

To: Our Clients and Friends

April 7, 2010

Pharmaceuticals, Medical Devices and Biologics Regulatory and Policy Bulletin



Top News

Tax Credit in Health Reform Law May Benefit BioPharmas

In addition to establishing a legal framework for biosimilars and allowing for 12 years of marketing exclusivity for innovator products, the new health reform law also established other mechanisms which could provide benefits to pharmaceutical and biotech companies, including tax credits and research funding. The law established the 'Therapeutic Discovery Project Credit,' which allows companies a tax credit for up to 50 percent of their research expenses for the years 2009 and 2010. The credit is capped at \$1 billion total over the two year period, and there is not currently a cap on the total credit a single company can receive. In addition, the law creates a 'Cures Acceleration Network' which will grant money to industry and academia to help speed development. The program would provide a company working in an area of high unmet need to receive up to \$15 million each year to fund its development programs.

Court Finds Eli Lilly, Sandoz Can't Use Preemption Defense

The U.S. District Court for the Central District of California has ruled that Eli Lilly and Sandoz cannot use a federal preemption defense to win dismissal of a product-liability case related to generic Prozac. The Court ruled that the drugmakers were not prohibited from revising the drug's labeling to include new warnings.

Issa Seeks Information on Health Reform Deals

Representative Darrell Issa, the ranking Republican on the House Oversight Committee, has [written letters](#) to five special interest groups asking them for information regarding the deals they reached on health reform. Issa sent the letters to the AMA, AFSCME, the U.S. Chamber of Commerce, the American Hospital Association and PhRMA. The letters asked the groups to for details regarding their meetings with the White House and Democratic leaders and the arrangements that were reached as a result of the negotiations.

Pfizer Settlement Less than Tough, CNN Reports

CNN is reporting that, although federal officials painted their enforcement efforts against Pfizer's marketing of Bextra as demonstrating their commitment to tough enforcement, the agreement reached between the company and the federal government was less harsh than it could have been. According to CNN's report, to avoid Pfizer from being excluded from Medicare and other federal programs, Pfizer incorporated an entity on the same day that Pfizer agreed it would plead guilty. That new entity, and not Pfizer, would be excluded from Medicare under the agreement.

Health Reform Trumps Whistleblower Limits Set by Supreme Court

On March 30, the Supreme Court ruled that whistleblower suits seeking to recover misspent government funds should be dismissed if they are based on information in state or local government administrative reports. This decision apparently will not apply to future cases, however, as the recent health reform law includes a provision that specifies that qui tam suits should be dismissed only if based upon publicly disclosed federal reports.

Federal Government Seizes Misbranded Products

U.S. Marshals, at the request of the FDA, [seized a range of consumer products](#) at Beehive Botanicals Inc. in Haywood, Wisconsin, on the grounds that they were misbranded and are unapproved new drugs. Beehive Botanicals, the manufacturer of the products, which included creams, capsules, tablets, throat spray, and other consumer items claimed on its website, on the products' labeling, and in the products' promotional materials that the products could be used to diagnose, cure, treat, and prevent diseases such as cancer, liver or kidney disease, insomnia, bone fractures, and skin disorders. Michael Chappell, FDA's acting associate commissioner for regulatory affairs, stated that the seizure demonstrates that the FDA will seek enforcement action against companies that promote therapeutic benefits of products not having been evaluated or approved by the FDA.

The FDA has been interacting with the company regarding its labeling since at least March 2007, when the agency issued the company a [warning letter](#) requesting that drug claims about its products be removed from its Web site and product labeling. During a later inspection conducted between September 2009 and October 2009, the FDA found that drug claims were being made for the products through related websites.

FDA Outlines Import Safety Initiative, Goals

Tim Ulatowski, director of the Office of Compliance in FDA's device center, and other FDA staff outlined some of the FDA's upcoming initiatives to improve import safety and address the challenges the agency faces with globalization. CDRH has defined several goals for 2010, including hiring a permanent associate director for international affairs, encouraging more and better sharing of foreign inspection data, developing a new single audit program with Health Canada and Australia's Therapeutic Goods Association, and sharing adverse event information globally and coordinating pre-market reviews with foreign partners.

