TRENDS-in-MEDICINE

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by 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…

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NOTE: Subscribe to ***Trends-in-Medicine*** for a report on **Ophthotech's Fovista** for wet age-related macular degeneration (AMD).

SHORT TAKES

- **AC IMMUNE SA – Roche** is buying the rights to an investigational Alzheimer's medication from AC Immune that is designed to block the tau protein and prevent tau tangles in the brain. In 2006, Roche bought the rights from AC Immune to crenezumab, which blocks beta amyloid plaques in the brain.

- **Antipsychotics –** The FDA is concerned about an increasing response to placebo in clinical trials of schizophrenia medications. An analysis by FDA researchers of 32 schizophrenia trials, published in the ***Journal of Clinical Psychiatry***, found that from 1991 to 2008 the response to placebo has been increasing and may be discouraging pharmas from developing new antipsychotics.

- **CELGENE's Revlimid (lenalidomide) –** The company withdrew its European application to widen the use of this multiple myeloma drug as maintenance therapy after the Committee for Medicinal Products for Human Use (CHMP) questioned Revlimid's link to secondary cancers. Celgene reportedly plans to file a new application when it has more clinical data showing the drug's benefits.

- **CSL's Fluvax –** The preliminary findings of a two-year study suggested an excessive immune response to the inactive viral component of this flu vaccine may be responsible for the nine-fold increase in fever and convulsions that occurred in children in the Southern Hemisphere after immunization.

- **DAIICHI SANKYO's Benicar (olmesartan) –** A Mayo Clinic study published in ***Mayo Clinic Proceedings*** linked this blood pressure medication to a potentially life-threatening gastrointestinal condition that mimics celiac disease. Symptoms (nausea, vomiting, diarrhea, and weight loss) improved when patients discontinued the drug.

- **Direct-to-consumer advertising –** A report by ***eMarketer*** predicted that online advertising and promotional spending by pharmas will hit $1.58 billion in 2012 but online spending growth will gradually decline over the next few years.

- **DUNE MEDICAL's MarginProbe –** The FDA's General and Plastic Surgery Advisory Committee voted 10-1 to recommend approval of this radiofrequency probe to help surgeons ensure that lumpectomy margins are clear.

- **GALAXY BIOTECH's (TAK-701, HuL2G7) –** After completing Phase I studies, **Takeda** decided to terminate its license for this cancer drug and return the worldwide

rights to Galaxy, which plans to continue development itself. HuL2G7 is a humanized monoclonal antibody against hepatocyte growth factor (HGF).

- **Hip implants** – The FDA received nearly 17,000 adverse event reports related to metal-on-metal hip implants from 2000 to 2011.

- **HIV drugs** – A study reported in the ***New England Journal of Medicine*** found that HIV-infected children may do better with an antiretroviral regimen of **Merck's Kaletra** (lopinavir) boosted by ritonavir than starting with the usual first-line therapy, **Boehringer Ingelheim's Viramune** (nevirapine).

- **HUMANA** and **NOVO NORDISK** formed a one-year research partnership to explore diabetes treatment and care.

- **INFINITY PHARMACEUTICALS' saridegib (IPI-926)** – The company halted trials of this investigational treatment for advanced, inoperable chondrosarcoma – as well as trials in myelofibrosis – after it failed to beat placebo on progression-free survival in a Phase II trial. Trials in pancreatic cancer were stopped earlier this year.

- **KV PHARMACEUTICAL's Makena (hydroxyprogesterone caproate)** – The FDA said it found no safety issue with compounded versions of this drug to prevent premature birth despite KV's concerns about potency and purity. However, the FDA said "approved hydroxyprogesterone caproate products such as Makena…provide a greater assurance of safety and effectiveness than do compounded products."

- **MEDGENICS' Infradure Biopump**, which uses a patient's tissue to facilitate production and delivery of therapeutic proteins, was granted orphan drug status to treat hepatitis D.

- **ONYX PHARMACEUTICALS' Kyprolis (carfilzomib)** – The FDA's Oncologic Drugs Advisory Committee voted 11-0 with one abstention that this multiple myeloma drug should receive accelerated approval.

- **Opioids** – A study published in ***Anesthesiology*** suggests that the respiratory depression and nausea that some opioid patients experience may have a genetic component. The researchers suggested that downstream molecular genetics may help identify patients who are more (or less) likely to benefit from these painkillers.

