Pharmaceutical & Medical Device Regulatory Update
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Top News

Pharmacists Involved in Fungal Meningitis Outbreak Charged with Second Degree Murder
This week, the U.S. Department of Justice ("DOJ") indicted 14 owners and senior officials of a Massachusetts pharmacy that manufactured and distributed contaminated drugs that killed 64 people in a 2012 fungal meningitis outbreak. The owner/head pharmacist and the supervisory pharmacist of the New England Compounding Center ("NECC") were charged with second degree murder, and 12 others were charged with racketeering, mail fraud, conspiracy, and other crimes. NECC's products were distributed nationwide, making more than 700 people ill and leading to 64 deaths from a rare and hard-to-treat spinal cord fungal infection. DOJ alleges that NECC's steroid injections for pain, which had been marketed as individually formulated products, contained mold and bacteria.

DOJ further alleges that both pharmacists knew the products were not sterile but conspired to cover it up by, for example, providing guidance on creating fake prescriptions. Investigations after the outbreak revealed NECC's staff failed to observe hygiene rules and took shortcuts in sterilization, among other violations.

The 2012 outbreak triggered congressional investigations and statutory changes on how FDA oversees compounding pharmacies. NECC filed for bankruptcy in 2012.

CONTACTS

Mark Mansour
Washington

Laurie A. Clarke
Washington

Cristiana Spontoni
Brussels

Colleen M. Heisey
Washington

Christopher M. Mikson
Washington

Emily K. Strunk
Washington

Katherine M. Llewellyn
Brussels

Stephanie L. Resnik
Washington

Brigid C. DeCoursey
Washington

Matthew R. Bowles
Washington

Brett Swearingen of the Washington Office assisted in the preparation of this Update.

Detailed Contact Information

RELATED PRACTICES

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FDA Issues Human Drug Compounding Guidance: Registration, E-Reporting, Fees
The FDA recently issued three guidance documents for human drug compounding outsourcing facilities registered with the FDA under section 503B of the Federal Food, Drug, and Cosmetic Act. The first document describes the process of electronic registration for outsourcing facilities. Facilities choosing to register should submit registration information using the existing structured product labeling ("SPL") format, and after initial registration must register annually between October 1 and December 31 of each year. The second document explains the requirements for electronic drug product reporting. In June and December of each year, registered outsourcing facilities should electronically submit drug product reports in SPL format using FDA's electronic submissions system. These reports should identify all drugs compounded at the outsourcing facility during the previous six months and provide specific information about each drug, including active ingredients, dosage, and route of administration. The third document details two fees registered outsourcing facilities will be required to pay beginning in fiscal year 2015. First, at the time of registration, facilities must pay an annual establishment fee equal to $15,000 multiplied by an inflation adjustment factor tied to FDA personnel costs and the Consumer Price Index for urban consumers. Entities that qualify as small businesses under the Act will pay only one-third of the annual fee. Second, an outsourcing facility must pay a reinspection fee each time it is subject to a reinspection equal to $15,000 multiplied by the inflation adjustment factor.

New Drug Risk Disclosure Requirements for Pregnant or Lactating Women
FDA has issued final labeling rules for human prescription drug and biological products. The "Pregnancy," "Labor and delivery," and "Nursing mothers" subsections of the "Use in Specific Populations" section of the labeling will be subject to new content and form requirements. The final rule requires the removal of the pregnancy categories A, B, C, D, and X from all human prescription drug and biological product labeling. Labeling for certain drugs must include a summary of the risks of using a drug during pregnancy and lactation, a discussion of the data supporting that summary, and relevant information to help health care providers make prescribing decisions and counsel women about the use of drugs during pregnancy and lactation. The final rule also requires the labeling to include relevant information about pregnancy testing, contraception, and infertility for health care providers prescribing for females and males of reproductive potential. FDA is also issuing a draft guidance to help drug and biological product manufacturers comply with the new labeling content and format requirements. ***Comments due February 2, 2015***.

