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

District Court Rules Against FDA in Off-Label Marketing Case

Last week, a federal judge in the Southern District of New York granted a preliminary injunction in favor of Amarin Pharma, Inc. ("Amarin") in its dispute against FDA asserting free speech rights to promote an approved drug for unapproved uses based on truthful and nonmisleading communications. The court held that, under Second Court precedent of *United States v. Caronia*, FDA may not prosecute a company for misbranding where the only conduct alleged is truthful and nonmisleading statements promoting "off-label" use. The decision reiterated the *Caronia* principle that prosecution of such conduct violates the First Amendment by unduly restricting commercial speech. Amarin has petitioned the court to restrain FDA from taking any enforcement action with respect to the company's proposed communications. The preliminary injunction allows for such marketing pending a decision on the merits but cautions Amarin that it bears the responsibility of ensuring that communications to doctors remain truthful and nonmisleading in the future. FDA has 60 days to appeal the district court's decision.

Germany Criminalizes Corruption in the Health Care System

On July 29, 2015, the German government adopted a draft act against corruption in the health care system ("Draft Act"), addressing in particular the relationships between life sciences companies and health care professionals. The Draft Act marks a step in the fight against corruption in Germany but, at the same time, raises a number of issues due to its

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UPCOMING EVENTS

September 17–18, 2015: Laura Laemmle-Wiedenfeld will give a presentation on *Damages and Penalties*

broad wording. The penalties are monetary fines or imprisonment, in certain serious cases, of between three months and five years of imprisonment. For more information on the Draft Act, see the recent Jones Day *Alert.*

FDA Revises Guidance on "Refuse to Accept" Policy

On August 4, 2015, FDA issued a revised version of its guidance document, *Refuse to Accept Policy for 510(k)s*, which outlines the criteria and processes the agency uses in determining whether 510(k) submissions meet the threshold for substantive review regarding substantial equivalence. FDA indicated the revisions should help reduce the number of submissions that are considered "administratively incomplete upon receipt." To that end, FDA made changes such as removing criteria deemed noncritical, allowing reviewer discretion where a file lacks certain noncritical information, separating or consolidating criteria into appropriate categories, and improving cross-references for the submission checklist. The revisions take effect October 1, 2015.

FDA Announces Quality Metrics Draft Guidance and Public Meeting

FDA recently released a draft guidance document titled, *Request for Quality Metrics*, designed to explain how the Center for Drug Evaluation and Research ("CDER") and the Center for Biologics Evaluation and Research ("CBER") collect and use quality metrics to support improvement and innovation in the pharmaceutical manufacturing industry. In conjunction with releasing and soliciting comments on the draft guidance document, FDA announced it will hold a public meeting on the topic on August 24, 2015.

Under the FCA at the CLE International Conference in San Francisco, CA.

October 1–2, 2015: Colleen Heisey will moderate a session titled *Challenging Hypotheticals*, at the Food & Drug Law Institute's program on Advertising and Promotion for the Pharmaceutical, Medical Device, Biological, and Veterinary Medicine Industries, in Washington, D.C.

October 15-16, 2015: Colleen Heisey will moderate a panel discussion on FDA guidance and policy at the *Medical Device Law 2015 Conference*, cosponsored by the American Bar Association, Medical Device Manufacturers Association, and FDLI, in Washington, D.C.

October 21, 2015: Maureen Bennett will give a presentation on *International Clinical Research Issues* to the Boston Bar Association's Health Law Education Committee.

October 24, 2015: Maureen Bennett will speak about "International Clinical Research Issues" at the ABA's Section of International Law fall meeting in Montreal, Canada.

RELATED PRACTICES

FDA Regulatory & Compliance Counseling

Health Care

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The draft guidance and meeting reflect FDA's efforts in the development and planned implementation of a quality metrics program launched under section 704 of the Federal Food, Drug, and Cosmetic Act, as amended by the Food and Drug Administration Safety and Innovation Act to enhance the agency's record-requesting authority in connection with drug establishment inspections.