- **POZEN's PA-32540 (immediate-release omeprazole + extended-release aspirin)** – The FDA's preliminary decision is that Pozen did not demonstrate bioequivalence for this investigational stomach ulcer drug to 325 mg aspirin. The FDA recommended Pozen seek approval for a lower-dose version, though that would need its own bioequivalence study for approval.

- **PRIMUS PHARMACEUTICALS' Limbrel (flavocoxid)** – A study published in the ***Annals of Internal Medicine*** found this arthritis treatment, a "medical food" marketed as a treatment for joint inflammation, was associated with several cases of clinically significant liver injury. All of the patients recovered when the flavocoxid was discontinued. The researchers urged physicians to discourage their patients from taking it.

- **Prostate cancer** – A study published in ***Cancer Discovery*** reported on a potential new pathway in prostate cancer. Researchers at the University of Virginia in Charlottesville showed that fusion RNAs can be generated without changes to DNA by a new mechanism that they called cis-SAGe (cis-splicing of adjacent genes). The data are highly suggestive for a causal role of the SLC45A3-ELK4 fusion RNA in prostate cancer. *Could this be the Bcr-Abl of prostate cancer?*

- **RANBAXY LABORATORIES** is in trouble with the FDA again, just five months after signing a consent decree. The FDA suspended Ranbaxy from selling, manufacturing, or marketing products from its plant in Maharashtra, India, for four days for failure to maintain proper storage conditions. *Will the FDA review the consent decree now?*

- **ST. JUDE MEDICAL's Durata** – The company said that, after investigation, the lead failure reported to the FDA was due to external abrasion (e.g., from a calcified heart valve or contact with another lead), not the inside-out abrasion that led to the recall of the Riata leads.

- **VALEANT PHARMACEUTICALS** is buying **OraPharma**, whose products include **Arestin** (minocycline hydrochloride), an antibiotic to treat periodontitis.

- **WALGREENS** is buying a 45% interest in **Alliance Boots** in an effort to create a global pharmacy chain. Walgreens has an option to gain full control of Boots in ~3 years. Together, the two chains have >11,000 stores and 370 distribution centers in 12 countries.

- **XANODYNE PHARMACEUTICALS' Zipsor (diclofenac)** – **Depomed** bought the rights to this painkiller.

NEWS IN BRIEF

Bariatric surgery
– similar results with all three surgeries

*What is the best approach to bariatric surgery – Roux-en-Y gastric bypass, sleeve gastrectomy, or banding (e.g., **Allergan's Lap-***

Band)? A study of the BOLD database, which has data on >500,000 bariatric surgery patients, was presented at the American Society for Metabolic and Bariatric Surgery (ASMBS), and the analysis found that 30-day mortality was highest with bypass and lowest with banding. Banding also was the safest in terms of serious complications, reoperation, and readmission, with bypass having the highest rates of complications, and the sleeve falling in the middle.

Bariatric Surgery Comparison			
Measurement	**Bypass**	**Sleeve**	**Banding**
Primary endpoint: 30-day mortality	0.14%	0.08%	0.03%
Length of stay	2.3 days	1.9 days	0.7 days
Serious complications	1.25%	0.96%	0.25%
Reoperation	2.73%	1.7%	0.65%
Readmission to hospital	4.62%	3.61%	1.38%

Last year, the Centers for Medicare and Medicaid Services (CMS) decided it would only cover sleeve gastrectomy when performed in a clinical trial, but CMS agreed to revisit that decision after patients complained. A final decision is expected June 29, 2012.

Interestingly, ~70% of bypass and banding patients had private insurance vs. 57% of the sleeve gastrectomy patients, reflecting a large number of patients who paid for the procedure themselves because CMS did not cover it.

BOEHRINGER INGELHEIM's Pradaxa (dabigatran) – new bleeding data

A new retrospective sub-analysis of the pivotal RE-LY trial, published in ***Circulation***, found similar rates of peri-procedural (7 days prior to 30 days post) bleeding and thromboembolic complications (e.g., stroke or systemic embolism) in non-valvular atrial fibrillation patients undergoing a surgical or invasive procedure treated with Pradaxa as with warfarin, even though there is no drug/agent to reverse the action of Pradaxa as there is for warfarin.