FDA Proposes Rule to Require Electronic Distribution of Prescribing Information
In December 18, 2014, *Federal Register*, FDA published a proposed rule to require electronic distribution of product-prescribing information intended for health care professionals, amending the current drug labeling regulations to move beyond the distribution of prescribing information in paper form at the time the product is dispensed. FDA is also proposing to eliminate the inclusion of prescribing information for health care professionals in paper form as part of the dispensed package, except where specifically authorized such as a product intended for use in an emergency room or a product that may be stockpiled for an emergency. As proposed, the electronic distribution requirements would not apply to patient labeling (including patient package inserts and Medication Guides) or to prescribing information accompanying promotional labeling, which would continue to be provided in paper form. Under the proposed rule, manufacturers would be required to submit prescribing information to FDA for posting on FDA's publicly available labeling repository website (labels.fda.gov) every time there is a change in the labeling, to review the labeling posted at FDA's website to verify that the correct version of the labeling appears in the repository, and to promptly notify FDA if the correct version is not posted. Comments due March 18, 2014.

FDA and China Agree to Collaborate on Inspections
FDA Commissioner Hamburg visited China last month and signed an agreement with Chinese officials to collaborate on inspections in China. This agreement builds on a 2007 agreement to "frame the work [FDA] inspectors will do in China and create mechanisms for collaboration on inspections." FDA is also engaging with Chinese universities and other stakeholders to create training opportunities. During her visit to China, Hamburg spoke at

Peking University, where FDA has established an advanced degree program in international pharmaceutical engineering management to accelerate modernization of the industry. According to Hamburg, "discussions ranged from how best to advance biomedical product innovation, expand access to important pharmaceuticals through generic and biosimilar regulatory pathways, and how coordinated action, along with using new, state-of-the art technologies and analytical methods, will more effectively protect the public from substandard or counterfeit products." China also recently agreed to approve visas to allow for more FDA inspectors to enter the country, after nearly two years of delays. The additions will more than double FDA's current China staff from 13 to 33.

Biotech and Generic Drug Firms Compromise on Substitution Language
FDA has not yet approved a biosimilar, let alone decided whether a biosimilar is interchangeable with a biologic reference product. But brand-name biologic companies and those pursuing generic versions of the reference products have been battling over whether pharmacists must notify doctors when making a substitution, an additional step that could restrict patient access to biosimilars. The parties recently reached an agreement in lobbying states for regulations pertaining to substitution. The compromise language, which closely resembles the recently passed Massachusetts law, allows the pharmacist to notify the prescriber of the substitution "within a reasonable time following the dispensing of a biological product," rather than before the product is dispensed. The compromise also allows for the use of technology, conveying the information to prescribers using electronic medical records systems.

NIH Proposes Expanded Clinical Trial Data Reporting
In an effort to enhance the transparency of clinical trials, the National Institutes of Health ("NIH") released a draft policy requiring all NIH-funded clinical trials to meet the ClinicalTrials.gov registration and reporting requirements. The new policy is an expansion of a 2007 law to cover unapproved, unlicensed, and uncleared products, responding to concerns about transparency in government-funded studies. HHS also released a separate but related notice of proposed rulemaking implementing the reporting requirements. In a teleconference on the release date, NIH Director Francis S. Collins said: "When a lot of dollars and people's time—and volunteers are putting themselves potentially at some sort of risk situation by taking part in a trial of an uncertain application—we need to be sure that the results of that are finding their way into the view of the public and of other researchers as quickly as possible."

