Pharmaceutical & Medical Device Regulatory Update
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Top News

FDA Issues Draft Guidance and Draft Memorandum of Understanding on Compounding

FDA recently issued five new documents related to drug compounding and repackaging to provide compliance information to pharmacies, physicians, and outsourcing facilities engaged in the compounding of human drugs. Under the Drug Quality and Security Act ("DQSA"), which was enacted in response to a deadly fungal meningitis outbreak, human drug products compounded by or under the direct supervision of a licensed pharmacist in a registered outsourcing facility can qualify for exemptions from FDA's drug approval requirements and certain other drug labeling and track and trace requirements. These provisions created a new section 503B of the Federal Food, Drug, and Cosmetic Act ("FDCA"). However, to qualify for these exemptions under 503B, outsourcing facilities, also referred to as compounding pharmacies, must meet several conditions. Many of the specific requirements and parameters provided for compounding under the DQSA remained unclear. The new documents are intended to provide clarification to such issues.

- Read More

New NIH Advisory Panel Will Develop Million-Person Cohort for White House Precision Medicine Initiative

At a recent National Institutes of Health ("NIH") workshop, the agency announced that an advisory panel will be formed to perform the million-subject research cohort that is an essential part of the

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UPCOMING EVENTS

president's Precision Medicine Initiative. The initiative is intended to foster development of a new model of health care delivery that targets treatments to patient subgroups identified by their genetic makeup and other characteristics. It was announced during the January 20 State of the Union address, when the president requested significant funds as a part of his fiscal year 2016 budget. To that end, as part of NIH's implementation of the initiative, the agency intends to create "a cohort of unprecedented scale" that will help researchers better understand all the factors that play out in health and disease more efficiently and implement ways to improve health outcomes, NIH Director Francis S. Collins stated during a press conference held at the workshop.

FDA Permits Marketing of the First Direct-to-Consumer Genetic Test in the Nation

After previously issuing a warning letter to 23andMe for marketing a genetic test to consumers without FDA clearance or approval, the agency authorized the company to market its Bloom Syndrome carrier test, which is a direct-to-consumer ("DTC") genetic test to determine whether a healthy person has a variant in a gene that could lead to their offspring inheriting the disorder. This is the first FDA authorization for a DTC genetic carrier test. In a press release, the agency stated, "[t]he FDA believes that in many circumstances it is not necessary for consumers to go through a licensed practitioner to have direct access to their personal genetic information. Today's authorization and accompanying classification, along with FDA's intent to exempt these devices from FDA premarket review, supports innovation and will ultimately benefit consumers."

FDA plans to issue a notice announcing the agency's intent to exempt those tests from premarket notification that will provide for a 30-day comment period.

Other News

FTC Fines Two Cancer Risk Detection Apps

CBER Publishes 2015 Guidance Agenda

Deadly Bacteria Leads FDA to Issue Advisory on Endoscopes

Georgia Senate Passes Bill for Automatic Substitutions of Biosimilar Drugs

FDA to Reopen Comment Period and Hold March Meeting on Proposal for Updating Safety Information on Generic Labeling

FDA Appoints Jonathan Jarow as Acting Director of Office of Medical Policy

NIH to Test Experimental HIV Vaccine for Safety, Immune Response in South Africa

FDA, NIH Work Group to Develop Plan for Improving Study Subgroup Data

FDA Issues New Guidance, Will Exercise Enforcement Discretion on Low-Risk Device Data

March 4, 2015: **Cristiana Spontoni** will speak at the ABA Life Sciences Legal Summit on "Negotiating an Effective Clinical Trial Agreement and Limiting Litigation Exposure."

March 4–7, 2015: **Michael Carvin** will speak at the American Bar Association's 16th Annual Conference on Emerging Issues in Healthcare Law.

April 22–23, 2015: **Cristiana Spontoni** will speak at the 1st Annual Women Leaders in Life Sciences Law Conference program on "Pharmaceutical and Medical Device Regulatory Developments, Issue Spotting: Updates on the Substantive Legal Developments Affecting Life Sciences Companies in 2015 and Beyond."