Substudy of RE-LY Trial			
Measurement	**Pradaxa**	**Warfarin**	**Relative Risk**
Peri-procedural major bleeding	5.1%	4.6%	1.09
Major bleeding	3.3%	9.0%	0.36
Stroke	0.5%	0.6%	0.71
CV death	0.5%	0.5%	1.01
Systemic embolism	0.1%	0.1%	1.01
Myocardial infarction	0.5%	0.3%	1.61
Pulmonary embolism	0.1%	0.2%	0.67
Minor bleeding	9.0%	7.8%	1.15
Fatal bleeding	0.1%	0.1%	1.01
Major bleeding by time of drug discontinuation prior to surgery			
<24 hours	6.8%	15.4%	0.44
24-48 hours	3.3%	9.0%	0.36
48-72 hours	4.5%	5.7%	0.79
>72 hours	6.2%	3.6%	1.70

In the study, nearly half of the Pradaxa patients underwent surgery within two days of interrupting treatment vs. 11% of warfarin patients. The most common surgeries/procedures were pacemaker or defibrillator insertion (10.3%), dental procedures (10.0%), diagnostic procedures (10.0%), cataract removal (9.3%), colonoscopy (8.6%), and joint replacement (6.2%).

BRISTOL-MYERS SQUIBB's Eliquis (apixaban) – possible ways to reverse it

Laboratory research presented in an American Heart Association webinar suggests that there may be three ways to reverse this anticoagulant prior to surgery, though the strategy still needs to be proven in humans: Adding prothrombin complex concentrates (PCCs, 50 IU/kg), activated prothrombin complex concentrates (aPCCs, 75 IU/kg), and recombinant Factor VII (rFVIIa, 270 µg/kg). They found:

- PCC and aPCC seemed more efficient than rFVIIa at restoring the generation of thrombin.
- rFVIIa was the quickest to produce a compact blood clot, followed by aPCC and PCC.
- rFVIIa was most effective in studies with blood circulating through a damaged blood vessel, followed by PCC and aPCC.

HISTOGENICS' NeoCart Autologous Cartilage Tissue Implant (ACTI) – very promising Phase II results

The two-year results of a Phase II trial, published in the ***Journal of Bone and Joint Surgery***, found that this implant – autologous bioengineered neocartilage grown outside the body using a patient's own cells – which is designed for patients with Grade II chondral injury to the femur, had better efficacy than microfracture surgery, which works by creating tiny fractures in the underlying bone. And NeoCart was just as safe. A multicenter Phase III trial is underway comparing NeoCart to microfracture surgery.

IDENIX PHARMACEUTICALS

- **IDX184.** The company announced interim data from a 31-patient cohort of an ongoing Phase IIb trial of this nucleotide inhibitor given with pegylated interferon and ribavirin to treatment-naïve hepatitis C patients. Of the patients who had an eRVR at Weeks 4 and 12 and then received 12 weeks of additional triple therapy, all four (100%) at the 100 mg

dose and four of five (80%) at the 50 mg dose achieved SVR4. The other patients entered a 36-week PegIFN/RBV treatment phase.

- **IDX719.** The company announced that this NS5A inhibitor for hepatitis C successfully completed a 3-day, 64-patient proof-of-concept trial, showing pan-genotypic activity, with up to a 3.7 $\log_{10}$ IU/mL viral load reduction in genotype 1 patients, up to 4.1 $\log_{10}$ drop in genotype 2, up to 3.4 $\log_{10}$ drop in genotype 3, and up to 3.9 $\log_{10}$ drop in genotype 4.

Inferior vena cava (IVC) filters – maybe not a good idea in bariatric surgery

An analysis of data from a Michigan registry of 1,045 bariatric surgery patients who got an IVC filter prophylactically found that use of these filters during bariatric surgery significantly ***increased*** the risk of a venous thromboembolism (VTE) vs. a matched cohort of patients who did not get a filter (1.8% vs. 0.4%). The VTE rate with a filter also was higher than in an analysis of 29,409 unmatched patients who did not get a filter.

In addition, there was also a trend toward higher mortality with the filters, more pulmonary embolisms, more deep vein thrombosis, more complications, and more serious complications.