Federal Circuit Affirms Dismissal of Biosimilars DJ Action
In a much-anticipated decision, on December 5, 2014, the Federal Circuit issued its ruling in the first case before it involving biosimilars. In that case, Sandoz filed suit in the Northern District of California seeking a declaratory judgment ("DJ") that certain patents were invalid, unenforceable, and would not be infringed by the marketing of a biosimilar to Enbrel. When suit was filed, a 351(k) application had not yet been filed with FDA for approval of the biosimilar. The district court dismissed the DJ action for lack of a justiciable case or controversy and also on the ground that the suit was barred by the patent litigation provisions of the Biologics Price Competition and Innovation Act ("BPCIA"), 42 U.S.C. §262. The latter provisions, which have become known in the industry as the "patent dance," include a specific procedure for parties to litigate patent disputes involving biosimilars after a 351(k) application is filed with FDA. The Federal Circuit affirmed the dismissal on the ground that DJ jurisdiction was lacking, but specifically stated, "[w]e do not address the district court's interpretation of the BPCIA." The decision comes on the heels of a December 1, 2014, dismissal of a similar suit filed by Celltrion in the Southern District of New York involving its biosimilar to Remicade. The district court dismissed the case for lack of DJ jurisdiction and also for being outside the procedures of the BPCIA. As matters now stand, industry continues its wait to see which biosimilar application will be the first to give rise to patent litigation under the "patent dance" provisions of the BPCIA.

FDA Seeks Comments on Criteria for "First Generic" Submissions
FDA has opened a public docket to request comments on its newly proposed criteria for "first generic" abbreviated new drug application ("ANDA") submissions. There are two

criteria for a "first generic" ANDA for the purposes of review prioritization: (i) a first-to-file ANDA eligible for 180-day exclusivity, or for which there are no blocking patents or exclusivities; and (ii) for which there is no previously approved ANDA for the drug product. FDA stated that "[e]stablishing clear criteria for this review prioritization category will allow FDA to appropriately prioritize ANDA submissions and track them in a manner consistent with the review prioritization commitments FDA made pursuant to GDUFA." FDA also hopes to stem industry confusion with clearer criteria and promote "more consistent identification of 'first generic' submissions." FDA specifically seeks comments on whether FDA should change the review prioritization for an ANDA that no longer meets the "first generic" criteria during its review, e.g., the validity of a patent may be upheld in litigation, thereby blocking approval until patent expiry. ***Comments due December 19, 2014***.

EU Regulatory Authorities Pull Marketing Authorizations for Bioequivalence Study Fraud

A number of EU Member States regulatory authorities have suspended the marketing authorizations of certain medicines whose studies were conducted at a site in Hyderabad, India of GVK Biosciences, a contract research organization. The move follows an investigation by the French medicines agency ANSM, which identified deficiencies and raised concerns about the reliability of bioequivalence studies conducted at GVK's Hyderabad site between 2008 and 2014. The World Health Organization's pre-qualification team subsequently opened an investigation to determine the authenticity of such studies.

The European Medicines Agency ("EMA") confirmed in a press release that it is currently reviewing findings of noncompliance with good clinical practice at this site and determining the impact on medicines authorized on the basis of studies performed at the site. It also clarified that such suspensions taken at the national level are precautionary measures until the review is finalized. An EMA recommendation on whether the marketing authorizations of the concerned medicines should be maintained, varied, suspended, or withdrawn across the EU is expected to be issued January 2015. Under EU law, clinical trials conducted in countries outside of the EU and used in Marketing Authorization Applications in the EU must be conducted under standards equivalent to the ethical principles and principles of good clinical practice applied to clinical trials in the EU.

Japan Amends Drug and Medical Device Law

A material amendment to the law regulating drugs and medical devices in Japan was recently implemented. The amendment addresses three main areas: (i) establishing a fast-track authorization process for regenerative medicine products, (ii) restructuring medical device regulations, and (iii) establishing reporting obligations for package inserts for drugs and medical devices. Jones Day's *Commentary* on the amendments provides additional information.

Draft Guidance Issued on ANDA Applicants Obtaining Letter from FDA Stating Safety Protections Comparable to REMS

FDA recently released draft guidance on the process by which an ANDA applicant may obtain a letter from FDA to facilitate the ANDA's efforts to obtain reference listed drug ("RLD") product for bioequivalence testing. By way of background, FDA notes that in some instances, RLD sponsors have refused to sell drug product to ANDA applicants on the ground that doing so would violate the elements to assure safe use ("ETASU") requirements of the product's risk evaluation and mitigation strategy ("REMS"). Historically, at the request of the potential ANDA applicant, FDA has (i) reviewed the bioequivalence study protocols to assess whether the proposed safety precautions are comparable to the ETASU, and if so, (ii) issued letters to RLD sponsors stating so and indicating that supplying the drug product would not be considered a violation of the REMS. The draft guidance document distills FDA's practice to writing to clarify procedures and allow consideration by stakeholders. FDA emphasizes that requesting such a letter is not a legal requirement and that the guidance is intended to clarify the process if the ANDA applicant chooses to do so. ***Comments due February 3, 2015***.

