TRENDS-in-MEDICINE

May 22, 2011

by D. Woods and Lynne Peterson

Quick Takes

…Highlights from this week's news relating to drugs and devices in development that are not covered in other *Trends-in-Medicine* reports…

SHORT TAKES

- **ABBOTT's Trilipix (fenofibric acid) –** The FDA's Endocrinologic and Metabolic Drugs Advisory Committee voted 13 to 9 to recommend that Trilipix keep its approval for use with statins while a new study tests the combination's cardiac effects. Trilipix came under question when the ACCORD study found that adding a similar fibrate to statins gave no additional protection to the heart.
- **Accountable Care Organizations (ACOs) –** A study prepared for the American Hospital Association (AHA) said that kick-starting an ACO could cost more than the Centers for Medicare and Medicaid (CMS) thought – as much as $11.6 million to $26.1 million, which is far more than the $1.8 million estimated by CMS in its proposed rule for startup and one year of operating expenses.
- **ACCUMETRICS' VerifyNow P2Y12 test –** European regulators granted a CE Mark for this point-of-care system to measure platelet reactivity.
- **ADVANTAGENE's ProstAtak –** The FDA approved a special protocol assessment (SPA) for Phase III testing of this drug in men with newly diagnosed prostate cancer. The company plans to enroll 711 patients and to release findings by 2015.
- **ALIMERA SCIENCES' Iluvien (sustained-release fluocinolone acetonide)** was resubmitted to the FDA as a treatment for diabetic macular edema (DME). The FDA had rejected the drug, which is licensed from pSivida, in December 2010 for efficacy and safety reasons. The FDA is expected to take six months to review the resubmission.
- **ALLERGAN's Botox (onabotulinumtoxinA) –** A proposed bill in New Jersey would ban physicians from giving Botox for cosmetic purposes to people under age 18.
- **BEDFORD LABORATORIES' and ADIENNE's Thiotepa (phosphorothioyltriaziridine for injection) –** Bedford has a shortage of this drug due to manufacturing delays. Adienne, in conjunction with the FDA, will import the European version, Tepadina, temporarily. Tepadina contains the same active ingredient as Thiotepa but comes in two vial sizes.
- **BRISTOL-MYERS SQUIBB's Taxol (paclitaxel) –** Indiana University researchers have identified a genetic biomarker called RWDD3, which causes neuropathy in some breast cancer patients who take a class of chemotherapy drugs called taxanes, which includes Taxol. Researchers said the discovery may lead to a blood test to see if a patient is at risk of developing neuropathy.

Trends-in-Medicine
Stephen Snyder, *Publisher*
2731 N.E. Pinecrest Lakes Blvd.
Jensen Beach, FL 34957
772-334-7409
Fax 772-334-0856
www.trends-in-medicine.com
TrendsInMedicine@aol.com

- **Cardiac death in African Americans –** Duke University researchers have found a common gene variant in African Americans that may be associated with the development of life-threatening heart arrhythmias.

- **Carotid stenting –** A CREST trial substudy published in ***Lancet Neurology*** found that the peri-procedural risk of events appears to be higher in women who have carotid artery stenting vs. those with carotid endarterectomy. Men showed little difference.

- **DBV TECHNOLOGIES' Viaskin –** The EPIT study, published in the ***Journal of Immunology***, found that this skin patch system for allergen-specific immunotherapy is safe for desensitizing people against peanut allergy. Other clinical trials are under way. Viaskin works by maintaining an allergen on a person's intact skin for repeated and prolonged periods in order to obtain desensitization.

- **DTaP protection decreases over time –** A five-year study of Kaiser Permanente data on 22,700 patients ages 4-11 showed that the protective power of the diphtheria, tetanus, acellular pertussis vaccination (DTaP) wanes with time. Researchers said that each year that goes by after vaccination is associated with a 36% increased risk of getting pertussis.

- **DUNE MEDICAL's MarginProbe System –** A PMA was filed for this system designed to ensure that all cancerous tissues at the edges (margins) of breast tumors are removed during surgery. The FDA is giving this product expedited review.