IVC Filters in Bariatric Surgery Patients

Measurement	IVC filter patients	Patients with no IVC filter
VTE	1.8%	0.4%
Mortality	0.07%	0.02%
Pulmonary embolism	0.7%	0.2%
Deep-vein thrombosis	1.2%	0.3%
Disabling complications	1.1%	0.5%
Serious complications	5.7%	3.7%

Jonathan Finks, MD, who presented the findings at the ASMBS meeting, concluded, "In bariatric surgery, the risks of IVC filter insertion exceed the benefits, and their use should be discouraged." However, other bariatric surgeons disagreed with these findings and reported positive experiences with the devices.

JOHNSON & JOHNSON

- **Gynecare TVT.** A study published in the ***New England Journal of Medicine*** found this vaginal sling, used to treat pelvic organ prolapse, cuts the risk for subsequently developing incontinence by ~50%. However, women who got the sling were at a higher risk for complications, such as difficulty emptying the bladder, urinary tract infection, bladder perforation, and bleeding.
- **Xarelto (rivaroxaban).** The FDA rejected this anticoagulant, developed in partnership with **Bayer**, for the treatment of acute coronary syndrome (ACS), issuing a complete response letter. In May 2012, the FDA's Cardiovascular and Renal Drugs Advisory Committee voted 6-4 against this expanded label for Xarelto, saying the data were insufficient and there was concern about bleeding.

Mammograms – who's right, the AMA or the USPSTF?

Should you or shouldn't you do preventive mammogram screenings? The U.S. Preventive Services Task Force (USPSTF) says routine mammography screening for breast cancer is unnecessary in women under age 50. The American Medical Association's House of Delegates disagrees, coming out in support of screening women starting at age 40.

The House of Delegates also adopted a resolution expressing "concern regarding recent recommendations by the USPSTF on screening mammography and prostate specific antigen (PSA) screening and the effects these recommendations have on limiting access to preventive care for Americans."

MEDTRONIC's Activa – DBS holds up over 3 years

A randomized, 159-patient study published in ***Neurology*** found that deep brain stimulation of the globus pallidus interna (GPi) or subthalamic nucleus (STN) appears to help people with Parkinson's disease over the long term (3 years). In the study, deep brain stimulation of both areas improved motor symptoms by 32% over 3 years, and deep brain stimulation of the GPi region was associated with a slower decline in thinking skills. In an accompanying editorial, Michele Tagliati, MD, from Cedars-Sinai Medical Center pointed out that ~50% of the initial participants were lost to follow-up, though she said the study did provide more reliable evidence that the treatment is stable over time.

MERCK

- **Health outcomes effort.** The company is collaborating with **Geisinger Health System** on ways to improve patient health outcomes by providing employees time and energy ***but not drugs***. Groups of Geisinger and Merck employees will work to improve patients' adherence to care plans, expand patients' role in making decisions about their conditions, share information among extended-care teams, and improve clinical-care processes.
- **Children's Claritin (loratadine).** The Public Health Advocacy Institute and 10 other groups filed a complaint with the Federal Trade Commission (FTC) charging that Merck advertised this allergy medicine directly to children,

using animated characters from the movie "Madagascar 3: Europe's Most Wanted." The groups suggested that children may confuse grape-flavored Claritin with candy.

- **Vorapaxar.** A 3,787-patient substudy of the larger TRA2P-TIMI-50 trial was presented in an American Heart Association Emerging Science Series webinar. The substudy found that this antiplatelet agent (a PAR-1 antagonist) reduced the rate of deep-vein thrombosis (DVT) and the need for leg revascularization significantly better than placebo in patients with peripheral artery disease (PAD). However, the drug did not significantly reduce the risk of heart attack or stroke, and it was associated with more serious bleeds.

  Marc Bonaca, MD, MPH, a cardiologist from Harvard Medical School, said, "This is the first outpatient therapy that has been shown to reduce the risk of blood clots and the need for artery-opening revascularization procedures in the legs of patients with PAD."

Substudy of TRA2P-TIMI-50		
Measurement	**Vorapaxar**	**Placebo**
MACE	11.3% (p=Nss)	11.9%
Hospitalization for blood clots in limbs	2.3%	3.9%
Revascularization	18.4%	22.2%
Moderate/severe bleeding	7.4%	4.5%

Nanoparticles – linked to RA

Researchers in Ireland and the U.S. National Institute for Occupational Safety and Health (NIOSH) reported that exposure to nanoparticles can seriously affect health, linking them to rheumatoid arthritis (RA), chronic lung inflammation, and other autoimmune diseases. The two sets of researchers found identical responses in human cells and in mice: a transformation of the amino acid arginine into citrulline, a protein that appears to be the trigger for autoimmune conditions. Further study is needed to see if all nanoparticle types cause this problem and to identify therapeutic/preventive approaches.