FDA Issues Draft Guidance on DSCSA Reporting Requirements

FDA recently issued draft guidance for prescription drug wholesale distributors and third-

party logistics providers on annual reporting requirements under the Drug Supply Chain Security Act of 2013 ("DSCSA"). For each facility, the DSCSA requires wholesaler distributors to provide that facility's name, address, and contact information, the state license number, and any significant disciplinary actions against the facility by a state or federal agency. The DSCSA requires third-party logistics providers to provide the name, address, and state license number for each facility. In addition, FDA is also requesting wholesale distributors and third-party logistics providers to provide a unique facility identifier (a D-U-N-S® number is preferred), the date that the state license(s) expire, and documents associated with any disciplinary actions. The initial report for wholesale distributors should be submitted between January 1, 2015, and March 31, 2015, and for third-party logistics providers between November 27, 2014, and March 31, 2015. Subsequent annual reports for both wholesale distributors and third-party logistics providers should be submitted each year between January 1 and March 31. ***Comments due February 9, 2015***.

FDA also recently issued draft guidance on the pharmaceutical security provisions of the DSCSA, which requires manufacturers, repackagers, wholesale distributors, and dispensers to exchange transaction information, transaction history, and a transaction statement—in paper or electronic format—when engaging in transactions involving prescription drugs in finished dosage form. This requirement goes into effect on January 1, 2015, for manufacturers, repackagers, and wholesale distributors, and on July 1, 2015, for dispensers. ***Comments due January 27, 2015***.

Other News

Annual Registrations and Listings for Medical Device Establishments Due 12/31/14

PhRMA Releases Principles on Conduct of Clinical Trials and Related Communications

FDA Delays Ruling for Generic Labeling Proposed Rule

FDA Issues Guidance on REMS Drugs for Generic Development

Device Company Pleads Guilty to Selling Without Regulatory Approval, Will Pay $80M

Senate Circulates Bill to Block Medical App Oversight

FDA Report to Congress: Too Many Frivolous Petitions

EMA Issues Guidance on Obtaining Unpublished Documents

FDA Issues Additional Guidance on Compounding Facilities

23andMe Approved in UK

FDA Discourages Laparoscopic Morcellation for Uterine Fibroids

FDA Approves New Abuse-Deterrent Hydrocodone Product

HHS Updates Federal Health IT Strategic Plan

Patients Suffer from Medicine Shortages throughout EU

European Medicines Agency Welcomes New Head of Administration

Emergency Safeguards for Avian Influenza in The Netherlands and the UK

2015 British Pharmaceutical Code of Practice Published

European Court of Justice: Defective Product Liability Does Not Preclude National Legislation

EMA Management Board Discusses Next Steps After Judgment of EU Civil Service Tribunal

EU Court Confirms French Order Restricted Competition in Clinical Biology Analysis

Regulatory Notices

FDA Issues Final Rule Revising Requirements for Pregnancy and Lactation Labeling
In the December 4, 2014, *Federal Register*, FDA issued a final rule amending its regulations governing the content and format of human prescription drug and biological products for indications involving reproduction.

FDA Opens Docket for Comments on "First Generic" ANDA Proposed Criteria
In the November 19, 2014, *Federal Register*, FDA opened a public comment on proposed criteria for "first generic" ANDA submissions. ***Comments due December 19, 2014***.

EMA Conflicts of Interests: New Policy
On November 20, 2014, EMA published a revised policy on handling declarations of interests for scientific committee members and experts. The revised policy, which was endorsed by the EMA Management Board in March 2014, takes into account input from stakeholders at the Agency's September 2013 public workshop and aims to strike a more balanced approach to the handling of conflicts of interests. The new policy enters into force on January 30, 2015.