- **ENZON PHARMACEUTICALS' PEG-SN38 –** Clinical work on this potential metastatic colorectal cancer treatment has been halted by the company, which said it wants to focus on treatments with "nearer-term commercial potential," such as a mid-stage trial in metastatic breast cancer and an early-phase pediatric cancer study. Enzon did not rule out further work in metastatic colorectal cancer at a later date.

- **E-prescribing –** At the end of 2010, a SureScripts report found 34% of office-based prescribers and 36% of office-based physicians were using e-prescribing, with cardiologists leading the way.

- **EPO –** Intravenous erythropoietin in patients with ST-segment elevation MI (STEMI) who had successful reperfusion with primary or rescue PCI did not reduce infarct size and was associated with higher rates of adverse cardiovascular events, according to research published in the ***Journal of the American Medical Association (JAMA)***. There is concern about an increase in infarct size in an older patient subgroup.

- **Erectile dysfunction drugs –** PDE5 inhibitors – **Pfizer**'s Viagra (sildenafil), **Lilly**'s Cialis (tadalafil), and **Bayer**'s Levitra (vardenafil) – have been linked to hundreds of sudden hearing loss cases globally, according to researchers. Forty-seven suspected cases of sensorineural hearing loss (a rapid loss of hearing in one or both ears) were linked to the drugs.

- **Fat gene –** U.K. researchers found that a gene linked to diabetes and cholesterol, known as KLF14, is a "master regulator" gene that controls the behavior of other genes found in body fat. *Perhaps we'll see new obesity drugs directed at this in the future.*

- **GENERAL ELECTRIC's AdreView (radiotracer iodine-123-metaiodobenzylguanidine, MIBG)** may help risk assessment in patients with heart failure according to a meta-analysis that showed that MIBG scintigraphy had a high negative predictive value for adverse clinical events. MIBG is approved by the FDA for the detection of primary or metastatic phechromocytoma or neuroblastoma as an adjunct to other diagnostic tests.

- **GERD –** State-of-the-art medication and surgery are equally effective in managing symptoms of chronic gastroesophageal reflux disease (GERD), according to a study (funded by **AstraZeneca**) of 554 patients in ***JAMA***. In the study, 92% of patients taking AstraZeneca's Nexium (esomeprazole) remained adequately controlled vs. 85% of patients who had laparoscopic anti-reflux surgery, a non-significant difference.

- **ICDs –** A study published in ***HeartRhythm*** showed that patients with an implantable cardioverter defibrillator (ICD) and sleep-disordered breathing (SDB) are more likely to develop nighttime life-threatening ventricular arrhythmias. The study also found an increase in appropriate ICD use among SDB patients, suggesting SDB patients should be screened for predominant nighttime ICD therapy.

- **JOHNSON & JOHNSON/TIBOTEC THERAPEUTICS' Edurant (rilpivirine, TMC-278)** was approved in combination with other antiretroviral drugs for HIV-1 in treatment-naïve adults.

- **LANTHEUS MEDICAL IMAGING's flurpiridaz F 18 –** Phase II data presented at the International Conference of Non-Invasive Cardiovascular Imaging (ICNC) in Amsterdam indicated that this myocardial perfusion imaging PET agent is safe and superior to SPECT when it comes to image quality, diagnostic certainty, and sensitivity for detection of coronary artery disease.