PFIZER

- **Prevnar 13.** The Centers for Disease Control and Prevention's Advisory Committee on Vaccine Practices (ACVP) unanimously recommended that immunocompromised adults – those with AIDS, cancer, organ transplants, advanced kidney disease, etc. – be given this pneumococcal vaccine, including people who have already had **Merck's Pneumovax 23** to give them broader protection. However, the ACVP has not yet decided if all adults ≥age 50 should get Prevnar 13.
- **Social media.** Pfizer is discontinuing enrollment in its effort to use social media to recruit patients for clinical trials. One year after launching this trial-in-a-box concept to recruit patients for a trial of **Detrol** (tolterodine) in overactive bladder, Pfizer has given up.
- **Tafamidis meglumine.** The FDA rejected this experimental treatment for transthyretin familial amyloid polyneuropathy (TTR-FAP), a rare genetic disorder that causes progressive and fatal nerve failure, issuing a complete response letter (CRL) that said another trial is needed to prove efficacy.
- **Japan.** **Takeda** is stopping its distribution of 13 Pfizer drugs in Japan at the end of 2012, with Pfizer taking over the sales.

ROCHE

- **Avastin (bevacizumab).** A 1,600-patient Canadian study, published in the ***Canadian Journal of Ophthalmology***, found that patients who got Avastin for wet age-related macular degeneration were 12 times more likely to develop serious intraocular inflammation (with some even losing their vision entirely) than patients who got the approved VEGF inhibitor **Lucentis** (ranibizumab).
- **Erivedge (vismodegib, GDC-0449).** A small study reported at the American Association for Cancer Research's Pancreatic Cancer Conference found that 10 of the 20 evaluable pancreatic cancer patients given this hedgehog inhibitor followed by standard chemotherapy with **Lilly's Gemzar** (gemcitabine) had objective responses or stable disease (5 objective responses and 5 stable disease, with PFS 50%). The researchers reported that some patients who progressed on Erivedge alone had a major response to the combination. And the researchers found that pre-treatment levels of sonic hedgehog predicted treatment response to the combination, suggesting that could be a good predictive biomarker for the regimen.
- **Perjeta (pertuzumab).** The company announced that the Phase III CLEOPATRA study showed adding Perjeta to **Herceptin** (trastuzumab) + docetaxel improved overall survival, a secondary endpoint in the trial, in women with HER2+ metastatic breast cancer.
- **Autism.** The company plans to collaborate with **Seaside Therapeutics** on the development of medications to treat autism spectrum disorders and fragile X syndrome. Roche is getting exclusive rights to Seaside's patents and the option to license commercial rights. This covers mGluR5 antagonists (including RG-7090, which is in Phase II in

fragile X). However, Seaside retains exclusive rights to this GABA-B agonist program (e.g., STX-209, which is in Phase III in fragile X and Phase IIb in autism), though Roche has options to license STX-209.

- **Investigation.** Roche is being investigated by the European Medicines Agency (EMA) for not informing regulators about ~80,000 adverse events involving U.S. patients taking Roche drugs, including 15,161 deaths. Roche said the division that received the reports didn't send them to the safety department. The EMA said it is not known whether the deaths were due to natural disease progression or were drug-related.

SANOFI

- **Plavix (clopidogrel).** In a viewpoint article in the ***Journal of the American Medical Association***, Paul Gurbel, MD, of Sinai Hospital of Baltimore and colleagues suggested that the only patients benefiting from the anti-thrombotic effects of Plavix may be smokers. They raised the question of whether Plavix should ***only*** be prescribed to smokers, with non-smokers getting **Lilly's Effient** (prasugrel) or **AstraZeneca's Brilinta** (ticagrelor) instead, since those drugs have not shown any interaction with smoking status.

  The authors pointed out that subanalyses of large-scale clinical trials have consistently shown substantial reductions in morbidity and mortality with clopidogrel in smokers but not in non-smokers, saying, "These observations raise concerns about the costs and potential risks incurred by treating nonsmokers with clopidogrel." Dr. Gurbel suggested a prospective study comparing Effient and Plavix by smoking status.