EMA Releases Practical Guidance on Access-to-documents Requests
On November 24, 2014, EMA released a practical guide detailing the process for requesting access to unpublished documents held by the Agency.

FDA Request Comments on Demographic Subgroup Data
In the November 24, 2014, *Federal Register*, FDA requested public comments on Demographic Subgroup Data for FDA Approved Products on its website. The website is designed to improve the availability and transparency of clinical trial demographic subgroup data. FDA is requesting comments on the format, content, and overall usability of the site to determine whether this approach is user friendly to the public. Comments due January 23, 2015.

FDA Issues Privacy Act Report on Commissioning of State and Local Officials
In the December 8, 2014, *Federal Register*, FDA published a notice regarding its new system of records containing information about state and local officials who have applied for an FDA commission that would allow them to assist FDA with its regulatory compliance and enforcement efforts. FDA will use the records in this system to assess qualifications of commissioning candidates, initiate background investigations, record the status of applications, and track the status of commissioned officials.

FDA Issues Clinical Data Standards
In the November 19, 2014, *Federal Register*, FDA announced it had released a document titled, *Validation Rules for Study Data Tabulation Model (SDTM) Formatted Studies*, intended to improve the standardization and quality of clinical data submitted to Center for Drug Evaluation and Research, as well as to improve the predictability of data quality and usefulness. ***Comments due December 19, 2014***.

FDA Extends Comment Period on Two-Phased Chemistry Draft Guidance
In the December 9, 2014, *Federal Register*, FDA announced an extension of the comment period on *Two-Phased Chemistry, Manufacturing, and Controls Technical Sections*. ***Comments due February 17, 2015***.

Corrections and Amendments to Prior FDA Notices

- Misstated name of an organization in *Report on the Standardization of Risk Evaluation and Mitigation Strategies*

FDA Determinations that Drugs Not Withdrawn from Sale for Safety or Effectiveness

- FIZERPEN (Penicillin G Potassium) Injection, 1 Million Units/Vial

FDA Withdraws Approval of 23 NDAs and 68 ANDAs from Multiple Applicants
In the December 5, 2014, *Federal Register*, FDA withdrew its approval of 23 new drug applications ("NDAs") and 68 ANDAs from multiple applicants. The holders of the applications notified the Agency in writing that the drug products were no longer marketed and requested the approval of the applications be withdrawn.

FDA Withdraws Approval of ANADA for Oxytetracycline Powder
In the December 15, 2014, *Federal Register*, FDA withdrew its approval of an abbreviated new animal drug application ("ANADA") for an oxytetracycline soluble powder used to make medicated drinking water for livestock and poultry. FDA withdrew the approval at the sponsor's request because this product is no longer manufactured or marketed.

FDA Amends Animal Drug Rules to Reflect NADAs, ANADAs, and Sponsorship Changes
In the December 15, 2014, *Federal Register*, FDA amended the animal drug regulations to reflect approval actions for new animal drug applications ("NADAs") and ANADAs during September and October 2014. The amendments also reflect a change of sponsorship of six NADAs and four ANADAs, the voluntary withdrawal of approval of an ANADA, and a correcting amendment.

