

To: Our Clients and Friends

March 26, 2010

Pharmaceuticals, Medical Devices and Biologics Regulatory and Policy Bulletin



Top News

House Passes Health Reform Bill

On Sunday, the House passed the health reform bill, which was signed into law by President Obama on Tuesday. However, the House had to vote again on changes to the landmark overhaul of the country's health system after the Senate's parliamentarian rejected two provisions in the measure. The House passed the reconciliation bill Thursday evening in a 220-207 vote.

Device industry analysts are reporting that the final device industry tax will be manageable by the sector at large, but that costs will fall more heavily on smaller companies. The provision applies a 2.3% excise tax on manufacturers or distributors for each device sale made to a hospital or other customer. The only exemptions from the tax are for sales of products sold at retail directly to consumers, along with all eyeglasses, contact lenses and hearing aids.

Perhaps the most significant FDA-related provision in the bill is the approval pathway for biosimilars, which will allow drug makers to rely in part on other products' clinical data to gain approval. Stakeholders expect FDA to be cautious with its new authority, and the agency has sent mixed signals about whether it is ready to begin reviewing biosimilars.

Republicans have unveiled a new "Repeal and replace" campaign slogan for use in the coming November elections. In addition, state Attorneys General in Florida, Alabama, Nebraska, North Dakota, Pennsylvania, South Dakota, South Carolina, Texas, Utah, Washington, and Michigan have indicated that they will challenge the legislation's constitutionality, saying that the expansion of state-run Medicaid illegally places a fiscal burden on their budgets. Virginia Attorney General Kenneth T. Cuccinelli has also indicated that he will challenge the legislation.

Hamburg: FDA Will Invest in, Advance Regulatory Science

FDA Commissioner Margaret A. Hamburg has indicated that one of her top priorities is to enhance the agency's regulatory science capabilities by investing in regulatory science. Hamburg stated at the Pharmaceutical Research and Manufacturers of America (PhRMA) annual meeting that the FDA must advance its regulatory science in order to allow the pharmaceutical industry to continue to make full use of advances in science and technology.

Participants Call for More Input, Interaction with FDA

Participants, including AdvaMed, the Medical Device Manufacturers Association and the Medical Imaging and Technology Alliance (MITA), called for increased interaction between industry and the agency and greater opportunities for input, in a listening session with the FDA's Transparency Task Force. The meeting addressed longstanding concerns with the agency's process for keeping companies abreast of its most current regulatory expectations.

FDA May Seek Additional REMS Authority

An FDA official has signaled to House lawmakers that the agency might want additional authority to dictate the specifics of a Risk Evaluation and Mitigation Strategy in order to stem lengthy negotiations with drug makers and might also seek changes to how it handles REMS for generics drugs. A coalition representing local and regional pharmacists is urging the agency to include consultations with local pharmacists as a key part of Risk Evaluation and Mitigation Strategies, raising concerns about requirements in recent REMS that patients obtain their medications from a specialty pharmacy network.

FDA to Oversee Genzyme Factory

Genzyme has announced that the [FDA is preparing](#) to fine the [company](#) and will take a larger role in overseeing its operations at its factory in Boston following recent manufacturing problems.

FDA May Tighten Standards for Home Glucose Meters

FDA officials indicated at a March 16-17 public meeting that the agency may tighten standards for market clearance and CLIA waivers of home-use blood glucose meters. Doctors and researchers at the meeting agreed that FDA's current minimum accuracy criteria for blood glucose meters cleared for home use are not sufficient for insulin dosing decisions.

Committee Meets to Discuss Trial Design for Investigation of LABAs

The March 10-11 meeting of the Pulmonary-Allergy Drugs and Drug Safety and Risk Management Advisory Committees focused on potential study design for trials to investigate the potential for serious outcomes - such as hospitalization, intubation or death - with the use of long acting beta-2 adrenergic agonists (LABAs). The FDA announced that it is taking steps to control risks associated with the drugs, including requiring a class-wide Risk Evaluation and Mitigation Strategy and working through the agency's Safe Use partners to monitor whether actual use adjusts based on the new safety measures. However, at the meeting, some committee members questioned whether classical clinical trials are the best method for gathering the desired information.

