

To: Our Clients and Friends

April 13, 2010

## Pharmaceuticals, Medical Devices and Biologics Regulatory and Policy Bulletin



### **Top News**

#### **FDA to Increase Prosecutions**

The FDA has stated that it will increase prosecutions against corporate officials as part of a drive to improve its Office of Criminal Investigations. The statement came in the midst of the release of a GAO report critical of the agency, which recommended that the office be assigned measurable performance goals and undergo regular monitoring.

#### **Office of Oncology Drug Products Undergoing Reorganization**

The FDA's Office of Oncology Drug Products is currently undergoing a reorganization aimed at making its structure more similar to the rest of the review offices in the Center for Drug Evaluation and Research. Under the reorganization, the office will be organized by cancer specialty and the new hematology division will begin to absorb products from the other two oncology divisions and will include hematologic malignancies in a manner similar to the organization of academic medical centers. The reorganization of the drug review divisions is also set to allow medical imaging staff to assume a broader role in consulting on trials that use medical images as an endpoint.

#### **FDA Violation Letter Indicates that it Considers Webcasts as Promotional Materials**

The recent notice of violation letter that the FDA sent to Biogen Idec may indicate that the FDA is gearing up to treat all social media interactions, including webcasts, as promotional materials – even when the purpose of such webcasts is to inform physicians. At issue in the letter are eight Biogen webcasts, which were ostensibly used to update treating neurologists on the safety profile of Tysabri for multiple sclerosis. DDMAC found that the webcasts included numerous statements that minimized the risk of PML.

#### **Canada's Molybdenum Announcement May Affect Device Industry**

The imaging industry is beginning to worry about the development of alternative sources of molybdenum 99, used to produce the most widely used diagnostic isotope. Canada's National Research Universal (NRU) has announced that it will no longer produce the isotope after 2016.

## CMS to Release Guidance on Medicaid Rebates

CMS has indicated that it will release in the near future a guidance document that will announce whether states can keep a percentage of rebates on brand-name drugs purchased through managed care organizations. The document will also explain how the agency plans to retroactively collect Medicaid drug rebates from states, which previously kept the savings from any discounts they negotiated beyond the federal government's original 15.1 percent floor.

## FDA Considering SAFEKIDS Expansion

The FDA has released a request for information that indicates that the agency is considering an expansion of its Safety of Key Inhaled and Intravenous Drugs in Pediatrics (SAFEKIDS) Initiative, a research program that studies the effects of sedatives and anesthetics on children and infants, and particularly on their neurocognitive development.

## Congresswoman to Push FDA to Use Independent Research for New Drugs

Congresswoman Rosa DeLauro (D-CT) has indicated that she intends to push the FDA to use independent science to assess the safety and efficacy of new therapies, rather than relying on the industry's statements. A spokesperson from DeLauro's office indicated that DeLauro also intends to meet with FDA Chief Scientist Jesse Goodman to discuss the agency's renewed focus on regulatory science.

## Judge Orders Abbott to Turn Over Emails Relating to Depakote Marketing

A US District Judge has [ordered Abbott Laboratories](#) to turn over emails involving the marketing of its drug Depakote to the Justice Department. The Department is currently investigating whether the company marketed the drug for unapproved, or off-label, treatment for agitation and aggression in the elderly. The case against the company is currently pending in US District Court in the Western District of Virginia.

## China Creates New Center for Device Standards

China has created a new Management Center for Medical Device Standards within China's State Food and Drug Administration. The Center will oversee the formulation and revision of device standards, organize a national technical committee to research device standards systems, and propose standardization policies. The Center is also expected to provide technical advice on medical device nomenclature, classification and unique device identifiers.

## Publications

The FDA has published a [draft guidance for industry](#) entitled "Draft Guidance for Industry on Guidances for the Validation of Analytical Methods Used in Residue Depletion Studies."

The FDA has published a [draft guidance for industry](#) entitled "Draft Guidance for Industry on Studies to Evaluate the Metabolism and Residue Kinetics of Veterinary Drugs in Food-Producing Animals: Comparative Metabolism Studies in Laboratory Animals."

The FDA has published a [draft guidance for industry](#) entitled "Draft Guidance for Industry on Studies to Evaluate the Metabolism and Residue Kinetics of Veterinary Drugs in Food-Producing Animals: Marker Residue Depletion Studies to Establish Product Withdrawal Periods."

The FDA has published a [draft guidance for industry](#) entitled "Draft Guidance for Industry on Studies to Evaluate the Metabolism and Residue Kinetics of Veterinary Drugs in Food-Producing Animals: Metabolism Study to Determine the Quantity and Identify the Nature of Residues (MRK)."

The FDA has published a [guidance](#) entitled "Q4B Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions; Annex 10: Polyacrylamide Gel Electrophoresis General Chapter." The guidance was prepared under the auspices of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH).

