Pharmaceutical & Medical Device Regulatory Update
Issue 18 | November 2014 JONES DAY

Jones Day Event

On November 20 and December 4, **Dr. Christian Fulda** will present a webinar on EMA Disclosure of Marketing Authorization Data.

Top News

Amgen Sues Sandoz Over "Patent Dance" for First Biosimilar Application
Last week, Amgen filed a complaint in federal court against Sandoz, the first domestic biosimilar applicant that seeks to issue a biosimilar version of an Amgen product. A few days later, Amgen filed a Citizen Petition with FDA. Both actions by Amgen arise out of an application filed by Sandoz under the Biologics Price Competition and Innovation Act ("BPCIA") to obtain approval to market a biosimilar version of Amgen's NEUPOGEN® (filgrastim). Amgen maintains that Sandoz has not complied with the patent litigation provisions of the BPCIA mandating the biosimilar applicant to provide the biologics license application holder with a complete copy of its biosimilar application within 20 days after acceptance for filing by FDA. Rather, according to Amgen, Sandoz allegedly informed Amgen that this process is "optional" and offered to "voluntarily" provide the biosimilar application with certain limitations. These filings are the latest developments in a series of ongoing disputes involving biosimilar applications and the patent litigation provisions of the BPCIA, the latter of which have become known as the "patent dance."

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UPCOMING EVENTS

Nov. 12: **Colleen Heisey** will moderate an ABA Health Law Section webinar on off-label marketing and free speech, focusing on the impact of *Caronia*.

Nov. 13: **Alexis Gilroy** will speak in New York City on telehealth issues at a dermatology course at Memorial Sloan Kettering Cancer Center.

Incoming GOP Senate Will Likely Press FDA to Ease Up on Regulation

As a result of this week's midterm elections, the incoming Republican majority will likely try to challenge FDA on several fronts, seeking to ease regulatory burdens for drug and device manufacturers. Some Republicans, for instance, have criticized FDA's new plan to start regulating laboratory developed tests. Other critics have argued that too much regulation can overly burden industry in getting new drugs and devices to market in the midst of health crises. The trade press has made a variety of predictions as to how the incoming GOP Senate could affect FDA-regulated industries. Politico predicts the GOP sweep could provide a fresh start for health IT, and it also notes the GOP may prefer a voluntary risk framework rooted in an industry-led approach for implementing the Food and Drug Administration Safety and Innovation Act of 2012 ("FDASIA"). Vox, for its part, compiled a summary of how the marijuana initiatives (including those for medical use) fared in the midterm elections. In Arizona, voters passed right-to-try legislation, permitting dying patients to use medications that have successfully completed Phase I clinical testing but have not received final FDA approval. It remains to be seen how Republicans will prioritize easing the regulatory burden on industry, but the change in Senate dynamics is likely to have an impact on drug and device makers.

Nov. 13–14: **Dr. Christian Fulda** will speak in Brussels, Belgium on European and U.S. transparency standards at the FDLI Conference.

November 20: **Laurie Clarke** will speak at an ABA Health Section webinar on medical device fundamentals.

RELATED PRACTICES

FDA Regulatory & Compliance Counseling

Health Care

Life Sciences

WEBINAR
EMA Disclosure of Marketing Authorization Data

November 20, 2014
December 4, 2014

Details

FDA Issues Guidance for Industry on Delaying, Refusing Drug Inspections

Last week, FDA issued a guidance for industry on the circumstances that constitute delaying, denying, limiting, or refusing a drug inspection, as required by the FDASIA. In July 2013, FDA issued a draft guidance on the issue. In response to public comments on the draft guidance, FDA revised the final version to clarify the expectations regarding the types of actions, inaction, and circumstances under which FDA would consider a drug adulterated. Examples of delaying, denying, or limiting an inspection that may cause drugs to be adulterated include failing to produce requested records within the timeframe specified by FDA without reasonable explanation, preventing the FDA inspector from beginning the inspection, and restricting entry to a portion of the facility without reasonable explanation. The guidance also adds a nonexhaustive list of examples of what may constitute "reasonable explanations" for such actions, inactions, or circumstances that could otherwise be considered delaying, denying, or limiting inspection, or refusing to permit entry or inspection. For example, the guidance provides that a "potentially reasonable explanation" may include when a facility refuses to allow FDA investigators access to aseptic processing areas until the investigator accommodates the facility's documented gowning procedures.

FDA Hosts Webinar to Clarify Draft Guidance on LDTs

On October 23, 2014, FDA held a webinar to clarify the two draft guidance documents that were released on October 3, 2014, regarding the proposed regulation of laboratory developed tests ("LDTs"). FDA made several clarifying statements during the webinar, both during the presentation and in the subsequent lengthy question and answer session. The recorded webinar, transcript, and slides are posted on FDA's website. Katherine Serrano from the Office of In Vitro Diagnostic Device Evaluation and Safety, Center for Devices and Radiological Health, walked participants through the timeline set out in the draft guidance documents, explaining when certain requirements would be in effect. The

slide presentation included several helpful charts that simplified the requirements of the draft guidance.