- **Semuloparin.** The FDA's Oncologic Drugs Advisory Committee voted against approval of this anti-clotting agent in chemotherapy patients, saying the data didn't provide meaningful support or approval.

TEVA's Copaxone (glatiramer acetate) – less frequent dosing may be possible

The international GALA trial of >1,400 patients found this multiple sclerosis drug may not have to be injected daily, suggesting that a higher dose (40 mg/1 ml) three times a week may be sufficient. The trial of this less-frequent dosing regimen met its primary endpoint, reducing the annualized relapse rate by 34.4% vs. placebo. All of the secondary endpoints were met, except for a reduction in brain atrophy. A 1-year open-label extension of the GALA trial is underway.

Vitamin D – the debate continues on its role

Should you or shouldn't you take vitamin D and calcium supplements? The USPSTF says there is no benefit to low doses for fracture prevention. However, a meta-analysis found a mortality benefit to the combination.

In a ***MedPageToday.com*** survey, 55% of respondents said they would recommend patients take both vitamin D and calcium, 27% said they would tell patients to forget supplements and eat a balanced diet, 10% said they would tell patients to take the combination but only at high doses, and 8% said they would do something else.

REGULATORY NEWS

Congressional panel blames drug shortages on FDA

The House Committee on Oversight and Government Reform issued a report that charged that the nationwide shortages of critical drugs, especially oncology drugs, is largely the FDA's fault because the Agency failed to ensure that enforcement and compliance activities were conducted properly.

The report found that the FDA's regulatory process effectively forced the shutdown of 30% of the total manufacturing capacity of four of the largest makers of generic injectable drugs: **Bedford Laboratories**, **Hospira Pharmaceuticals**, **Sandoz Pharmaceuticals**, and **Teva Pharmaceuticals**.

The report also put some of the blame on:

- The Medicare Modernization Act, which dramatically reduced Medicare's reimbursement for generic drugs, especially older generics, making some of them unprofitable.
- Group purchasing organizations (GPOs), which negotiate big contracts to purchase drugs, concentrating the market since only large manufacturers can produce drugs at the price negotiated by the GPOs and still make a profit.

The committee recommended a "common-sense approach" to regulation be restored at the FDA – by allowing inspection problems that do not pose an immediate threat to public safety to be corrected under close supervision rather than taking actions that lead companies to shut down manufacturing lines.

FDA issues new guidance on genotoxicity testing for small molecules

The FDA issued new guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals – small molecules, not

biologics – meant for human use. The revised guidance, which is designed to improve risk characterization of carcinogenic effects, describes internationally agreed-upon standards for follow-up testing and interpretation of positive results *in vitro* and *in vivo* in standard genetic toxicology. The new approach is designed to reduce the risk of false negative results for compounds with genotoxic potential while also recognizing that a positive test does not necessarily mean a compound poses a genotoxic/carcinogenic hazard to humans.

HHS pilots IT program

The Department of Health and Human Services' Health IT division is launching a pilot program in Indiana and Ohio to give doctors, pharmacists, and emergency departments real-time access to patient prescription records. Currently, the lag time can be up to 30 days.

FDA approvals/clearances

- **KFx MEDICAL** received 510(k) clearance for a 5-millimeter tissue fixation anchor designed for small joint (ankle and foot) surgeries. The device is part of the company's **AppianFx** implant line.
- **LENSAR's LensAR Laser System**, a next-generation cataract surgery laser system, was granted 510(k) clearance for anterior capsulotomy and laser phacofragmentation.
- **PFIZER's Lyrica (pregabalin)** – The FDA approved an expanded indication for this painkiller to treat pain due to spinal cord injuries. This is the first FDA-approved treatment for neuropathic pain from spinal cord injury.
- **ST. JUDE MEDICAL's Amplatzer** – The latest version of this vascular plug (AVP 4) was approved.
- **SIEMENS HEALTHCARE's Somatom Definition Edge**, a single-source CT scanning device with a maximum rotation speed of 0.28 seconds, received 510(k) clearance.
- **SUREFIRE MEDICAL's Surefire high-flow microcatheter**, which is designed to fit in small vessels, was granted 510(k) clearance.