The FDA has published the [CDRH Ombudsman's](#) 2009 annual report.

The FDA has published its listing of [March 2010 510\(k\) Clearances](#).

The FDA has published a [webinar](#) to better inform stakeholders about the Prescription Drug User Fee Act program.

A recent study published in the *Journal of the American Medical Association* found that the proportion of complex, device-intensive spine surgeries has increased in recent years compared to simpler procedures, resulting in more complications and higher costs but not necessarily more benefit.

PricewaterhouseCoopers has published a report, entitled *HealthCast 2020: The Customization of Diagnosis, Care and Cure*, finding that a rise in chronic disease; technology-enabled mass customization; and improved understanding of the impact of genetic, behavioral and socio-economic factors on health will lead to a beneficial climate for device and diagnostic companies.

In an [annual report](#) to HHS, New York State's Attorney General Andrew Cuomo stated that his Medicaid Fraud Control Unit recovered more than \$283 million and obtained 148 criminal convictions in 2009.

## Approvals

The FDA has granted approval to HeartWare International to recruit 54 additional patients for a clinical study of its Ventricular Assist System.

The FDA has approved an expanded indication for Salix Pharmaceuticals' Xifaxan to reduce the risk of recurrence of overt hepatic encephalopathy in patients with liver failure.

## Recalls, Warnings, and Notifications

The FDA has updated its online information concerning the [Class I recall](#) of Teleflex Incorporated - Arrow International Custom Intravenous (IV) Administration Products (IV Tubing Sets and Accessories) and Certain Arrow Arterial Embolectomy Catheters.

The FDA has published an [update](#) on "Follow up to the Public Health Alert about Changes to the Heparin Sodium USP Monograph."

The FDA has published [updated information about triclosan](#) for consumers. The FDA is currently conducting a scientific review of triclosan, a common ingredient added to many consumer products to reduce or prevent bacterial contamination, in light of animal studies raising questions about triclosan's safety.

The FDA has issued a warning [letter](#) to Guidewire Technologies for not following sterilization procedures, adequately validating processes and conducting quality audits.

The FDA has issued a warning letter to Biological Controls for several quality system (QS) and documentation failures, including failure to establish a quality policy or audit procedures.

The FDA has issued a warning letter to Salix Pharmaceuticals for omitting risk information and suggesting that its Metozolv orally disintegrating tablet is safer and more effective than evidence has demonstrated.

The FDA has issued a warning letter to Edwards Lifesciences for failure to report within required time frames six serious adverse events linked to its annuloplasty rings and a replacement heart valve.

## Business News

CMS has determined that it will suspend Aetna from enrolling new Medicare patients or marketing its plans, in part due to the company's improper processing of expedited appeal requests. The company was also cited for failing to provide transitional drug assistance to beneficiaries who received coverage in 2009 for certain drugs that the company cut from its formulary in 2010.

Arizona-based TGen Drug Development (TD2) and the UK's Horizon Discovery Limited have announced that they have formed a partnership to customize treatments for individuals with cancer.

Biogen Idec Inc. is set to start [clinical trials](#) this year for a screening tool to assess the odds that a patient taking the multiple sclerosis treatment Tysabri will get progressive multifocal leukoencephalopathy. Biogen has indicated that it is preparing for clinical trials involving 9,000 people to determine the rates of false positives and false negatives.

Merck KGaA's CEO Karl-Ludwig Kley has stated that the [company's purchase](#) of U.S. biotechnology equipment supplier Millipore Corp. for \$6 billion is "worth every euro," and announced that the deal will likely close in the second half of 2010. The company has also indicated that it will resubmit its cladribine application to the FDA as soon as possible. The FDA rejected the application in November.

Sanofi Aventis announced that its expanded R&D centre in China opened for business last week.

An FDA official has reported that injectable and once-weekly versions of the diabetes drug Byetta may be tied to [increased cancer risk](#).

The FDA is drawing criticism for its policy that allowed URL Pharma to brand its old, unapproved gout drug colchicine as Colcrys and use that FDA approval to block competitors from marketing their versions, which allowed the company to increase the price of the drug.

Novartis and Roche Holding have warned U.K. officials that they might halt their operations in the country, in protest of strict rules on drug pricing and safety trials.

Some reports are predicting that comparative-effectiveness research (CER) could increase the value of pharmaceuticals and biologics by holding alternative therapies to the same standards. HHS Secretary Kathleen Sebelius recently indicated that CER could also be used to test the value of complementary and alternative medicines.

Louis Jacques, director of CMS' coverage and analysis group, suggested at a recent conference that sponsors hold joint meetings with the FDA and Centers for Medicare & Medicaid Services early on to discuss clinical trial designs.