FDA Teams with Researchers to Compile Drug Data

The FDA is teaming up with outside investigators to conduct a study on the safety and effectiveness of certain medications when taken during pregnancy. The study, unveiled in December as the Medication Exposure in Pregnancy Risk Evaluation Program, will unite researchers at Harvard's HMO Research Network Center for Education and Research in Therapeutics, Kaiser Permanente and Vanderbilt University and collect insurance records from 11 million sites. The records will be pooled and evaluated for safety signals associated with certain drugs, or types of drugs, often taken by women while pregnant.

FDA Advisory Committee Recommends Updating Renal Testing Guidance

The Pharmaceutical Science and Clinical Pharmacology Advisory Committee recommended at a recent meeting that the FDA amend its new renal testing guidance to reflect real-world conditions. The committee also recommended that the agency change its patient selection criteria for one segment of pharmacokinetics studies on the effect of renal impairment on drug dosing.

FDA Considers Safeguards for CT Radiation

At a recent public meeting, groups representing radiologists, imaging technicians and physicists urged the FDA and industry to offer more tools to protect patients from potential radiation overexposure during medical imaging. The FDA is currently considering several different safeguards that could be added to the equipment to ensure that it does not deliver

radiation in excess of the optimal dose. These safeguards include dose display and reporting features, access controls, alerts on dose levels, and default settings. Devicemakers are warning, however, that incorporating too many new safeguards into imaging equipment could make the devices too expensive for the market.

FDA Will Not Change Employee Investigation Process

The FDA has informed Republican members of the House that the agency does not intend to stop using criminal investigators to investigate allegations of non-criminal employee misconduct, despite the House members' concerns about the negative impact of this practice on agency morale and whistleblowers. The agency stated that its handling of alleged misconduct by Office of Criminal Investigations employees is consistent with its approach for other agency staff.

Pharma Industry Comments on Web Advertising

As the FDA wrestles with how to address online ads for pharmaceuticals, several industry members are encouraging the agency to use a formal rulemaking process, rather than a guidance, to set standards for the industry. The industry also emphasized that companies should not be held responsible for online statements that they cannot control.

Industry Comments on FDA Draft Guidance on IRBs

In comments to the FDA's January 2010 draft guidance on institutional review boards (IRBs), the industry pushed back on the agency's attempt to make sponsors responsible for providing information that IRBs need for continuing reviews. Merck noted that sponsors already provide IRBs timely notification of protocol amendments, investigator brochure updates and informed consent risk profile revisions. The company also stated that IRBs may not have the technical capability to receive information from sponsors' annual IND submissions in common electronic technical document format and that such submissions may contain confidential corporate information. BIO commented that the guidance may overload IRBs with technical requirements, which might be better left to data monitoring committees.

Grassley Asks Sebelius to Investigate Phantom Pharmacies

Senator Charles Grassley has written a letter to Secretary Kathleen Sebelius inquiring about the failure of HHS to investigate complaints relating to "phantom pharmacies," which bill millions of dollars in false Medicare bills and then vanish. Grassley's letter cited examples of the claims about such pharmacies, mostly based out of Florida and California.

Jury Finds Pfizer Liable for Termination of Whistleblower

A federal jury in Hartford, Connecticut, [awarded \\$1.37 million in damages](#) to a former Pfizer scientist who alleged that she was fired for raising safety concerns. The jury found that Pfizer violated laws protecting free speech and whistle-blowers by retaliating against the scientist as a result of her raising those concerns. The case has brought increased attention to the safety of workers in the biotechnology industry, and the new head of the federal Occupational Safety and Health Administration has indicated that the agency is considering new requirements for employers to help protect such workers.

Publications

The FDA is announcing the availability of a [guidance](#) entitled "Q4B Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions; Annex 7: Dissolution Test General Chapter" and of a [guidance](#) entitled "Q4B Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions; Annex 9: Tablet Friability General Chapter."

CDER's ombudsman has published its [2009 annual report](#), which outlines the most common complaints the office received from industry, law firms, researchers, consumers and health care professionals. The report also notes that more CDER employees are turning to the ombudsman for help in resolving scientific differences of opinion.

DOT's Pipeline and Hazardous Materials Safety Administration published a proposed [rule](#) that would require manufacturers to declare and label products containing small lithium-ion and lithium-metal cells as Class 9 hazardous

materials when shipping them on planes. Devicemakers are stating that the rule could cost them millions of dollars and lead to cutbacks in expansion, innovation, and R&D.