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

RELATED PRACTICES

FDA Regulatory & Compliance Counseling

Health Care

Life Sciences

Systems

GAO Reports to Congress on FDA Device Oversight, Globalization, and Drug Shortages

European Federation of Pharmaceutical Industries and Associations, the European Confederation of Pharmaceutical Entrepreneurs, and the European Association for Bio-Industries Complain with the European Commission about Italy's Promotion of the Off-Label Use of Medicines

European Health Care Stakeholders Announce the Establishment of the European Medicines Verification Organisation Aimed at Securing the Legitimate Pharmaceutical Supply Chain Against the Risk of Falsified Medicines

A Coalition of Companies (Langland, Mendor, and Sanofi) is Participating in What is Expected to be Europe's First Clinical Trial to be Conducted Remotely

Regulatory Notices

FDA Solicits Comments on Draft Standard MOU Regarding Distribution Policies for Compounded Drugs
In the February 19, 2015, *Federal Register*, FDA released, for public comment, a draft standard MOU entitled "Memorandum of Understanding Addressing Certain Distributions of Compounded Human Drug Products Between the State of [insert State] and the U.S. Food and Drug Administration." In order for a compounding pharmacy to qualify for exemption to certain requirements of the FDCA, its drug products must be compounded in a state that has entered into an MOU with FDA regarding distribution of such products. This draft standard MOU describes the responsibilities of a state that chooses to enter into the MOU with respect to investigating and responding to complaints related to compounded human drug products distributed outside the state and in addressing the interstate distribution of inordinate amounts of compounded human drug products. In connection with its issuance of the new draft standard MOU, FDA announced the withdrawal of an earlier draft standard MOU entitled "Memorandum of Understanding on Interstate Distribution of Compounded Drug Products," issued in January 1999. ***Comments due June 19, 2015***.

FDA Solicits Information to Facilitate Development and Qualification of Biomarkers in Human Drugs
In the February 13, 2015, *Federal Register*, FDA issued a notice seeking information to facilitate development and qualification of biomarkers in areas related to human drug therapeutics, consistent with policy goals of the Prescription Drug User Fee Act. FDA encourages interested groups and individuals to submit information on specific medical and biological areas where novel biomarkers can be identified that would meaningfully advance drug development. The survey provides more detailed information requests. ***Comments due April 14, 2015***.

FDA Publishes Modification to Recognized Consensus Standards for Medical Devices
In the February 11, 2015, *Federal Register*, FDA issued a publication containing modifications to the list of standards FDA recognizes for use in premarket reviews ("FDA Recognized Consensus Standards"). Specifically, this publication adds a list of recognized standards relevant to safety considerations to mitigate the risks of misconnections with small-bore connectors intended for enteral applications. The publication, entitled "Modifications to the List of Recognized Standards, Recognition List Number: 039," will assist manufacturers that elect to declare conformity with consensus standards to meet certain requirements for medical devices.

EMA Publishes Fact Sheet on Metal-on-Metal Hip Implants
The European Medicines Agency ("EMA") has published a new fact sheet on the safety of metal-on-metal hip implants. The fact sheet provides a summary of the opinion on "The safety of metal-on-metal joint replacements with a particular focus on hip implants" of the European Commission's Scientific Committee of Emerging and Newly Identified Health

Risks.

EMA Establishing Task Force on International Standards for Identification of Products
EMA is establishing a task force for the implementation of international standards for the identification of medicinal products for human use in the EU. The task force will be made up of representatives of the agency, national competent authorities, the pharmaceutical industry, and service providers. ***Parties interested in participating are invited to submit their expressions of interest by March 6, 2015***.

EMA Recommended Changes to Product Information to be Available in All EU Languages
EMA has begun translating its recommended changes to product information based on the assessment of safety signals into all official languages of the EU. The initiative is aimed at accelerating the implementation of changes to product information with a view to contributing to easier access to information for patients.

FDA Publishes List of Approved PMA Applications
In the February 11, 2015, *Federal Register*, FDA published a list of premarket approval applications ("PMAs") that were approved between July 1, 2014, and September 30, 2014. By law, FDA is required to publish a quarterly list of available safety and effectiveness summaries of PMA approvals and denials that were placed on the internet and made available via FDA's Division of Dockets Management.