- **MERCK's Victrelis (boceprevir)** – The FDA approved this protease inhibitor, making it the first direct-acting antiviral drug to treat hepatitis C virus (HCV). Then, just days later, European regulators also approved Victrelis.
- **Parkinson's disease** – The stomach bacteria responsible for ulcers, *Helicobacter pylori* (*H. pylori*), could play a role in Parkinson's disease, according to data presented at the American Society for Microbiology meeting.
- ***PFĒNEX* INC's CRM 197 carrier protein** – The company submitted a biologics master file (BMF) to the FDA for the cGMP grade carrier protein to support the development of conjugate vaccine products by its partners.
- **PFIZER and EISAI's Aricept (donepezil)** – Public Citizen's Health Research Group asked the FDA to immediately withdraw the 23 mg dose of this Alzheimer's medication, charging that it is more toxic and less beneficial than the 10 mg dose. Public Citizen also asked the FDA to warn doctors that patients should not take two 10 mg pills if Aricept 23 mg is taken off the market.
- **Radiation** – The American College of Radiology launched a CT Dose Index registry that will help facilities track the radiation doses patients get from CT and to gauge their emitted doses vs. other institutions.
- **ROCHE/GENENTECH's Avastin (bevacizumab)** – The company said it wants to do a clinical trial to show that Avastin + paclitaxel is effective in women with advanced breast cancer. It also wants to evaluate a biomarker to see which patients are most likely to benefit from Avastin. An FDA advisory committee is scheduled to discuss the FDA's decision to withdraw the breast cancer indication on June 28-29, 2011.
- **Rural ERs** – Twenty-seven percent of rural hospital emergency departments closed between 1990 and 2009 because of competition, safety-net status, and a low profit margin, according to a study published in ***JAMA***.
- **SHIRE's Vyvanse (lisdexamfetamine dimesylate)** – The FDA sent the company a warning letter saying that Shire is misbranding this attention-deficit/hyperactivity disorder (ADHD) drug by suggesting it is safer and more effective than has been demonstrated.
- **TAKEDA's Actos (pioglitazone)** – The FDA's adverse event reporting system (the AERS database) showed 138 cases of bladder cancer in patients who took this diabetes medication between 2004 and 2009, and >20% of those cases involved Actos. The FDA began a safety review of Actos last year after early data from a long-term study showed an increased risk of bladder cancer in patients who had taken Actos the longest.
- **Targeted cancer pills** – A study conducted by Avalere Health and published in the ***Journal of Oncology*** found that patients prescribed cancer pills – including **Roche/Genentech**'s Tarceva (erlotinib) and Xeloda (capecitabine) and **Merck**'s Temodar (temozolomide) – are not filling their prescriptions, due largely to cost and copays.
- **VIVUS' Qnexa (phentermine/topiramate)** – A study published in ***JAMA*** showed little risk of birth defects in children of women who took the newer anti-epileptic drugs, including topiramate. The FDA did not approve Qnexa to treat obesity in October 2010 because of health concerns, including birth defects and increased heart rate.

NEWS IN BRIEF

ABBOTT's RX Herculink Elite renal stent system – safe

Data from the HERCULES trial showed clinically and statistically significant blood pressure reduction in patients with multidrug-uncontrolled hypertension was associated with low in-stent restenosis and complication rates. However, brain natriuretic peptide (BNP) was a weak predictor of systolic blood pressure (SBP) response. The study showed that there was no correlation between pre-procedural BNP levels, change in BNP levels, and clinically important reduction in SBP after renal artery stenting.

9-Month HERCULES Trial Results

Measurement	Results
Device success rate	96%
Procedure success rate	99.2%
Clinical success rate	94.8%
Freedom from major adverse events and re-intervention	94.8%

ACORDA THERAPEUTICS' and BIOGEN IDEC's Ampyra/Fampyra (dalfampridine) – more approvals

This drug to improve walking ability in adult multiple sclerosis (MS) patients is FDA approved in the U.S. and sold there by Acorda as Ampyra. This week the drug received marketing approval from regulators in Australia and Europe. It will be sold in these countries/regions by Biogen as Fampyra. The issue in Australia will be getting it reimbursed.

ADHD drugs – no higher CV risk

Researchers reported in ***Pediatrics*** that there does not appear to be an increased risk of cardiovascular (CV) events, including sudden death or ventricular arrhythmia, in children and teens taking ADHD medications. Rates of validated stroke and MI

were too low to make comparisons between ADHD and non-ADHD users.

CV Risk with ADHD Drugs		
Measurement	Per 10,000 patient-years	
	ADHD users	Non-ADHD users
Sudden death or ventricular arrhythmia	0.06%	0.04%
Death from any cause	1.79%	3.00%

AMYLIN PHARMACEUTICALS' and LILLY's Byetta (exenatide) – a marriage in trouble

Amylin is suing Lilly, its partner for this diabetes treatment, for allegedly engaging in anti-competitive practices by agreeing to help **Boehringer Ingelheim** develop and market a competing product, Tradjenta (linagliptin), which gained FDA approval earlier this month. Amylin's lawsuit also accuses Lilly of breaching an obligation to maximize sales of Byetta. Amylin asked a federal court to prevent Lilly from assigning the same sales team to both products.