The EU's Directorate General for Health and Consumers has indicated that it expects to have a proposal for recasting the MDD by the first half of next year, with adoption by the European Commission by the end of 2011.

Drugmakers are asking the FDA to widen the scope of a draft [guidance](#) on assessing the abuse potential of drugs that affect treatment areas such as mood or the central nervous system to include all drugs that may be misused.

Approvals

The FDA has [approved](#) TachoSil, the first absorbable fibrin sealant patch for use in cardiovascular surgery to prevent mild and moderate bleeding from small blood vessels, when standard surgical techniques are ineffective or impractical.

The FDA has approved a new formulation of Purdue Pharma LP's painkiller OxyContin. The new formulation is designed to be more difficult to crush or dissolve, in order to prevent tampering.

Guidant announced that it will plead guilty to two federal misdemeanor counts that the company failed to properly disclose changes made to some implantable heart devices. Under the deal, Guidant will pay more than \$296 million but will not have to pay restitution to patients. U.S. District Judge Donovan Frank has stated that he will rule on whether [to accept the plea and settlement agreement](#) within three weeks when he decides whether to put the company on probation and order restitution.

The FDA has granted fast-track review designation to perifosine, Aeterna Zentaris and Keryx Biopharmaceuticals' experimental treatment for refractory advanced colorectal cancer.

Unilife received 510(k) clearance from the FDA for its Unitract 1 milliliter Insulin Syringe manufactured in Lewisberry, Pa.

Recalls, Warnings, and Notifications

FDA reviewers of Daxas have expressed concern about suicide and suicide attempts by clinical-trial recipients of the drug.

Acino Pharma has indicated that it has no plans to recall generic products made with clopidogrel from a company facility in India where good manufacturing practice violations were identified, despite a recommendation by the European Medicines Agency's Committee for Medicinal Products for Human Use.

The FDA has issued a warning letter to HMI Industries for good manufacturing practice violations related to its air-filtration devices, including failure to conduct quality audits.

The FDA has completed its initial assessment of defective titanium alloy imported from China and has recommended that devicemakers determine the impact of the material specification problem and take corrective actions as appropriate. The agency has indicated that it is continuing to monitor titanium alloy imported from China and that it is continuing to encourage manufacturers to remain vigilant in their supplier controls.

Merck Serono, a division of Merck KGaA, has suspended enrollment and treatment of patients in ongoing worldwide studies of its therapeutic vaccine Stimuvax, following a suspected unexpected serious adverse reaction. The FDA has placed a clinical hold on the investigational NDA for Stimuvax.

Business News

The Wall Street Journal is reporting that it is expected that the generic drug market will experience a surge in competition and potential complications, due to an increase in brand name drugs going off patent and the introduction of generics by large pharmaceutical companies in response to their drugs going off patent.

A jury has awarded Edwards Lifesciences Corp. \$73.5 million in a case brought by the company against Medtronic Inc. for violating a patent on Edwards' Sapien XT heart valve.

KV Pharmaceutical Co. is continuing to find itself [under scrutiny by the FDA](#) for failing to report to the FDA that it was making oversize tablets that could be harmful to patients. The company's products were pulled from pharmacy shelves, its manufacturing has been idle for 15 months, and it has shed nearly 75 percent of its workers.

Medical technology company CareFusion Corp. has announced that it will purchase Medegen for \$225 million in cash. CareFusion has stated that the acquisition is intended to boost the company's ability to compete on claims of reducing hospital-acquired infections.

Sources are reporting that, although the new health law sets the federal upper limit for Medicaid generic drug reimbursement at 175 percent of the average manufacturer price, which should be sufficient to allow pharmacies to cover the cost of buying the drugs, it is unclear whether state-level reimbursement will be lower. Pharmacies have indicated that they are worried that lower state-level reimbursement might result in a loss to them on the drugs.

Repros Therapeutics has asked the FDA to lift a clinical hold on uterine fibroid drug Proellex.

Sanofi-Aventis has announced that its French manufacturing operations will focus on vaccine and biotech drugs, and that emphasis will be shifted away from synthetic chemistry-based production.

PPD has announced that it has added capabilities at the facility acquired from Merck & Co and improved integration of other sites to create a Vaccines & Biologics Center of Excellence.