European Commission Experts Told They Cannot Look at Pricing and Reimbursement Issues
The Commission Expert Group on Safe and Timely Access to Medicines for Patients ("STAMP") held its first meeting on January 27, 2015. STAMP has been set up to provide advice and expertise to the European Commission services in relation to the implementation of the EU pharmaceutical legislation and will exchange views and information about the experience of Member States, examine national initiatives, and identify ways to use the existing EU regulatory tools more effectively, with the aim to improve safe and timely access to and availability of medicines for patients. However, under its remit or directive, the group may not consider pricing and reimbursement issues.

FDA Issued the Following Draft and Final Guidance Documents
Investigating and Reporting Adverse Reactions Related to Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) Regulated Solely Under Section 361 of the Public Health Service Act and 21 CFR part 1271, February 20, 2015, *Federal Register*. ***Comments due April 21, 2015***.

Draft Guidance for Entities Considering Whether to Register as Outsourcing Facilities Under Section 503B of the Federal Food, Drug, and Cosmetic Act, February 19, 2015, *Federal Register*. ***Comments due May 20, 2015***.

Draft Guidance for Industry: Mixing, Diluting, or Repackaging Biological Products Outside the Scope of an Approved Biologics License Application, February 19, 2015, *Federal Register*. ***Comments due May 20, 2015***.

Draft Guidance for Industry: Repackaging of Certain Human Drug Products by Pharmacies and Outsourcing Facilities, February 19, 2015, *Federal Register*. ***Comments due May 20, 2015***.

Draft Guidance for Industry: Adverse Event Reporting for Outsourcing Facilities Under Section 503B of the Federal Food, Drug, and Cosmetic Act, February 19, 2015, *Federal Register*. ***Comments due May 20, 2015***.

Guidance for Industry and FDA Staff: Immediately in Effect Guidance Document: Classification and Requirements for Laser Illuminated Projectors (LIPs), February 18, 2015, *Federal Register*.

Guidance for Industry: Complicated Urinary Tract Infections: Developing Drugs for Treatment, February 17, 2015, *Federal Register*.

Draft Guidance for Industry: Alcoholism: Developing Drugs for Treatment, February 12, 2015, *Federal Register*. ***Comments due April 13, 2015***.

Draft Guidance for Industry and FDA Staff: Premarket Studies of Implantable Minimally Invasive Glaucoma Surgical (MIGS) Devices, February 11, 2015, *Federal Register*. ***Comments due May 12, 2015***.

Draft Guidance for Industry: Individual Patient Expanded Access Applications: Form FDA 3926, February 10, 2015, *Federal Register*. ***Comments due April 23, 2015***.

Guidance for Industry: Complicated Intra-Abdominal Infections: Developing Drugs for Treatment, February 10, 2015, *Federal Register*.

FDA Announced that the Following Collections Have Been Submitted to OMB
- Export of Food and Drug Administration Regulated Products: Export Certificates
- Food and Drug Administration Recall Regulations

FDA Has Determined that the Following Drug Products Were Not Withdrawn from Sale for Reasons of Safety or Effectiveness
- SUBUTEX (buprenorphine hydrochloride)

Upcoming Meetings, Workshops, and Conferences

Drugs and Biologics
FDA/Society of Clinical Research Associates Conference on Food and Drug Administration Clinical Trial Requirements, Regulations, Compliance, and Good Clinical Practice, **March 11–12, 2015**, San Francisco, CA.

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

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

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

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

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

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

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

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

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

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

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

Advisory Committees
February 27, 2015: General and Plastic Surgery Devices Panel of the Medical Devices Advisory Committee Meeting (to discuss information regarding the panel-track PMA supplement to expand the indication for use for an injectable implant device to include subdermal implantation for hand augmentation to correct volume deficit in the hands)

March 4, 2015: Vaccines and Related Biological Products Advisory Committee Meeting (to discuss and make recommendations on the selection of strains to be included in the influenza virus vaccines for the 2015–2016 influenza season)

March 4, 2015: Science Board to the FDA Meeting (to provide the Board with progress reports on certain activities and to seek input regarding approaches to regulatory science training coordination)