Pharma Companies Facing Increased Litigation Relating to False Patent Marking

In recent months, pharmaceutical companies have been hit with a wave of whistleblower suits claiming they intentionally included expired patents on their product labeling to deter competition. The complaints arose after a December ruling by the U.S. Court of Appeals for the Federal Circuit that that the false marking statute explicitly permits qui tam actions to allow individuals to help control false marking. Since the decision, eleven pharma companies have been sued for false patent marking.

Ontario Government Taking Measures to Lower Prices of Generics

The Ontario government has introduced legislation to curb the price of generic drugs that would ban the \$750 million paid annually by generic drug manufacturers to pharmacies on taxpayer-funded drugs for welfare recipients.

Obama May Nominate Berwick as CMS Administrator

Reports are circulating that the White House may announce its nomination of Harvard professor and pediatrician Donald Berwick to serve as CMS Administrator.

Publications

The CDER Ombudsman's Office has published its [2009 Annual Report](#).

The FDA has updated its listing of [Individual Product Bioequivalence Recommendations](#).

A recent study published in the [American Journal of Roentgenology](#) found that X-rays fail to spot as much as nearly a third of fractures in the bones of the hip and pelvis.

An editorial published in the *Journal of the American Medical Association* is calling for industry-sponsored drug research to be analyzed by scientists [without ties to the company](#) developing a product.

Consumer advocates have stated their support for revising the FDA drug approval process to mandate active comparator trials, as proposed in a recent article in the *Journal of the American Medical Association*. The article argues that requiring active comparator trials as part of the FDA approval process would reduce the amount of "tax-payer-funded" comparative effectiveness research needed and could cut down on health care costs.

A study published in [BMJ](#) found that, although the 2001 Consolidated Standards of Reporting Trials (CONSORT) statement, led to improvement in reporting, the overall quality of reporting remained inadequate.

An article published in the *Journal of the American Medical Association* has found that clinical trials that finish early due to positive treatment effects often have misleading findings.

GAO has published a report recommending that the FDA clarify its goals in planning and management, as well as set better performance standards to boost oversight of drugs, medical devices and food.

IMS Health has published a report recommending that pharmaceutical companies more aggressively target emerging markets, including Venezuela, Poland, Argentina, Vietnam, South Africa, Thailand, Indonesia, Romania, Egypt, Pakistan and Ukraine, as these countries stand to contribute 48 percent of annual market growth in 2013.

Japan's Pharmaceuticals and Medical Devices Agency has posted a presentation advising that manufacturers of active pharmaceutical ingredients (APIs) seeking to sell their products in Japan must receive accreditation as a foreign manufacturer from the country's Ministry of Health, Labour and Welfare.

Approvals

An FDA advisory panel has [recommended approval](#) for Medtronic's MRI-safe pacemaker.

The FDA has approved the use of Salix Pharmaceuticals' Xifaxan to treat adults with hepatic encephalopathy.

The FDA has approved a resubmission plan for Transcept Pharmaceuticals' insomnia drug Intermezzo that involves new packaging to foil inadvertent re-dosing and a next-day highway driving study.

An FDA advisory panel has recommended that Boston Scientific's cardiac resynchronization therapy defibrillators (CRT-Ds) be approved for use in some healthier heart failure patients.

Recalls, Warnings, and Notifications

The FDA is [recommending that healthcare professionals temporarily suspend the use of Rotarix](#), a [vaccine](#) used to prevent rotavirus disease. FDA's [recommendation](#) is a precaution taken while the agency learns more about the situation. The agency has learned that DNA from porcine circovirus type 1 (PCV1) is present in Rotarix.

The FDA has notified healthcare professionals that the agency [has been notified by Boston Scientific](#) that it has stopped shipment and started recalling all of its implantable cardioverter defibrillators (ICDs) and cardiac resynchronization therapy defibrillators (CRT-Ds) that have not yet been implanted.

The FDA is warning patients and healthcare providers about the [potential for increased risk of muscle injury](#) from the cholesterol-lowering medication Zocor (simvastatin) 80 mg. Although muscle injury (called myopathy) is a known side

effect with all statins, the warning highlights the [greater risk of developing muscle injury](#), including rhabdomyolysis, for patients when they are prescribed and use higher doses of this drug.