CDRH is currently attempting to create a clear approval path for pediatric circulatory support devices, while also examining any potential neurological side effects. To assist with its determination of whether and how to tie neurological function and neurocognitive assessments into clinical trials, the agency is turning to industry.

Cell Therapeutics, Inc. has indicated that it intends to pursue an expanded access program for its non-Hodgkin's lymphoma drug Pixuvri while it conducts a new combination therapy trial to satisfy concerns raised by the FDA in a "complete response" letter the company received on the drug's NDA.

Steris has indicated that it is seeking clarification from the FDA regarding the 510(k) clearance letter it issued for Steris' new System 1E device and the caveat in the letter that the device "should not be used on devices that must be sterile."

CareFusion has indicated that its planned acquisition of needleless intravenous infusion device maker Medegen for \$225 million acquisition will improve its ability to compete on claims of reducing hospital-acquired infections.

At a recent summit, economists and industry analysts warned that a comprehensive review of manufacturer models for pricing and putting a valuation on medical devices is set to occur now that health care reform is law. They also warned that, as hospitals face increasing pressure to limit the costs of a patient's episode of care, technologies that do not fit easily within new Medicare incentives will face greater price and market pressures. Industry is also reporting concerns that market-based fees and increased Medicaid rebates will start several years before drug manufacturers will see any benefit of an expanded market from health care reform, further increasing price pressures.

Industry reports are indicating that medical device acquisition activity is poised to rebound and possibly accelerate through the rest of 2010.

The FDA's decision not to accept Forest's proposed revised indication for Daxas appears to be a primary reason behind the rejection of the drug by the Pulmonary-Allergy Drugs Advisory Committee, which voted 9-6 that the drug was effective and 9-6 that the drug was safe, but 10-5 rejecting the cost-benefit ratio.

The Wall Street Journal is reporting that the FDA is currently considering for approval lorcaserin, Qnexa and Contrave, three new anti-obesity drugs.

Javelin Pharmaceuticals Inc. announced that it received a better acquisition offer from Hospira Inc. and plans to end a competing bid made by Myriad Pharmaceuticals Inc.

Roche Holding AG has indicated that it plans to [continue licensing medicines in 2010](#), and that it expects to sign a similar number of deals to 2009's 65 agreements.

As drug and device companies begin to [disclose payments made to doctors](#) who act as consultants or speakers, some online companies are finding a business opportunity in monitoring and reporting on those companies' databases.

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## Public Meetings

### FDA to Host Public Workshop

The FDA has announced that it will host a public workshop entitled "Developing Guidance on Naming, Labeling, and Packaging Practices to Reduce Medication Errors." The purpose of the public workshop is to initiate constructive dialogue and information sharing among regulators, researchers, the pharmaceutical industry, health care organizations, health care professionals, and others from the general public about the design of drug and therapeutic biologic container labels, carton labeling, and product packaging, and practices to develop proprietary names to reduce medication errors. The workshop will be held on Thursday and Friday, June 24 and 25, 2010, from 8:30 a.m. to 5 p.m. each day. Register to make a presentation at the workshop by May 25, 2010. More information is available at <http://edocket.access.gpo.gov/2010/2010-8233.htm>.

### FDA to Host Cardiovascular Workshop

The FDA is announcing a public workshop entitled "FDA/NHLBI/NSF Workshop on Computer Methods for Cardiovascular Devices: The Integration of Nonclinical and Clinical Models." The workshop will include a smaller, optional session entitled "Microstructure Modeling Session." The FDA is cosponsoring the workshop with the National Heart Lung and Blood Institute of the National Institutes of Health and the National Science Foundation. The optional session will be held on June 9, 2010, from 1 p.m. to 5:30 p.m. and the public workshop will be held on June 10 and 11, 2010, from 8 a.m. to 5 p.m. in Rockville, Maryland. More information is available at <http://edocket.access.gpo.gov/2010/2010-8311.htm>.

### FDA to Hold Public Meeting on ICH

The FDA is announcing a public meeting entitled "Preparation for ICH Steering Committee and Expert Working Group Meetings in Tallinn, Estonia" to provide information and receive comments on the International Conference on Harmonisation (ICH) as well as the upcoming meetings in Tallinn, Estonia. The meeting will be held on Wednesday, May 5, 2010, from 2:30 p.m. to 4:30 p.m. in Rockville, Maryland. More information is available at <http://edocket.access.gpo.gov/2010/2010-8379.htm>.

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## More Information

Archived issues of the Bryan Cave Pharmaceuticals, Medical Devices and Biologics Regulatory and Policy Bulletin and other FDA news bulletins are available at [www.bryancave.com](http://www.bryancave.com) on the [FDA Practice Bulletins web page](#).

If you have any questions regarding any of these issues, please contact:

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