OPDP Warning Letter Targets Social Media Campaign

FDA's Office of Prescription Drug Promotion ("OPDP") issued two warning letters regarding pharmaceutical product promotion in a two-week timeframe, most recently citing social media posts. On August 7, 2015, OPDP wrote a warning letter regarding claims made in a social media campaign by a reality TV star about a product intended to treat the nausea and vomiting associated with pregnancy in women who do not respond to conservative management. The celebrity had endorsed the product with descriptive posts on her Facebook, Instagram, and Twitter accounts. A complaint about the material was submitted to FDA via its Bad Ad Program, and in the warning letter, OPDP stated it considered the material false or misleading because it omitted risk information and material facts. In addition, on July 27, 2015, OPDP warned another company regarding a professional sales aid, which the agency asserts omits risk information, fails to adequately convey the product's indication, and makes unsubstantiated claims. In each letter, FDA has requested

the companies issue corrective messaging, which should be distributed using the same media, and generally for the same duration and frequency as the original material. These actions follow a relatively quiet period from OPDP; while the office has issued several untitled letters in 2015, the last-posted warning letter was from September 2014.

FDA Releases User Fee Rates for FY2016
On August 3, 2015, FDA announced fiscal year 2016 ("FY2016") user fee rates for animal drugs, animal generic drugs, biosimilars, generic drugs, medical devices, human drug compounding outsourcing facilities, and prescription drugs, which are listed in the attached chart. The fee rates are effective October 1, 2015, and will remain in effect through September 30, 2016.

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Other News

Technologists Explore Impact of FDA's First Approved 3D-Printed Drug

EMA Seeks Comments on Fast-Track Routes for Medicines that Address Unmet Needs

FDA Approves Nonsurgical Temporary Balloon Device to Treat Obesity

Hospitals, Others Advised About Medical Device Cybersecurity Vulnerabilities

EU and Swiss Regulators Sign Confidentiality Arrangement for Improved Oversight of Medicines

EMA Consults on Draft Guidance on Arrangements Necessary to Implement Regulation (EC) No 507/2006

FDA Announces New Search Tool for Agency's Guidance Documents

Regulatory Updates

FDA Announces Classification of Internal Tissue Marker
In the August 5, 2015, *Federal Register,* FDA announced the classification of the Internal Tissue Marker into class II (special controls). Various testing measures and labeling will be required to mitigate the identified risks of adverse tissue reaction, ineffective marking, and improper use.

FDA Classifies External Upper Esophageal Sphincter Compression Device
In the August 4, 2015, *Federal Register,* FDA published its classification of the external upper esophageal sphincter compression device into class II (special controls). Biocompatibility assessment, labeling, and other methods will be required to mitigate the identified risks of adverse tissue reaction, overcompression, and malfunction.

FDA Classifies *Trichomonas Vaginalis* Nucleid Acid Assay
In the August 4, 2014, *Federal Register,* FDA announced the classification of *Trichomonas vaginalis* nucleic acid assay into class II (special controls). Device description requirements, performance studies, and labeling will be required and are explained in the FDA document, "Class II Special Controls: Nucleic Acid Amplification Assays for Detection of *Trichomonas vaginalis.*" Identified risks, such as false test results, require special controls to provide reasonable assurance of safety and effectiveness.

FDA Announces FY2016 Rates
In the August 3, 2015, *Federal Register,* FDA announced rates for FY2016 through a series of notices:

- Prescription Drug User Fees

- Abbreviated New Drug Applications (ANDAs), Prior Approval Supplements to Approved ANDAs, Drug Master Files, Generic Drug Active Pharmaceutical Ingredient Facilities, Finished Dosage Form Facilities
- Medical Device User Fees
- Outsourcing Facility Fees
- Food Safety Modernization Act Domestic and Foreign Facility Reinspection, Recall, and Importer Reinspection Fees
- Animal Generic Drug User Fees and Payment Procedures
- Animal Drug User Fee Rates and Payment Procedures
- Biosimilar User Fee Rates

FDA Extends Comment Period on Risk Assessment
In the July 30, 2015, *Federal Register,* FDA announced the extension to the comment period for the risk assessment titled, "Multicriteria-Based Ranking Model for Risk Management of Animal Drug Residues in Milk and Milk Products." FDA requests comments to help improve the ranking model approach, the scientific data and assumptions used to inform scoring used in the model, the selection of animal drugs evaluated, and the clarity and the transparency of the risk assessment. ***Comments are now due October 27, 2015.***

FDA Issued the Following Draft and Final Guidance Documents:
Guidance for Industry: Over-the-Counter Pediatric Oral Liquid Drug Products Containing Acetaminophen, August 5, 2015, *Federal Register.*

Guidance for Industry: Recommendations for Premarket Notification (510(k)) Submissions for Nucleic Acid-Based Human Leukocyte Antigen Test Kits Used for Matching of Donors and Recipients in Transfusion and Transplantation, August 3, 2015, *Federal Register.*

Revised Draft Guidance for Industry (Revision 2): Brief Summary and Adequate Directions for Use: Disclosing Risk Information in Consumer-Directed Print Advertisements and Promotional Labeling for Prescription Drugs, August 6, 2015, *Federal Register*.
Comments are due October 5, 2015.