The Division of Drug Marketing, Advertising, and Communications (DDMAC) of the FDA has reviewed a Substance Abuse Patient Profile Sell Sheet (RAM-01071) (Sell Sheet) for RozeremTM (ramelteon) Tablets (Rozerem) submitted by Takeda Pharmaceuticals North America, Inc. and has found that the [Sell Sheet is false or misleading](#) because it makes unsubstantiated superiority presentations, omits and minimizes the risks associated with the use of Rozerem, omits material facts, and makes a misleading claim about Rozerem.

The FDA has issued a [warning letter](#) to Xian Libang Pharmaceutical Co., Ltd. related to a July 27-30, 2009 inspection of its active pharmaceutical ingredient (API) manufacturing facility, Xian Libang Pharmaceutical Co., Ltd. located at ShanXi, China.

The Medicines Company and the FDA are notifying healthcare professionals of the [expansion of the nationwide recall](#) of Cleviprex (clevidipine butyrate) injectable emulsion.

Merck KGaA has stated that it has [suspended all studies](#) of the experimental therapeutic cancer vaccine Stimuvax after a patient with multiple myeloma developed encephalitis while taking it.

Merck KGaA has stated that it is [reviewing heart risks](#) of its drug Erbitux in response to a request by the European Medicines Agency.

A CMS advisory panel has concluded that high doses of erythropoiesis-stimulating agents used to treat anemia increased heart risks in patients with chronic kidney disease.

The FDA has issued a warning letter to G3 for good manufacturing practice (GMP) issues that need to be resolved.

Business News

The United States Patent and Trademark Office has once again [denied](#) the Medicines Company's request to extend the life of the patent protecting its blood thinner Angiomax.

Reckitt Benckiser Group PLC has announced that it is repurchasing rights to narcotic addiction treatments Suboxone, Subutex, and Temgesic from Merck & Co. at a price of 100 million British pounds.

AstraZeneca has stated that it is purchasing the right to sell 18 of Torrent's portfolio of generic pharmaceuticals in nine "key emerging markets" under its own branding.

AP and the Wall Street Journal are reporting that ReGen Biologics, the maker of the Menaflex knee repair implant, is pushing back against the FDA's decision to reevaluate the agency's 2008 approval of the device. The company is challenging the agency's authority to reevaluate an earlier approval. The FDA decided to reevaluate its earlier approval in light of the Obama administration's finding that the prior approval had been influenced by lobbying from New Jersey lawmakers. On March 23, an FDA panel found that the device was likely safe and effective, despite shortcomings with the company's studies.

The US Circuit Court of Appeals for the Federal Circuit struck down a \$65 million ruling for Ariad Pharmaceuticals Inc. in its lawsuit alleging that Eli Lilly & Co. infringed Ariad patents. The court found that the patent claims were invalid due to inadequate written descriptions.

Covidien PLC announced that it [won a patent infringement lawsuit](#) against Applied Medical Resources Corp.

Stryker Corp. has stated that the FDA has indicated that the company has taken sufficient action to fix problems at its Mahway, NJ facility.

A jury has determined that Pfizer must pay [\\$142.1 million](#) for illegally promoting Neurontin for unapproved uses. Kaiser Foundation Health Plan Inc. and Kaiser Foundation Hospitals alleged that Pfizer misled them into believing Neurontin was effective for migraines, bipolar disorder and other conditions.

A high court in Brazil is currently considering when Pfizer Inc.'s patent on its drug Viagra will expire in Brazil, with the Brazilian government [arguing that the patent is set to expire](#) in June of this year.

CVS Caremark Corp. has indicated its [opposition to a bill](#) headed for consideration by the House Committee on Oversight and Government Reform, which would prevent pharmacy-benefits managers that own retail stores from bidding on the federal prescription-drug contract.

Mela Sciences has stated that the FDA has postponed the premarket approval of MelaFind, has imposed a 180-day extension for the review, and has asked for more details on the device.

Six plaintiffs have dropped accusations that Purdue Pharma prevented generic competition for its painkiller OxyContin through misrepresentations to the PTO and sham patent litigation.