FDA Issued the Following Draft and Final Guidance Documents

- *Guidance for Industry: Vaginal Microbicides: Development for the Prevention of HIV*. November 18, 2014, *Federal Register*.
- *Guidance for Industry: Citizen Petitions and Petitions for Stay of Action Subject to Section 505(q) of the Federal Food, Drug, and Cosmetic Act*. November 18, 2014.
- Guidance for Industry: Fees for Human Drug Compounding Outsourcing Facilities Under Sections 503B and 744K of the FD&C Act. November 24, 2014, *Federal Register*.
- *Revised Draft Guidance: Recommended Warning for Over-the-Counter Acetaminophen-Containing Drug Products and Labeling Statements Regarding Serious Skin Reactions*. November 28, 2014, *Federal Register*. ***Comments due January 27, 2015***.
- *Guidance for Industry: Registration for Human Drug Compounding Outsourcing Facilities Under Section 503B of the Federal Food, Drug, and Cosmetic Act*. November 24, 2014, *Federal Register*.
- *Draft Guidance for Industry: Drug Supply Chain Security Act (DSCSA) Standards for the Interoperable Exchange of Information for Tracing of Certain Human, Finished, Prescription Drugs: How to Exchange Product Tracing Information*. November 28, 2014, *Federal Register*. ***Comments due January 27, 2015***.
- *Guidance for Industry: Scale-up and Post-approval Changes (SUPAC): Manufacturing Equipment Addendum*. December 2, 2014, *Federal Register*.
- *Draft Guidance for Industry: Pregnancy, Lactation, and Reproductive Potential: Labeling for Human Prescription Drug and Biological Products-Content and Format*. December 4, 2014, *Federal Register*.
- *Draft Guidance for Industry: How to Obtain a Letter from FDA Stating that Bioequivalence Study Protocols Contain Safety Protections Comparable to Applicable REMS for RLD*. December 5, 2014, *Federal Register*. ***Comments due February 3, 2015***.
- *Draft Guidance for Industry: General Clinical Pharmacology Considerations for Pediatric Studies for Drugs and Biological Products*. December 9, 2014, *Federal Register*. ***Comments due February 9, 2015***.
- *Draft Guidance for Industry: DSCSA Implementation: Annual Reporting by Prescription Drug Wholesale Distributors and Third-Party Logistics Providers*. December 9, 2014, *Federal Register*. ***Comments due February 9, 2015***.
- *Guidance for Industry: Patient Counseling Information Section of Labeling for Human Prescription Drug and Biological Products—Content and Format*. December 10, 2014, *Federal Register*.
- *Guidance for Industry and Food and Drug Administration Staff Recommendations for Labeling Medical Products to Inform Users That the Product or Product*

Container Is Not Made With Natural Rubber Latex. December 2, 2014, *Federal Register*.
- *Draft Guidance for Industry: Bacterial Detection Testing by Blood and Blood Collection Establishments and Transfusion Services to Enhance the Safety and Availability of Platelets for Transfusion*. December 9, 2014, *Federal Register*. ***Comments due February 9, 2015***.
- *Guidance for Industry: Changes to an Approved Application: Biological Products: Human Blood and Blood Components Intended for Transfusion or for Further Manufacture*. November 21, 2014, *Federal Register*.
- *Immediately in Effect Guidance Document: Product Labeling for Laparoscopic Power Morcellators*. November 25, 2014, *Federal Register*.
- *Draft Guidance for Industry: Electronic Product Reporting for Human Drug Compounding Outsourcing Facilities*. November 24, 2014, *Federal Register*. ***Comments due January 23, 2015***.
- *Guidance for Industry and FDA Staff: Infusion Pumps Total Product Life Cycle*. December 2, 2014, *Federal Register*.
- *Guidance for Industry and Food and Drug Administration Staff: Design Considerations for Devices Intended for Home Use*. November 24, 2014, *Federal Register*.
- *Guidance for Industry: Pharmacovigilance of Veterinary Medicinal Products Electronic Standards for Transfer of Data*. December 10, 2014, *Federal Register*.
- *Bioequivalence Recommendations for Budesonide Extended-Release Tablets*. December 11, 2014, *Federal Register*.

FDA Announced that the Following Collections Have Been Submitted to OMB

- Risk and Benefit Perception Scale Development
- Humanitarian Use Devices
- Notification of the Intent To Use an Accredited Person Under the Accredited Persons Inspection Program

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

- Administrative Practices and Procedures; Formal Evidentiary Public Hearing
- FDA Medical Products Reporting Program

Upcoming Meetings, Workshops, and Conferences

Drugs and Biologics

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.

Public Meeting on Chagas Disease Patient-Focused Drug Development, **April 28, 2015**, in Silver Spring, MD to obtain patient input on the impact of Chagas disease on daily life and patients' views on currently available therapies.