Draft Guidance for Industry: Dissolution Testing and Specification Criteria for Immediate-Release Solid Oral Dosage Forms Containing Biopharmaceutics Classification System Class 1 and 3 Drugs, August 3, 2015, *Federal Register.* ***Comments are due October 2, 2015.***

Draft Guidance for Industry: Request for Quality Metrics, July 28, 2015, *Federal Register.*
Comments are due September 28, 2015.

Draft Guidance for Industry: Bracketing and Matrixing Designs for Stability Testing of New Veterinary Drug Substances and Medicinal Products, July 31, 2015, *Federal Register.*

FDA Announced that the Following Collections Have Been Submitted to OMB:
- Registration and Product Listing for Owners and Operators of Domestic Tobacco Product Establishments and Listing of Ingredients in Tobacco Products
- Guidance for Industry: Adverse Event Reporting for Outsourcing Facilities Under Section 503B of the Federal Food, Drug, and Cosmetic Act

FDA Announced that the Following Collections Have Been Approved by OMB:
- State Enforcement Notifications

EU Regulatory Notices

EMA Recommends 10 New Medicines Marketing Authorization
During its July 2015 meeting, the European Medicines Agency ("EMA") Committee for Medicinal Products for Human Use ("CHMP") recommended for marketing authorization 10 new medicines. These include: Praluent (alirocumab), to lower high levels of cholesterol in the blood of people who are unable to control their cholesterol despite taking optimal

doses of statins or who cannot take statins; Intuniv (guanfacine), to treat attention deficit hyperactivity disorder in children and adolescents aged 6 to 17 years old; Cresemba, for the treatment of aspergillosis and mucormycosis; and Zerbaxa (ceftolozane/tazobactam), for the treatment of complicated intra-abdominal infections, acute pyelonephritis, and complicated urinary tract infections. The CHMP also gave a positive scientific opinion in respect of Mosquirix (*Plasmodium falciparum* and hepatitis B vaccine), the first vaccine for malaria to be assessed by a regulatory agency for use outside the EU.

EMA Publishes Guideline on Processing of Renewals in the Centralized Procedure
On July 28, 2015, EMA published a draft guideline on the processing of renewals in the centralized procedure. The guideline, which is not legally binding, has been developed by the CHMP with the aim of giving procedural guidance to marketing authorization holders. ***Public comments are due September 14, 2015***.

EMA to Publish Public-Friendly Herbal Medicine Information
EMA has announced that it will systematically publish summaries of the recommendations of its Committee on Herbal Medicinal Products ("HMPC") regarding the medicinal uses of an herbal substance in easy-to-understand, public-friendly language with the aim of helping the public make informed choices when using such medicines for self-medication. The summaries will include information on the herbal substance assessed, HMPC's conclusions on its recommended uses, the data supporting the recommendations, and the potential side effects associated with the use of the herbal substance.

EMA Call for Civil Society Members for Two Committees
The Health and Food Safety Directorate-General of the European Commission has launched calls for expressions of interest to represent civil society in two scientific committees of EMA: the Pharmacovigilance Risk Assessment Committee, which is responsible for assessing all aspects of the risk management of medicines for human use, and the Committee for Advanced Therapies, which is responsible for assessing the quality, safety, and efficacy of advanced-therapy medicinal products and for following scientific developments in the field. ***Expressions of interest are due September 30, 2015***.

Upcoming Meetings, Workshops, and Conferences

Public Meeting on "Evidentiary Considerations for Integration of Biomarkers in Drug Development," **August 21, 2015**, in Baltimore, MD.

Public Meeting on Quality Metrics, **August 24, 2015**, in Silver Spring, MD.

Public Workshop titled, "Surrogate Endpoints for Clinical Trials in Kidney Transplantation," **September 28, 2015**, in Arlington, VA.

FDA/CDC/NLM Workshop on Promoting Semantic Interoperability of Laboratory Data, **September 28, 2015**, in Silver Spring, MD.

Sixth Annual Coalition Against Major Diseases/Food and Drug Administration Scientific Workshop, **October 15, 2015**, in Silver Spring, MD.

