, and other heritable bleeding disorders will be held on **September 22, 2014**, in Silver Spring, MD.

Public Meeting on Patient-Focused Drug Development for idiopathic pulmonary fibrosis will be held on **September 26, 2014**, in Silver Spring, MD.

Medical Devices
Public Workshop on Hemostatic Medical Devices for Trauma Use will be held **September 3–4, 2014**, in Silver Spring, MD.

International Medical Device Regulators Forum will be held **September 15–19, 2014**, in Washington, DC.

Public Workshop on Additive Manufacturing of Medical Devices: An Interactive Discussion on the Technical Considerations of 3D Printing will be held **October 8–9, 2014**, in Silver Spring, MD.

Advisory Committees
July 30–31, 2014: Gastroenterology and Urology Devices Panel of the Medical Devices Advisory Committee

July 31, 2014: Blood Products Advisory Committee Meeting

August 1, 2014: General and Plastic Surgery Devices Panel of the Medical Devices Advisory Committee Meeting

August 14, 2014: Pulmonary-Allergy Drugs Advisory Committee Meeting

September 23, 2014: Pediatric Advisory Committee Meeting

October 16, 2014: Joint Meeting of the Psychopharmacologic Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee Meeting

October 20, 2014: Dermatologic and Ophthalmic Drugs Advisory Committee

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

Workshops, Meetings, and Conferences (Biologics)

Workshops & Conferences (Medical Devices)

FDA Advisory Committee Calendar

Enforcement Updates

Recent Product Recalls
Recent medical product recalls include a medical device due to inconsistent performance and because the firm had not obtained premarket clearance. An injection drug product was also recalled due to the presence of particulates.

Click here for a complete listing of FDA Recalls.

Recent Warning Letters
FDA continues aggressively citing medical device manufacturers for violating Quality System Regulation requirements. FDA recently posted warning letters to five medical device firms for such infractions. Some of the letters included other violations, such as failure to comply with listing requirements or medical device reporting requirements. Two firms were also cited for not obtaining premarket approval, 510(k) clearance, or an investigational device exemption for its device prior to marketing.

FDA warned a compounding pharmacy for multiple violations and noted that the pharmacy continued to violate the law in spite of previous warnings from FDA. FDA also sought a permanent injunction against a company for illegally distributing over-the-counter vaginal drug products without required FDA approvals.

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 letter to a drug company after reviewing the company's sponsored Google link. OPDP determined the company's sponsored link provided evidence that the drug is intended for a new use for which it lacks approval, and for which its labeling does not provide adequate directions for use, rendering the drug misbranded within the meaning of the FDCA.

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

Recent Drug and Device Approvals
FDA approves Beleodaq to treat rare, aggressive form of non-Hodgkin lymphoma (July 3, 2014).

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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Top Stories

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Historically, compounding pharmacies have been small shops that custom-mixed specific drugs for specific patients; these pharmacies were subject primarily to state pharmacy regulation. More recently, some facilities claiming to be compounding pharmacies have been conducting operations resembling those of drug manufacturers, which are heavily regulated by FDA. The lack of oversight over these compounding pharmacies is considered a key factor in the circumstances that culminated in a 2012 meningitis outbreak that resulted in the death of 64 people and sickened nearly 700 more. The outbreak was traced to products made at a compounding pharmacy.

Earlier this month FDA issued a proposed rule that would add 25 products to the list of drugs that may not be legally compounded under statutory exemptions to the FDCA because these products have been found unsafe or not effective since FDA last published a final rule regarding the list in 1999.

FDA also issued two guidance documents explaining provisions of DQSA, which modified FDCA sections 503A and 503B. The guidance documents describe how the Agency intends to regulate individuals and pharmacies that compound drugs (regulated under section 503A), and sterile drug compounders, also known as outsourcing facilities (regulated under section 503B). Section 503A exempts state-licensed pharmacies, which primarily distribute within their state and compound drugs in response to specific

individual prescriptions, from certain FDA requirements such as new drug approval, current good manufacturing practice ("cGMP"), and some labeling requirements. Section 503B exempts outsourcing facilities from new drug approval requirements and some labeling and distribution requirements but requires these facilities to register with FDA, subjects them to cGMP requirements, and restricts their compounding activities to drugs on FDA's "clinical need list." FDA issued a final guidance for individuals and pharmacies intending to compound drugs reiterating the requirements of section 503A, describing interim policies for provisions that require further FDA action, and providing a nonexhaustive list of potential enforcement actions against those who do not comply with FDCA requirements. A separate draft guidance for outsourcing facilities that will register with FDA under FDCA section 503B describes cGMP requirements related to sterility assurance programs and general safety measures for compounded products.

In addition, FDA is reopening the nomination process for two lists of bulk drug substances (active pharmaceutical ingredients, or APIs) that may be used to compound drug products under FDCA sections 503A and 503B. According to FDA, the original December 2013 request did not receive adequate responses. Interested parties may submit nominations through September 30, 2014.

Finally, in addition to developing the new regulatory tools, FDA continues to demonstrate that oversight of certain compounding activities is a priority for the Agency through its compliance and enforcement programs. FDA has been increasing its monitoring of compounding pharmacies through inspections, and the Agency regularly issues warning letters to facilities it determines are not in compliance with FDA regulations and the FDCA as amended by DQSA.

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Off-label use of certain drugs is relatively common among the medical community, but the lengthy and expensive clinical trial process often deters drug manufacturers from seeking formal approval for these alternative uses. FDA generally prohibits companies from promoting their products to approved indications as reflected in the current prescribing information.

Although current rules allow drug makers to share unabridged peer-reviewed journal articles with physicians (as long as they are distributed separately from promotional materials), FDA officials recently explained in a notice and response to a citizen petition that the Agency is working to harmonize its public health regulatory mission with the interests in the dissemination of truthful and nonmisleading information. FDA plans to revise guidance documents to better address how pharmaceutical firms should respond when they receive unsolicited information requests from physicians about off-label uses.