CABG rates decline, PCI steady – impact unclear

Researchers found a 15% decrease in coronary artery bypass graft (CABG) surgery rates in hospitals from 2001 to 2008, but percutaneous catheter-based intervention (PCI) rates did not change. The University of Pennsylvania School of Medicine researchers published the results of a serial cross-sectional study of the Healthcare Cost and Utilization Project's Nationwide Inpatient Sample (NIS) in ***JAMA***. One researcher said the data imply a "sizeable shift in cardiovascular clinical practice patterns away from surgical treatment toward percutaneous, catheter-based interventions. This raises concerns, given that recent data from a national trial indicated that CABG surgery remains the better choice for patients with previously untreated three-vessel or left main coronary artery disease."

COURAGE trial – has had little effect

An observational study published in the ***Journal of the American Medical Association*** found that clinical practice has changed little since the COURAGE study, comparing medical therapy to stenting, was first presented. The authors wrote, "It is unknown to what degree optimal medical therapy (OMT) is applied before PCI in routine practice or whether its use increased after the COURAGE trial…Our study demonstrated that less than half of patients undergoing PCI are taking OMT before their procedure, despite the guideline-based recommendations to maximize OMT and the clinical logic of doing so before PCI so that the need for additional symptom relief from revascularization can be appreciated. Even after publication of the COURAGE trial, little change in this practice pattern was observed."

Fewer than half of patients with stable coronary artery disease undergoing PCI were receiving OMT before PCI, and about two-thirds were receiving OMT at discharge after PCI, with relatively little change in practice patterns after COURAGE.

GENZYME's Campath (alemtuzumab) – beats standard therapy for less risky renal transplant patients

Researchers writing in the ***New England Journal of Medicine*** said that kidney transplant patients taking Campath for antibody induction therapy did better compared to conventional therapies, with a significantly lower risk of rejection after one year for patients on Campath vs. those on **Thomson Healthcare**'s Simulect (basiliximab) or rabbit antithymocyte globulin. Researchers said that Campath was not associated with an increased rate of overall infections and that there were no differences in terms of bacterial infections or opportunistic viral infections.

Campath in Kidney Transplant Patients			
Measurement	Campath	Conventional therapy	p-value
Biopsy confirmed acute rejection			
At 6 months	3%	15%	<0.001
At 12 months	5%	17%	<0.001
At 3 years	13%	20%	0.03
Other results			
Rate of rejection at 3 years	10%	22% (basiliximab)	0.003
Efficacy (composite of freedom from biopsy, confirmed acute rejection, death, or graft loss at 3 years)	85% for low risk	76% for low risk	0.04
Rate of serious infection events	35%	22%	0.02

GLAXOSMITHKLINE's Avandia (rosiglitazone) – FDA to finally severely restrict use

This Type 2 diabetes drug, which has been found to increase the risk of cardiac events – along with GSK's Avandamet (rosiglitazone + metformin) and Avandaryl (rosiglitazone + glimepiride) – will no longer be available in retail pharmacies after November 18, 2011. Under a new FDA-imposed risk evaluation and mitigation strategy (REMS), doctors will have to enroll patients in a special registry in order to receive the drug, which will be delivered only by mail order and only from certified pharmacies.

IMTHERA MEDICAL's aura6000 – positive Phase I results

Three-month Phase I results from a European study looking at this neurostimulation device for the treatment of obstructive sleep apnea (OSA) showed that patients had "marked improvement" in their baseline diagnostic apnea hypoponea index.