Medical Devices

Public Workshop on Framework for Regulatory Oversight of Laboratory Developed Tests, **January 8–9, 2015**, to discuss FDA's proposal for a risk-based framework for addressing the regulatory oversight of this subset of in vitro diagnostic devices).

Advisory Committees

December 18, 2014: Bone, Reproductive, and Urologic Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee (closed meeting to discuss whether FDA should permit further clinical development of an existing investigational drug product).

January 7, 2015: Oncologic Drugs Advisory Committee (to discuss the biologics license application for a proposed biosimilar to NEUPOGEN (filgrastim) to decrease the incidence for certain complications related to anti-cancer drugs).

January 12, 2015: Endocrinologic and Metabolic Drugs Advisory Committee (to discuss the safety and efficacy of NOCDURNA (desmopressin) for treatment of nocturia due to

nocturnal polyuria in adults who awaken two or more times each night to void.

January 22, 2015: Anti-Infective Drugs Advisory Committee Meeting (to discuss NDAs for isavuconazonium sulfate capsules and isavuconazonium sulfate for injection, for the proposed indications of treatment of invasive aspergillosis and mucormycosis).

February 20, 2015: Orthopaedic and Rehabilitation Devices Panel of the Medical Devices Advisory Committee (postponed from December 12, 2014).

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

Enforcement Updates

Recent Product Recalls
In recent weeks, a drug manufacturer recalled a lot of potassium chloride injections due to a complaint of mislabeling of the overpouch. A medical device manufacturer recalled surgical kits due to a packaging defect that may compromise the sterility of the product. Another device manufacturer recalled a donut gel pillow due to potential mold contamination.

Two medical device manufacturers issued corrections for their products. One manufacturer issued a correction for use of a monitory system, warning that certain medical conditions should not be tested with the system. Another device manufacturer issued a correction for defibrillation electrodes, warning of connector compatibility issues with certain defibrillator units.

View a complete listing of FDA Recalls.

Recent Warning Letters
Since we last reported on enforcement actions in early November, FDA posted warning letters to drug and device manufacturers, as well as one fertility center, for violations related to CGMP ("Current Good Manufacturing Practices"), QSR ("Quality Systems Regulations"), MDR ("Medical Device Reporting"), selling unapproved human and animal drugs, clinical investigations, and deviations from the regulations for human cells, tissues, and cellular and tissue-based products.

FDA continues to cite medical device manufacturers for CGMP and QSR violations, including failure to establish adequate procedures for design changes, inadequate handling of complaints, insufficient process controls, failure to establish and maintain procedures for corrective and preventative action, and failure to establish procedures for quality audits. Recipients of recently posted warning letters for CGMP and QSR violations, five of which are located overseas, included manufacturers of massage devices, catheters, surgical sutures, tests for Phadebact monoclonal GC, H. Influenza, and CSF, saline and heparin flush syringes, blood collection tubes, and intravenous sets, poles, and syringes. FDA also cited four medical device manufacturers for failure to follow the MDR regulations.

Drug manufacturers continue to receive warning letters for CGMP violations, as well as misbranded or unapproved drugs. CGMP violations include insanitary conditions and inadequate quality controls. FDA additionally warned two drug manufacturing facilities, both located in India, for CGMP violations related to the manufacture of active pharmaceutical ingredients. One of the facilities was also warned for failing to register the facility prior to offering the drug for import into the United States.

FDA continues to monitor compounding pharmacies, recently posting three warning letters, 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 pharmacies were additionally cited for violations relating to insanitary conditions, CGMP, and selling unapproved drug products.

FDA cited a clinical investigator of an investigational drug for failing to ensure the investigation was conducted according to the investigational plan. A fertility center received a warning letter for deviations from the regulations for human cells, tissues, and cellular and tissue-based products, including failure to screen donor specimens for infections and failure to determine as ineligible donors with risk factors for certain diseases.

Finally, FDA recently posted five warning letters to veterinary companies, three located overseas, that sell animal drugs online for marketing numerous unapproved new animal drugs.