Public Meeting on Patient-Focused Drug Development for Nontuberculous Mycobacterial Lung Infections, **October 15, 2015**, in Silver Spring, MD. ***Comments are due December 15, 2015.***

Medical Devices
Stakeholder Meeting—MDUFA Reauthorization, **September 15, 2015**, in Silver Spring, MD.

Public Workshop on Medical Device Patient Labeling, **September 29–30, 2015**, in Silver Spring, MD.

Public Workshop on Acute Ischemic Stroke Medical Devices Trials, **October 6, 2015**, in Silver Spring, MD.

Public Workshop titled, "Non-Microbial Biomarkers of Infection for In Vitro Diagnostic Device Use," **October 16, 2015**, in Silver Spring, MD.

Advisory Committees
Joint Meeting of the Anesthetic and Analgesic Drug Products Advisory Committee and the Drug Safety and Risk Management Advisory Committee, **September 10–11, 2015**, in Silver Spring, MD.

Pediatric Advisory Committee, **September, 16, 2015**, in Silver Spring, MD.

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 nonsurgical temporary balloon device to treat obesity (July 28, 2015)

For additional information on drug and device approvals and clearances, please visit FDA's web pages on Drug Approvals and Databases (includes biologics) and Device Approvals, Denials, and Clearances.

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FDA User Fees—FY2016

	FY 2016	FY 2015	% Change
Animal drug user fee rates			
Animal drug application	$351,100	$400,600	-12.4
Supplemental animal drug application	$175,550	$200,300	-12.4
Annual product fee	$7,790	$8,075	-3.5
Annual establishment fee	$105,950	$104,150	1.7
Annual sponsor fee	$101,000	$94,450	6.9
Animal generic drug user fee rates			
Abbreviated generic animal drug application	$233,330	$189,200	23.3
Abbreviated generic animal drug application (50% of application fee)	$116,650	$94,600	23.3
Generic new animal drug product	$8,705	$8,500	2.4
Generic new animal drug sponsor paying 100% of the sponsor fee	$83,800	$80,900	3.6
Generic new animal drug sponsor paying 75% of the sponsor fee	$62,850	$60,675	3.6
Generic new animal drug sponsor paying 50% of the sponsor fee	$41,900	$40,450	3.6
Biosimilar user fee rates			
Initial biosimilar biological product development fee	$237,420	233,520	1.7
Annual biosimilar biological product development fee	$237,420	233,520	1.7
Reactivation fee	$474,840	467,040	1.7
Biosimilar biological product application requiring clinical data	$2,374,200	2,335,200	1.7
Biosimilar biological product application not requiring clinical data	$1,187,100	1,167,600	1.7
Biosimilar biological product supplement with clinical data	$1,187,100	1,167,600	1.7
Biosimilar biological product establishment fee	$585,200	569,200	2.8
Biosimilar biological product fee	$114,450	110,370	3.7
Generic drug user fee rates			
Abbreviated new drug application fee	$76,030	58,730	29.5

Prior approval supplement fee	$38,020	29,370	29.5
Drug master file fee	$42,170	26,720	57.8
Domestic active pharmaceutical ingredient facility fee	$40,867	41,926	-2.5
Foreign active pharmaceutical ingredient facility fee	$55,867	56,926	-1.9
Domestic finished dosage form facility fee	$243,905	247,717	-1.5
Foreign finished dosage form facility fee	$258,905	262,717	-1.5
Medical device user fee rates (standard)			
Premarket application, premarket report, efficacy supplement	$261,388	250,895	4.2
Panel-track supplement	$196,041	188,171	4.2
180-day supplement	$39,208	37,634	4.2
Real-time supplement	$18,297	17,563	4.2
510(k) premarket notification submission	$5,228	5,018	4.2
30-day notice	$4,182	4,014	4.2
513(g) request for classification	$3,529	3,387	4.2
Annual fee for periodic reporting on a class III device	$9,149	8,781	4.2
Annual establishment registration	$3,845	3,646	5.5
Outsourcing facility fee rates			
Small business establishment fee	$5,203	5,103	2.0
Non-small business establishment fee	$16,465	16,442	0.1
Reinspection fee	$15,610	15,308	2.0
Prescription drug user fee rates			
Application requiring clinical data	$2,374,200	2,335,200	1.7
Applications not requiring clinical data	$1,187,100	1,167,600	1.7
Supplements requiring clinical data	$1,187,100	1,167,600	1.7
Establishments	$585,200	569,200	2.8
Products	$114,450	110,370	3.7

Return to Homepage