Phase I Results with Aura6000

Measurement	Patients with improvement
Apnea hypoponea index (AHI) reduction	50.2%
Oxygen desaturation index (ODI) reduction	54.3%
Hypoponea index (HI) reduction	46.1%
Epworth Sleepiness Scale (ESS) reduction	50.5%
Quality of sleep improved	64.9%

INTERMUNE's Esbriet (pirfenidone) – positive data in diabetic nephropathy

An analysis published in ***The Lancet*** of two randomized trials found this antifibrotic agent had physiologic benefits in idiopathic pulmonary fibrosis (IPF). In one trial, the mean change in FVC at Week 72 was significantly lower in high-dose pirfenidone patients vs. placebo (-8% vs. -12.4%, p=0.001). In the other study, there were no statistically significant differences in FVC between pirfenidone and placebo. The new pooled analysis of the two studies found a significant change in FVC in favor of pirfenidone. The FDA rejected pirfenidone last year as a treatment for IPF.

Kaposi's sarcoma – new clues

Researchers at the University of Texas Health Science Center at San Antonio have discovered an important mechanism that controls the growth of Kaposi sarcoma-associated herpes virus (KSHV), saying it could mean that inexpensive antioxidants and anti-inflammatory drugs might potentially be used to prevent the flare-up of this cancer, which is common in AIDS patients. The research was published in ***PLoS Pathogens***.

KUDOS PHARMACEUTICALS' and ASTRAZENECA's olaparib (AZD-2281) – PARP inhibitor slows recurrent ovarian cancer

Data from a Phase II trial showed that this investigational DNA repair inhibitor almost doubled progression-free survival (PFS) in patients with relapsed, platinum-sensitive ovarian cancer. Patients taking olaparib had a median PFS of 8.4 months vs. 4.8 months for placebo patients. The agent is the first to show a benefit for maintenance therapy for patients with relapsed serious ovarian cancer responding to platinum-based regimens.

MEDTRONIC's RestoreAdvanced – helps paraplegic walk

A 25-year-old paraplegic man with spinal cord injury to C7-T1 was able to stand and even take a few steps using a Medtronic device to stimulate the spinal cord. The unprecedented movements offer hope that this technology, originally developed for pain management, can be further perfected to help other spinal cord injury patients. The news and details were reported in ***The Lancet***.

MERCK

- **HCV partnership** – Merck will collaborate with **Roche** to develop and market treatments for hepatitis C virus (HCV). Roche/Genentech will include Victrelis in its promotion of Pegasys (peginterferon alfa-2a) in a triple combination regimen – Vectrelis, Pegasys, and ribavirin. Victrelis was studied primarily in the clinical trials with Merck's PegIntron (peginterferon alfa-2b), but it can be used with either interferon. The agreement is non-exclusive. The companies also will work together to educate physicians and patients about HCV, including the diagnosis of the disease, which is believed to be widely underdiagnosed.
- **Zostavax** – The FDA approved Zostavax in 2006 for people age ≥60 and earlier this year for people age 50-59, but there are reports that it isn't easy for the new age group to find or get the vaccine. Some medical facilities reportedly are waiting for action by the Centers for Disease Control and Prevention (CDC) before agreeing to provide the vaccine to people age 50 to 59. The Advisory Committee on Immunization Practices, which makes vaccine recommendations to the CDC, will discuss the topic next month. In addition, many doctors do not carry the vaccine because it is not covered by Medicare Part B, even though it is covered (with some exceptions) by Medicare Part D.

Parkinson's-like diseases – possible pathway explanation

New research suggests that a pathway located at the base of the brain and is essential for coordination may be selectively damaged by the "friendly fire" of the body's immune response. Researchers at the University of Florida College of Medicine's Center for Translational Research in Neurodegenerative Disease said there is evidence of a direct link between chronic inflammation and Parkinson's pathology and that a small protein produced in response to infections called interferon-gamma can directly lead to the loss of brain cells that are selectively targeted in Parkinson's patients. *Watch for Parkinson's drugs to be developed targeting this protein.*

Percutaneous aortic valves – new safety concerns raised

Data presented at EuroPCR found that even moderate regurgitation after a transcatheter aortic valve replacement (TAVI) is associated with significantly increased early and longer-term mortality as well as acute kidney injury. Even mild regurgitation tended to reduce two-year survival vs. patients with no regurgitation post-procedure (68.0% vs. 81.3%, p=0.12).