After the slide presentation, FDA answered participants' questions. When asked whether the public should expect to see revised drafts of the guidance documents, FDA said it will depend on whether the public comment process prompts "significant" revisions. In response to questions about medical device user fees, Serrano said, "under the current agreement that we have with industry we would actually not be enforcing user fee requirements on laboratory developed tests" and "whether or not laboratory developed tests would be subject to user fees is a topic for discussion in future negotiations." But the draft guidance provides, "Submission of the registration and listing information must be accompanied by payment of the registration fee" in the context of LDT manufacturers who decide not to submit LDT notifications. So, whether laboratories must pay the medical device user fees is not yet clear.

During the slide presentation, FDA specifically requested public comment on the following issues: (i) whether the risk mitigations for Traditional LDTs was sufficient; (ii) whether the factors for determining Rare Disease LDT status are appropriate; and (iii) whether the risk mitigations for Unmet Needs LDTs are sufficient. FDA intends to hold a public meeting in early January 2015 to collect additional input. ***The public comment period for both draft guidance documents closes on February 2, 2015***.

Other News
Rand Corp Estimates Biosimilars Could Save $44 Billion Over 10 Years

FDA Unveils New Website on Postmarket Drug Sampling and Testing

FDA Approved Twice as Many De Novo Petitions in 2013 Due to Newly Established Pathway for Low-Risk Devices, Report Finds

FDA Encourages Development of Devices for Patients with Disabilities

Australia's Consumer Protection Agency Proposes Stronger Pharmaceuticals Marketing Code

NIH Launches New Website for Global Clinical Trials

Patient Advocacy Groups Band Together to Ensure Patients' Voices Heard in FDA Biosimilars Debate

FDA Regulations Increased 15 Percent from 2000 to 2012, Data Shows

Congressmen, Doctors, Pharmacists, and Patients Demand Explanation for Increase in Prices of Generic Drugs

Regulatory Updates

FDA Seeks Comments on Best Communication Practices Between IND Sponsors and FDA
In the October 29, 2014, *Federal Register*, FDA announced the establishment of a docket to receive suggestions, recommendations, and comments from interested parties, including academic institutions, regulated industry, and other interested organizations on best practices for communication between FDA and investigational new drug application ("IND") sponsors during drug development. FDA says it intends to issue draft guidance in the future on this topic. ***Comments due December 29, 2014***.

FDA Classifies Nucleic Acid-Based Devices for Detection of Antibiotic Resistant TB
In the October 22, 2014, *Federal Register*, FDA issued its classification of nucleic acid-based in vitro diagnostic devices for the detection of *Mycobacterium tuberculosis* complex

("MTB-complex") and the genetic mutations associated with MTB-complex antibiotic resistance in respiratory specimens devices into class II (special controls).

FDA Determines Certain Products Not Withdrawn for Safety or Effectiveness Reasons

- TOPICORT (desoximetasone) Cream
- DIAMOX (acetazolamide) intravenous, 500 milligrams (mg) base/vial, and DIAMOX (acetazolamide) tablets, 125 mg and 250 mg

FDA Amends Animal Drug Rules to Reflect August Approvals and Changes in Sponsorship

In the October 28, 2014, *Federal Register*, FDA issued a technical amendment to the animal drug regulations reflecting approval actions for new animal drug applications ("NADAs") and abbreviated new animal drug applications ("ANADAs") during August 2014. The animal drug regulations are also being amended to reflect a revised food safety warning and a change of sponsorship of two NADAs and one ANADA.

FDA Issued the Following Draft and Final Guidance Documents

Guidance for Industry Circumstances that Constitute Delaying, Denying, Limiting, or Refusing a Drug Inspection. October 22, 2014, *Federal Register*.

Draft Guidance for Industry Migraine: Developing Drugs for Acute Treatment. October 21, 2014, *Federal Register*. ***Comments due December 22, 2014***.

Draft Guidance for Industry Same Surgical Procedure Exception Questions and Answers Regarding the Scope of the Exception. October 23, 2014, *Federal Register*. ***Comments due December 22, 2014***.

Draft Guidance on Qualification of Biomarker Galactomannan in Studies of Treatments of Invasive Aspergillosis. October 27, 2014, *Federal Register*. ***Comments due December 26, 2014***.

Information Collection Activities

FDA Announced the Following Collections Have Been Submitted to OMB for Approval

Application for Participation in the Food and Drug Administration Commissioner's Fellowship Program

Correction: Notification and Recordkeeping Requirements for Exports

Adverse Experience Reporting for Licensed Biological Products; and General Records

State Petitions for Exemption From Preemption

Upcoming Meetings, Workshops, and Conferences

Drugs and Biologics

FDA Outreach Meeting for the Pediatric Cancer Advocacy Community will be held **November 18, 2014**, in Silver Spring, MD.