View FDA's Warning Letters homepage (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 stating its seizure medication's promotion was misleading, citing the inclusion of claims that the drug is more effective than has been demonstrated by substantial evidence. In this letter, FDA highlighted promotional claims associated with patient-reported outcomes used without apparent adequate substantiation. The untitled letter represents OPDP's 10th letter of 2014.

View a complete listing of 2014 OPDP Warning Letters.

Recent Notable Drug and Device Approvals/Clearances

FDA approves first pathogen reduction system to treat plasma (December 16, 2014)

FDA allows marketing of the first newborn screening test to help detect Severe Combined Immunodeficiency (December 15, 2014)

FDA clears test that helps predict the risk of coronary heart disease (December 15, 2014)

FDA grants CLIA waiver expanding the availability of rapid screening test for syphilis (December 15, 2014)

FDA expands approved use of Cyramza to treat aggressive non-small cell lung cancer (December 12, 2014)

FDA approves first test to confirm the presence of Human T-cell Lymphotropic Virus-I/II antibodies (December 11, 2014)

FDA approves Gardasil 9 for prevention of certain cancers caused by five additional types of HPV (December 10, 2014)

FDA approves Jakafi to treat patients with a chronic type of bone marrow disease (December 4, 2014)

FDA approves Blincyto to treat a rare form of acute lymphoblastic leukemia (December 3, 2014)

FDA allows marketing of noninvasive device to help evaluate heart blood flow (November 26, 2014)

FDA approves extended-release, single-entity hydrocodone product with abuse-deterrent properties (November 20, 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.

Jones Day FDA Regulatory & Compliance Counseling Contacts

Mark Mansour
Washington
+1.202.879.3883
mmansour@jonesday.com

Laurie A. Clarke
Washington
+1.202.879.3498
lclarke@jonesday.com

Cristiana Spontoni
Brussels
+32.2.645.14.48
cspontoni@jonesday.com

Colleen M. Heisey
Washington
+1.202.879.3449
cmheisey@jonesday.com

Christopher M. Mikson
Washington
+1.202.879.3669
cmikson@jonesday.com

Emily K. Strunk
Washington
+1.202.879.3778
estrunk@jonesday.com

Katherine M. Llewellyn
Brussels
+32.2.645.14.47
kllewellyn@jonesday.com

Stephanie L. Resnik
Washington
+1.202.879.5458
sresnik@jonesday.com

Brigid C. DeCoursey
Washington
+1.202.879.3651
bdecoursey@jonesday.com

Matthew R. Bowles
Washington
+1.202.879.3604
mbowles@jonesday.com

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Top News

FDA to Study Effects of Pill Aesthetics on Patient Compliance
FDA intends to survey pharmacists and patients to find out whether the shape, size, or color of a pill influences adherence to the prescribed dosing regimen. FDA previously issued a draft guidance recommending generic manufacturers make their pills look similar to the brand name drug, indicating its interest in how aesthetic changes in pill appearance are linked to health outcomes.

About 85 percent of all medications prescribed in the U.S. are generic drugs, and because generics are often treated interchangeably, the appearance of a patient's medication may change depending on the generic supplier.

According to the FDA information collection notice, "[s]tudies indicate that patients are more likely to stop taking their generic medications when they experience a change in their drugs' physical characteristics, leading to harmful clinical and public health consequences, as well as increased health care costs." FDA says it will ask pharmacists how often generic suppliers change and whether they employ strategies to help patients transition between pills with a different appearance. FDA will also poll patients, focusing on older adults with epilepsy, diabetes, hypertension, hyperlipidemia, depression, HIV, or combinations of these six conditions.

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CONTACTS

Mark Mansour
Washington

Laurie A. Clarke
Washington

Colleen M. Heisey
Washington

Christopher M. Mikson
Washington

Emily K. Strunk
Washington

Stephanie L. Resnik
Washington

Brigid C. DeCoursey
Washington

Matthew R. Bowles
Washington

Detailed Contact Information

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