Compared with no or mild periprosthetic aortic regurgitation, the moderate leakage cases were associated with worse outcomes. The principal investigator suggested these findings mean that "every effort should be made to downgrade a significant periprosthetic regurgitation and to avoid negative hemodynamic effects on the patient, especially in case of markedly impaired left ventricular ejection fraction."

U.K. Study of Perivalvular Leakage Risk with TAVI

Measurement	Moderate leakage	No or mild leakage	p-value
30-day mortality	19.0%	4.7%	0.019
1-year mortality	61.9%	22.1%	<0.001
Acute kidney injury	61.9%	17.0%	<0.001
Post-dilatation	57.1%	23.3%	0.002
MI	9.5%	1.9%	Nss, 0.07

While this was a single-center study of only 127 TAVI patients in Germany, another single-center study also raised safety questions. That Italian study found that moderate-to-severe perivalvular leaks were more common with valves too small for the annuli.

The Italian researchers looked at 79 CoreValve patients over two years and found that 32 had aortic regurgitation of ≥Grade 2 and 12 had ≥Grade 3. A mismatch with an annulus smaller than the valve was not associated with higher degrees of regurgitation (p=0.12), but valves smaller than the annulus showed a trend to higher (Grades 2-4) regurgitation (18.8% vs. 4.3% Grade 0/1, p=0.056).

Interestingly, higher implantation of the valve tended to be associated with less severe regurgitation while low implantation tended to be associated with more severe regurgitation (both p=0.05). Post-dilatation to reduce the degree of aortic regurgitation around the valve worked in 17 of 21 cases (80% success), but two patients required a second valve procedure.

PFIZER

- **Axitinib** – Data from the pivotal Phase III AXIS 1032 showed that this tyrosine kinase inhibitor worked better than **Bayer**'s Nexavar (sorafenib) in 723 patients with advanced kidney cancer. A study summary released in advance of the American Society of Clinical Oncology (ASCO) meeting in June said that patients taking axitinib lived a median of 6.7 months before tumor progression vs. 4.7 months for patients taking Nexavar.
- **Celebrex (celecoxib)** – People who took this pain medication over a three-year period were less likely to develop polyps that could lead to colorectal cancer, but their risk of cardiac problems increased, according to a study published in the ***American Journal of Gastroenterology***.
- **Chantix (arenicline)** – The FDA ordered Pfizer to refile thousands of adverse reaction reports, including suicide, linked to this smoking-cessation drug. Of the 1,055 events reported in 3Q09, 589 happened in previous years but were not entered into the FDA's Adverse Events Reporting System (AERS) until July 2010, according to the Institute for Safe Medication Practices. The filing is not expected to cause the FDA to change the Chantix label.
- **Crizotinib** – The FDA gave priority-review status for this treatment for patients with non-small cell lung cancer (NSCLC) who have a mutated ALK gene. Crizotinib was designated as an orphan drug in 2010. Pfizer also submitted crizotinib to Japanese regulators.

Radial approach – major bleeding remains a common complication

Despite the predominant use of the radial approach (84%) in percutaneous coronary intervention (PCI) in the 532-patient ABOARD trial, major bleeding – both occult and gastrointestinal – remained a common complication and was highly associated with mortality in non-ST elevation acute coronary syndrome patients treated with optimal anti-thrombotic therapy.

1-Month Safety with Radial Access in ABOARD Trial

One-month results	Incidence
Bleeding complications	5.4%
Occult bleeding	36.8%
Overt gastrointestinal bleeding	21%
Mortality	26.3%

RADI MEDICAL SYSTEMS' FemoSeal – fared well against manual compression

This femoral artery closure device may reduce large hematomas and speed closure compared to manual compression of the catheter access room, researchers reported at EuroPCR. The randomized study found that in-hospital hematomas >5 cm occurred in 2.2% of patients with the device vs. 6.7%

in patients getting manual compression alone. The device, which "sandwiches the wound with an anchor inside the artery and a cap outside," also reduced time to hemostasis by seven minutes vs. manual compression.