March 9, 2015: Dermatologic and Ophthalmic Drugs Advisory Committee (to discuss an NDA for a cytolytic drug for treatment of submental fat in adults and to discuss development of systemic pediatric treatments for atopic dermatitis that does not respond to topical therapies)

March 17, 2015: Arthritis Advisory Committee Meeting (to discuss biologics license application for a proposed biosimilar for treatment of moderately to severely active Crohn's disease in patients who have had an inadequate response to conventional therapy)

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

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

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

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

Recent Notable Drug and Device Approvals/Clearances

FDA Approves Closure System to Permanently Treat Varicose Veins (February 20, 2015)

FDA Permits Marketing of First Direct-to-Consumer Genetic Carrier Test for Bloom Syndrome (February 19, 2015)

FDA Approves Lenvima for a Type of Thyroid Cancer (February 13, 2015)

FDA Permits Marketing of Fecal Incontinence Device for Women (February 12, 2015)

FDA Clears System to Reduce Stroke Risk During Stent and Angioplasty Procedures (February 9, 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.

Enforcement Updates

Recent Product Recalls
Injection drug products continued to be recalled for various issues. In recent weeks, two injection drug products were recalled, one for potential sterility issues and a second because consumers observed particulates floating in some of the vials. Additionally, a medical device manufacturer that had recalled a peripheral infusion system in December 2014, due to a device error that arose from incorrect labeling, issued a second notice stating that the recall has now been classified by FDA as Class I.

View a complete listing of FDA Recalls.

Recent Warning Letters
Since we last reported on enforcement actions in January 2015, FDA posted warning letters to drug and device manufacturers for violations related to CGMP ("Current Good Manufacturing Practices"), QSR ("Quality Systems Regulations"), and MDR ("Medical Device Reporting"). The amount of warning letters declined compared to when we last reported in January 2015, with only four warning letters sent to medical device manufacturers and three to drug manufacturers since our last *Update*.

FDA continues to cite medical device manufacturers for CGMP and QSR violations, including those related to device designs, maintaining device master records, complaint procedures, post-sterilization inspections, and device packaging and shipping containers. Recipients of these warning letters included manufacturers of in vitro diagnostic devices, intravenous tubing sets, and convenience packs for surgical procedures. One medical device manufacturer was also warned for failure to follow the MDR regulations and for marketing medical devices without the necessary marketing clearance or approval.

Drug manufacturers continue to receive warning letters for CGMP violations as well as misbranded drugs. CGMP violations include those related to preventing contamination, maintaining a sterile environment, and ensuring laboratory records included complete data. One manufacturer was also cited for failing to submit field alert reports within three working days of receipt of information concerning any significant change or deterioration in a distributed drug product.

FDA continues to monitor compounding pharmacies. One such pharmacy was warned after investigators noted that the pharmacy was not receiving valid prescriptions for individually identified patients. The compounding pharmacy was cited for practices that render the pharmacy ineligible for statutory exemptions from the laws that generally apply to drug manufacturers. The compounding pharmacy was additionally cited for violations relating to insanitary conditions and CGMP.

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

The Office of Prescription Drug Promotion ("OPDP") has issued no new warning letters since the last *Update*.

View a complete listing of 2014 OPDP Warning Letters.

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The draft guidance on registration provides a comprehensive list of the conditions that must be met for an outsourcing facility to qualify for the 503B exemptions and clarifies that registering with the FDA as an outsourcing facility indicates the intent of that facility's compounded drugs to be compounded in accordance with, and regulated under, FDCA Section 503B. FDA issued two draft guidance documents to further outline policies not addressed in the laws on compounding—a draft guidance on repackaging describes FDA's enforcement policy for repackaging compounded drugs (not including biologics), and a draft guidance on biologics describes FDA's enforcement policy for biological products that are mixed or repackaged without an approved biologics license application. The draft guidance on reporting explains the requirements for adverse event reporting for outsourcing facilities. Finally, the draft memorandum of understanding ("MOU") describes the responsibilities of a state that elects to sign on to the MOU for handling complaints related to compounded drugs and distribution of statutorily determined "inordinate amounts" of compounded drugs.

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