The Seventh Annual Sentinel Initiative Public Workshop will convene on **February 5, 2015**, in Washington, D.C. to discuss a variety of topics on active medical product surveillance.

Medical Devices

Public Workshop on Regulatory Science Considerations for Software Used in Diabetes Management will be held **November 13, 2014**, in Silver Spring, MD.

Public Workshop on Brain-Computer Interface Devices for Patients with Paralysis and Amputation will be held **November 21, 2014**, in Silver Spring, MD.

Advisory Committees
November 14, 2014: Ophthalmic Devices Panel of the Medical Devices Advisory Committee (to discuss premarket approval of an interocular lens implant)

November 18, 2014: Drug Safety and Risk Management Advisory Committee (to discuss risk evaluation and mitigation strategies and elements to assure safe use of eculizumab (SOLIRIS))

November 19, 2014: Science Board to the FDA (to discuss data related to anesthetics and sedation drugs in children)

November 24–25, 2014: Anesthetic and Analgesic Drug Products Advisory Committee (to discuss the risk–benefit balance of epidural steroid injections for inflammation and pain management)

December 2–3, 2014: Blood Products Advisory Committee (to hear scientific data related to reconsideration of the current blood donor deferral policy for men who have had sex with another man since 1977, to hear information about the emergence of the chikungunya virus in the Western Hemisphere, and to hear information about rapid surveillance for Middle Eastern Respiratory Syndrome coronavirus)

December 4, 2014: Anti-Infective Drugs Advisory Committee Meeting Announcement (to discuss issues related to clinical development programs and clinical trial designs for antibacterial products for the treatment of patients with serious bacterial infections for which there are limited or no therapeutic options)

December 12, 2014: Orthopaedic and Rehabilitation Devices Panel of the Medical Devices Advisory Committee (to discuss premarket approval of a spine-spacing device)

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

Enforcement Updates

Recent Product Recalls
In recent weeks, drug manufacturers recalled certain lots of two injectable drug products, one due to the presence of particulate matter in one vial, and another because the product may have experienced temperatures outside the allowable range during shipment. A compounder of human and veterinary products also recalled certain unexpired sterile injectable and powdered products due to lack of sterility assurance.

A drug manufacturer recalled certain lots of several different intravenous solution products due to the potential for leakage that could lead to contamination, and an intravenous port manufacturer recalled two lots of plastic containers due to complaints it received about particulate matter in the sterile fluid path.

Finally, a drug repackaging company recalled a naproxen sodium product because some packages actually contained ibuprofen, and a baby wipe manufacturer issued a nationwide recall of its products due to potential bacterial contamination.

View a complete listing of FDA Recalls.

Recent Warning Letters
In the first warning letter that exercises new authority granted under FDASIA as the basis

of a violation, FDA cited a foreign pharmaceutical manufacturing facility for adulterated drug products because the manufacturer "refused inspection" by denying entry to FDA inspectors. (FDA also recently released guidance on this topic.) FDA subsequently placed the firm on import alert, also based on the new authority.

FDA continues to cite medical device manufacturers for violations of the Quality Systems Regulations ("QSR"), including inadequate handling of complaints, insufficient process controls, and lack of written testing plans to ensure product conformance. Recipients of recently posted warning letters for QSR violations included manufacturers of gas pressure regulators, balloon catheters, vascular implants, intravascular catheters, audiometers, a shock treatment life vest, and a pacifier-activated lullaby device. The manufacturer of the pacifier-activated lullaby device was also cited for unapproved modifications to a cleared medical device.

Drug manufacturers continue to receive warning letters for Current Good Manufacturing Practices ("CGMP") violations, as well as misbranded or unapproved drugs. CGMP violations include insanitary conditions and inadequate quality controls.

FDA continues to keep close watch on compounding pharmacies and recently posted yet another warning letter citing one such pharmacy for failing to obtain valid prescriptions for its compounded products, a practice that renders the pharmacy ineligible for statutory exemptions to laws that would otherwise apply to drug manufacturers. The compounding pharmacy was additionally cited for violations relating to insanitary conditions, CGMP, and selling unapproved drug products.

Finally, FDA also recently posted a warning letter to a veterinary company that sells animal drugs online, citing it for marketing numerous unapproved new animal drugs.

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

Since the last *Update*, the Office of Prescription Drug Promotion ("OPDP") issued an untitled letter to a drug manufacturer deeming the drug product misbranded because the manufacturer's promotional material omitted important risk information associated with the drug, contained unsubstantiated superiority claims, and omitted material facts.

View a complete listing of 2014 OPDP Warning Letters and Notices of Violations.

Recent Drug and Device Approvals/Clearances

First vaccine approved by FDA to prevent serogroup B Meningococcal disease (October 29, 2014)

FDA approves new treatment for rare form of hemophilia (October 24, 2014)

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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