Stenting carotid, coronary arteries – doubling up is safe

A long-term study of data from the prospective FRIENDS registry, published in the ***Journal of the American College of Cardiology: Cardiovascular Interventions***, found that combining stenting with carotid stenting is successful in complex, high-surgical-risk patients with both carotid and coronary artery disease (CAD). At long-term follow-up, patients with previous CAD had significantly higher rates of major cardiac and cerebrovascular events vs. patients with a first clinical episode (17% vs. 6%).

FRIENDS Registry Results

Measurement	30 days n=239	520 days
Composite death, MI, stroke	4.2%	N/A
Death	1.3%	4.2%
MI	1.3%	2.1%
Stroke	2.5%	3.8%

Wnt inhibitors identified – potential cancer approach

Researchers at New York University Langone Medical Center Cancer Institute have identified three novel small molecules that are inhibitors of the Wnt signaling pathway, which regulates several aspects of cell development and cancer. Previous studies have indicated that skin, breast, liver, and colon cancers are associated with abnormal signaling activity within the Wnt pathway.

REGULATORY NEWS

FDA unhappy with DTC advertising of genetic tests

The FDA sent warning letters to three makers of direct-to-consumer (DTC) genetic tests, saying the companies are promoting their products with unsupported claims. The FDA asked the companies to present proof of device approval or explain why they think they are exempt from FDA oversight. The companies and tests involved are:

- **American International Biotechnology Services' (formerly CBI Services) Sports X Factor Test Kit –** The company claims it can predict the risk for certain health conditions, including undiagnosed heart conditions.
- **Lumigenix –** Its tests reportedly uncover genetic risk factors for 79 diseases, and the company claims an ability to uncover increased risk for conditions such as lactose intolerance or even ovarian cancer.
- **Precision Quality DNA –** The company describes itself as a "DNA guidance service," warning consumers to "dodge the bullet with your name on it." The FDA is concerned about the company's claims that its tests can provide insight into a person's likely response to specific drugs and highlight risk factors based on key target genes.

States can challenge insurance premium increases

The Department of Health and Human Services (HHS) released a final rule allowing states to scrutinize insurance companies if they propose excessive increases in insurance premiums (>10% in a given year for small or individual health insurance plans). The rule does not apply to plans sold in the large group market, which already has some oversight.

While neither states nor the federal government can block an insurer from enacting a high rate hike, HHS hopes that publicizing a high rate hike may be enough of a deterrent for double-digit increases. Under the new rule, if an insurer hikes rates ≥10%, the insurer must publicly report it and justify it. Independent experts will scrutinize increases ≥10%. Starting in 2012, states can choose their own threshold at which a review would be triggered. If a state doesn't have the resources or authority to review the rates, then the federal government will take that role, HHS officials said.

European regulatory news

- **Leukaemia & Lymphoma Research**, a U.K.-based charity, is setting up a nationwide network of 13 clinical trial centers in an effort to improve poor survival rates for patients with a variety of hematologic blood cancers by making unapproved drugs available to more patients through clinical trials. The hub will be Birmingham University.
- **MERCK and JOHNSON & JOHNSON's Simponi (golimumab)** finally gained approval for use by the U.K.'s National Health Service (NHS). The U.K.'s National Institute for Health and Clinical Excellence (NICE) changed its mind about this rheumatoid arthritis (RA) treatment to allow its use in patients with moderate-to-severe RA who have failed other similar therapies. A NICE official said the approval was based on new clinical and cost evidence submitted by Merck, which markets it in Europe.
- **The European Society of Cardiology (ESC)** said Europe needs a "single, coordinated" system for regulating medical devices to ensure patient safety. ESC also called for a more stringent process for testing medical technologies.