Sanofi-Aventis U.S. and Albany Molecular Research have filed a request for a temporary restraining order and a preliminary injunction against Dr. Reddy's Laboratories to prevent the company from distributing a generic version of Allegra-D 24-hour extended-release tablets.

The Sorin Group has reached a tentative \$10 million settlement with the Justice Department to resolve a 2006 kickback investigation into its subsidiary, Ela Medical.

Novartis' strategy to expand its cardiovascular and metabolics business in advance of the expiration of the patent on its drug Diovan included running a lot of clinical trials to add indications and amass outcomes data. But several studies designed to expand use ended with negative results.

Boston Scientific has announced that it plans to submit a PMA for its third-generation platinum-chromium Taxus Element stent to the FDA by June.

Regulatory Notices

FDA Seeks Comments on Focus Groups, Labeling Guidance

The FDA is seeking comments on focus groups about drug products used by FDA to gauge public opinion, on a variety of subjects related to consumer, patient, or healthcare professional perceptions and use of drug products and related materials, including but not limited to, direct-to-consumer (DTC) prescription drug promotion, physician labeling of prescription drugs, Medication Guides, over-the-counter (OTC) drug labeling, emerging risk communications, patient labeling, online sales of medical products, and consumer and professional education. Comments are due May 21, 2010. More information is available at <http://edocket.access.gpo.gov/2010/2010-6172.htm>.

The FDA is also seeking comments on the information collection associated with the guidance "Hypertension Indication: Drug Labeling for Cardiovascular Outcome Claims," which is intended to assist applicants in developing labeling for outcome claims for drugs that are indicated to treat hypertension. Comments are due May 21, 2010. More information is available at <http://edocket.access.gpo.gov/2010/2010-6173.htm>.

FDA to Amend Medical Device Establishment Registration, Device Listing Regulations

The FDA is proposing to amend its regulations governing medical device establishment registration and device listing. The proposed revisions would modify FDA's current regulations at part 807 (21 CFR part 807) to reflect recent statutory amendments to the device registration and listing provisions of the Federal Food, Drug, and Cosmetic Act. Written or electronic comments on the proposed rule are due by June 24, 2010. More information is available at <http://edocket.access.gpo.gov/2010/2010-6662.htm>.

FDA Opens Comment Period on Guidance for Drug Induced Liver Injury

The FDA is opening a comment period for submission of suggestions for revising the guidance for industry published in the Federal Register July 30, 2009, entitled "Drug-Induced Liver Injury: Premarketing Clinical Evaluation." In addition, the FDA, along with the American Association for the Study of Liver Diseases (AASLD) and the Pharmaceutical and Research Manufacturers of America, is sponsoring a public conference to be held on March 24 and 25, 2010, to discuss and debate issues contained in the published guidance document. The public conference will be held on March 24, 2010,

from 8 a.m. to 6 p.m. and March 25, 2010, from 8 a.m. until 3:15 p.m. in Silver Spring, Maryland. More information is available at <http://edocket.access.gpo.gov/2010/2010-6701.htm>.

FDA Releases Guidances on Pharmacokinetics, IBS Treatment, Drug Labeling

The FDA has released a revised draft guidance for industry entitled “Pharmacokinetics in Patients With Impaired Renal Function--Study Design, Data Analysis, and Impact on Dosing and Labeling.” The draft guidance is intended to assist sponsors planning to conduct studies to assess the influence of renal impairment on the pharmacokinetics of an investigational drug. It provides recommendations on when studies should be conducted to assess the influence of renal impairment on the pharmacokinetics of an investigational drug, the design of such studies, and how such studies should be carried out. Comments should be submitted by May 21, 2010 in order to be considered before the FDA begins work on the final version of the guidance. More information is available at <http://edocket.access.gpo.gov/2010/2010-6171.htm>.

The FDA is announcing the availability of a draft guidance for industry entitled “Irritable Bowel Syndrome--Clinical Evaluation of Products for Treatment.” This guidance is intended to assist the pharmaceutical industry and other investigators who are conducting new product development for the treatment of IBS. Comments should be submitted by May 24, 2010, to ensure that the FDA considers them before it begins work on the final version of the guidance. More information is available at <http://edocket.access.gpo.gov/2010/2010-6310.htm>.