At the 2010 Horizons conference, CMS' Louis Jacques outlined for attendees some of the challenges for comparative effectiveness research, including the assumption that such research will always favor the lower cost option and creating valid comparisons from vastly different criteria.

Megan Moynahan, a CDRH specialist in cardiac electrophysiology devices, has stated that the FDA pilot program allowing agency staff to flag device safety concerns generated 250 "signals" of potential risks in 2009, and the program is slated for expansion by the end of 2010.

Apotex and Roxane have filed separate suits against HHS and FDA seeking a preliminary injunction to stop FDA from granting 180-day marketing exclusivity for generic versions of Merck's hypertension drugs Cozaar and Hyzaar.

Regulatory Notices

FDA Proposes Amendments to Neurological Device Regulations

The FDA is proposing to amend certain neurological device and physical medicine device regulations to establish special controls for these class II devices and to exempt some of these devices from the premarket notification requirements of the Federal Food, Drug, and Cosmetic Act. Comments are due by July 6, 2010. More information is available at <http://edocket.access.gpo.gov/2010/2010-7637.htm>.

The FDA is also announcing the availability of draft special controls guidance documents for 11 neurological and physical medicine devices. FDA has developed a draft special controls guidance document for each of the 11 devices, which describe a means by which the devices may comply with the requirement of special controls for class II devices. Comments are due by July 6, 2010, to ensure their consideration before the FDA begins work on the final version of the guidance. More information is available at <http://edocket.access.gpo.gov/2010/2010-7634.htm>.

FDA Determines Regulatory Review Periods for Lusedra, Fanapt, Toviaz

The FDA has determined that the regulatory review period for Lusedra is 2,405 days. Anyone with knowledge that any of the dates as published are incorrect may submit comments to the Division of Dockets Management and ask for a redetermination by June 4, 2010. Furthermore, any interested person may petition FDA for a determination regarding whether the applicant for extension acted with due diligence during the regulatory review period by October 4, 2010. More information is available at <http://edocket.access.gpo.gov/2010/2010-7516.htm>.

The FDA has determined that the applicable regulatory review period for Fanapt is 6,552 days. Anyone with knowledge that any of the dates as published are incorrect may submit comments to the Division of Dockets Management and ask for a redetermination by June 7, 2010. More information is available at <http://edocket.access.gpo.gov/2010/2010-7678.htm>.

The FDA has determined that the applicable regulatory review period for Toviaz is 2,395 days. Anyone with knowledge that any of the dates as published are incorrect may submit comments to the Division of Dockets Management and ask for a redetermination by June 7, 2010. More information is available at <http://edocket.access.gpo.gov/2010/2010-7679.htm>.

FDA Signs MOUs

The FDA is providing notice of a memorandum of understanding (MOU) between the FDA, U.S. Department of Health and Human Services and the Association of Minority Health Profession Schools, Inc. The purpose of the MOU is to establish the terms for collaboration to enhance the diversity pool of candidates and to promote shared interests in increasing science and public health internship opportunities for socio-economically disadvantaged students. The agreement became effective January 20, 2010. More information is available at <http://edocket.access.gpo.gov/2010/2010-7677.htm>.

The FDA has also signed an MOU with the U.S. Department of Health and Human Services and the National Alliance for Hispanic Health. The purpose of the MOU is to establish the terms for collaboration to enhance the diversity pool of candidates and to promote shared interests in increasing science and public health internship opportunities for socio-economically disadvantaged students. The agreement became effective January 21, 2010. More information is available at <http://edocket.access.gpo.gov/2010/2010-7673.htm>.

Public Meetings

Peripheral and Central Nervous System Drugs Advisory Committee

The Peripheral and Central Nervous System Drugs Advisory Committee will meet June 10, 2010, from 8 a.m. to 5 p.m. in Silver Spring, Maryland. More information is available at <http://edocket.access.gpo.gov/2010/2010-7698.htm>.

Amendment to Agenda for Joint Committee Meeting

There is an amendment to the notice of a joint meeting of the Arthritis Advisory Committee and the Drug Safety and Risk Management Advisory Committee to reflect a change in the Agenda portion of the document. More information is available at <http://edocket.access.gpo.gov/2010/2010-7697.htm>.

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.