FDA approvals/clearances

- **ABBOTT's RealTime hepatitis C test –** This PCR-based test measures HCV in both human plasma and serum, with a limit of quantification for both of 12 IU/mL.
- **BAYER's Natazia –** The first four-phase oral contraceptive in the U.S. contains two female hormones – estradiol valerate and dienogest (a progestin). In Europe it is approved and sold as Qlaira.
- **BIOMERIEUX's toxoplasmosis test –** This is the first test to help determine whether a pregnant woman or someone with swollen lymph nodes testing positive for toxoplasmosis, sometimes called cat scratch disease, developed the infection within the past four months. Toxoplasmosis is caused by the parasite *Toxoplasma gondii*.
- **IDAHO TECHNOLOGY's Q fever (Coxiella burnetii) diagnostic test** was cleared for use for military personnel serving overseas. Use of the test is limited to designated Department of Defense laboratories equipped with the Joint Biological Agency Identification and Diagnostic System (JBAIDS).
- **MAQUET CARDIOVASCULAR's Cardioroot –** This one-piece aortic root graft, used to repair or replace diseased and damaged aortas, received FDA 510(k) clearance as well as a CE Mark.
- **MEDICSIGHT's ColonCAD API program –** This computer-aided detection system designed to improve detection of polyps on CT colonography received 510(k) clearance.

Upcoming FDA Advisory Committees and Other Regulatory Meetings of Interest (*items in RED are new since last week*)		
Date	**Topic**	**Committee/Event**
	May 2011	
May 23	**Vertex Pharmaceuticals' telaprevir**, a treatment for hepatitis C	PDUFA date
May 29	**Roche/Genentech's Lucentis** (ranibizumab) – results of Phase III trial	EURETINA Congress in London
May 30	**Optimer Pharmaceuticals' fidaxomicin** for the treatment of *C. diff*	PDUFA date
	June 2011	
June 2-3	Approaches and endpoints for devices for **seizure detection, cognitive evaluation, and traumatic brain injury/concussion assessment**	Joint workshop of the FDA, the American Academy of Neurology, the American Epilepsy Society, and the National Academy of Neuropsychology
June 8-9	**Reprocessing medical devices**	FDA public workshop
June 17	**Celgene's Istodax** (romidepsin) – sDNA for peripheral T-cell lymphoma	PDUFA date
June 17	**Pfizer/King Pharmaceuticals' Acurox** (immediate-release oxycodone), a painkiller	PDUFA date
June 20	**Salix Pharmaceuticals' Xifaxan** (rifaximin) for non-constipation IBS	Company to meet with FDA on complete response letter
June 23	**Pfizer/King Pharmaceuticals/Pain Therapeutics' Remoxy** (tamper-resistant oxycodone CR) for pain	PDUFA date
June 23-24	**HCV drug development**	Workshop on Clinical Pharmacology of Hepatitis Therapy, Boston
June 28-29	**Roche/Genentech's Avastin** (bevacizumab), hearing on appeal of FDA's decision to withdraw the indication for metastatic breast cancer	FDA's Oncologic Drugs Advisory Committee (ODAC)
June 29	**Cellular and gene therapy products** for retinal disorders	FDA's Cellular Tissue and Gene Therapies Advisory Committee
	Other 2011 meetings/events	
July 11	**Novartis's Arcapta Neohaler** (indacaterol) long-acting beta agonist (LABA) for COPD	PDUFA date
July 20	**AstraZeneca's Brilinta** (ticagrelor), an anticoagulant	PDUFA date
August 20	**Regeneron's afilbercept** (VEGF Trap-Eye) for AMD	PDUFA date
August 25	**Shire's Firazyr** (icatibant) for hereditary angioedema	PDUFA date
August 30	**Seattle Genetics and Takeda's brentuximab vedotin** for two orphan indications – refractory Hodgkin's lymphoma and anaplastic large cell lymphoma (ALCL)	PDUFA date
2H11	**Abbott's RX Acculink** carotid stent	FDA final decision expected
Summer	Report on **FDA 510(k) reform**	Institute of Medicine
4Q11	**Ophthotech's ARC-1905** primary endpoint results in Phase I trial in dry AMD	Company announcement or medical conference presentation
4Q11	**Roche/Genentech's Lucentis** (ranibizumab) – Phase III HARBOR trial one-year data on the 2 mg dose in wet AMD	Company announcement or medical conference presentation
December	**Allergan's brimonidine tartrate intravitreal implant** – Phase II trial in dry AMD to complete	Company announcement or medical conference presentation
December 8	**Antares Pharma's Anturol Gel** (oxybutinin gel), a treatment for overactive bladder	PDUFA date
	2012 meetings/events	
February 2012	**Alcon's tandospirone** for dry AMD – Phase III final data expected	Company announcement or medical conference presentation