The FDA has released a guidance for industry entitled “Dosage and Administration Section of Labeling for Human Prescription Drug and Biological Products--Content and Format.” This guidance is one of a series of guidance documents intended to assist applicants in drafting prescription drug labeling in which prescribing information is clear and accessible and in compliance with the requirements in the final rule on the content and format of labeling for prescription drug and biological products. More information is available at <http://edocket.access.gpo.gov/2010/2010-6322.htm>.

FDA Amends Regulations to Reflect Change of Address

The FDA is amending its regulations to reflect a change in the address and telephone number for the Office of Combination Products (OCP). More information is available at <http://edocket.access.gpo.gov/2010/2010-6246.htm>.

FDA Issues Determination Regarding Didrex

The FDA has determined that DIDREX Tablets, 25 milligrams (mg), were not withdrawn from sale for reasons of safety or effectiveness. More information is available at <http://edocket.access.gpo.gov/2010/2010-6593.htm>.

Public Meetings

Endocrinologic and Metabolic Drugs Advisory Committee

The FDA has announced that the Endocrinologic and Metabolic Drugs Advisory Committee will meet on May 27, 2010, from 8 a.m. to 5 p.m. at the Inn and Conference Center, University of Maryland University College (UMUC), 3501 University Blvd. East, Adelphi, MD. More information is available at <http://edocket.access.gpo.gov/2010/2010-6169.htm>.

FDA to Host Joint Conference

The FDA is hosting a joint conference with the University of Rhode Island (URI) College of Pharmacy entitled “FDA and PAT for Pharma Manufacturing: FDA--Partnering with Industry.” The conference will be held on May 11 and 12, 2010, from 8 a.m. to 5 p.m. in Bethesda, Maryland. More information is available at <http://edocket.access.gpo.gov/2010/2010-6265.htm>.

FDA Announces Public Workshops

The FDA is announcing a public workshop entitled "Medical Device Epidemiology Network (MDEpiNet): Developing Partnership Between the Center for Devices and Radiological Health and Academia." The purpose of the workshop is to facilitate discussion among FDA and academic researchers with expertise in epidemiology and health services research on issues related to the methodology for studying medical device performance. The workshop will be held on April 30, 2010, from 8 a.m. to 5 p.m. in Silver Spring, Maryland. More information is available at <http://edocket.access.gpo.gov/2010/2010-6446.htm>.

The FDA Los Angeles District Office, in cosponsorship with the Society of Clinical Research Associates, Inc. (SoCRA) is announcing a public workshop entitled "FDA Clinical Trial Requirements, Regulations, Compliance, and Good Clinical Practices." The public workshop is intended to aid the clinical research professional's understanding of the mission, responsibilities, and authority of FDA and to facilitate interaction with FDA representatives. The public workshop will be held on Wednesday and Thursday, May 5 and 6, 2010, from 8 a.m. to 5 p.m. in Newport Beach, California. More information is available at <http://edocket.access.gpo.gov/2010/2010-6579.htm>.

The 2010 PDA/FDA Pharmaceutical Supply Chain Workshop will be April 26-28, 2010 in Bethesda, Maryland. More information is available at <http://www.pda.org/supplychain2010>.

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 on the [FDA Practice Bulletins web page](#).

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

Mark Mansour	Partner	mark.mansour@bryancave.com	1 202 508 6019	Washington
Megan A. Gajewski	Associate	megan.gajewski@bryancave.com	1 202 508 6302	Washington
Patrice M. Hayden	Associate	pmhayden@bryancave.com	1 202 508 6147	Washington
Emily K. Strunk	Associate	emily.strunk@bryancave.com	1 202 508 6360	Washington

This bulletin is published for the clients and friends of Bryan Cave LLP. To stop this bulletin, please reply to this email. To stop this bulletin and all future commercial e-mail from Bryan Cave LLP, please reply to: opt-out@bryancave.com and leave the message blank. Information contained herein is not to be considered as legal advice. Under the ethics rules of certain bar associations, this bulletin may be construed as an advertisement or solicitation.