FDA recalls/warnings

- **INNOVISION's Innocor Ergospirometry System, Cardiopulmonary Exercise Testing Option, and LCI Option for Innocor** – The company received a warning letter that the manufacturing of these devices did not meet current good manufacturing practice (cGMP) requirements at its plant in Denmark, particularly with respect to design control, training, and recordkeeping.
- **MEDIAGNOST GMBH Human Growth Hormone diagnostic kits** – The company received a warning letter that these tests did not meet cGMP requirements. In particular, the FDA found that the process used in the production of human growth hormone was not validated.
- **MERCK** recalled a batch of measles, mumps, and rubella vaccines because they were accidentally shipped prior to being approved for market release.
- **MILLAR INSTRUMENTS' disposable pressure transducer catheters** – The company received a warning letter that these devices did not meet cGMP requirements.
- **NIDEK MEDICAL PRODUCTS' Medical Mark5 Nuvo Lite Oxygen concentrators** – The voluntary recall of these devices because of capacitor-related fires was upgraded by the FDA to a Class I recall.
- **SIEMENS HEALTHCARE DIAGNOSTICS' *in vitro* diagnostic devices** – The company received a warning letter that these devices did not meet cGMP requirements and that the company did not reply in a timely manner to the FDA's previous warning letter. Just a couple of weeks ago, **Siemens** was reprimanded by the FDA for failure to respond in a timely manner to a different complaint at another facility. *Is Siemens deliberately trying to get on the FDA's bad side?*
- **TELEFLEX's surgical clips** to close the renal artery during transplant surgery – The FDA has contraindicated these surgical clips for patients undergoing laparoscopic kidney donor surgery.
- **TERUMO's Surshield Safety Winged intravenous infusion set and blood collection set** – The company received a warning letter that manufacturing of these devices at its Medical Products Hangzhou, China, plant did not meet cGMP requirements because, among other things, the validation test had not been approved.

Regulatory news from other countries

Singapore: The Health Sciences Authority issued draft guidance on a plan to adopt two registration procedures for Class B medical devices: expedited or immediate registration of low-to-moderate-risk devices. The proposal is open for comments through June 28, 2012.

Upcoming FDA Advisory Committees and Other Regulatory Meetings of Interest (*items in RED are new since last week*)		
Date	**Topic**	**Committee/Event**
	June 2012	
June 25	**QRxPharma's MoxDuo** (morphine + oxycodone) for pain	PDUFA date
June 27	**Arena Pharmaceuticals and Eisai's Lorqess** (lorcaserin) for obesity	PDUFA date
June 27	**Onyx Pharmaceuticals' carfilzomib**, a treatment for relapsed and refractory multiple myeloma	PDUFA date
June 27-28	Risk:benefit of **metal-on-metal hip replacement** and **resurfacing**	FDA's Orthopaedic and Rehabilitation Devices Advisory Committee
June 28	**Bristol-Myers Squibb's Eliquis** (apixaban), an anticoagulant for the prevention of stroke in Afib	PDUFA date
June 29	**Johnson & Johnson's Xarelto** (rivaroxaban) for acute coronary syndrome	PDUFA date
June 29	**Astellas Pharma's Betanis** (mirabegron) to treat overactive bladder	PDUFA date
June 29	**Sleeve gastrectomy** coverage reimbursement reconsideration	CMS decision date
	July 2012	
July 17	**Vivus' Qnexa** (phentermine + topiramate) for weight loss	PDUFA date (extended from April 17)
July 24	**GlaxoSmithKline's Tykerb** (lapatinib) **+ Roche's Herceptin** (trastuzumab), supplemental indication for HER2+ metastatic breast cancer	FDA's Oncologic Drugs Advisory Committee (ODAC)
July 25	Discussion of presurgical identification of clear-cell carcinoma of the kidney using an imaging test	FDA's Oncologic Drugs Advisory Committee (ODAC)
July 26	**Amarin's AMR-101** (omega-3 fish oil EPA) to treat hypertriglyceridemia	PDUFA date
July 26	**Horizon Pharma's Lodotra** (low-dose prednisone) for rheumatoid arthritis	PDUFA date
July 27	**Onyx Pharmaceuticals' Kyprolis** (carfilzomib) for multiple myeloma	PDUFA date
July 27	**Salix Pharmaceuticals and Progenics Pharmaceuticals' Relistor** (subcutaneous methylnaltrexone bromide) for chronic non-cancer pain	PDUFA date
July 30	**Regeneron's Arcalyst** (rilonacept) for gout	PDUFA date
July 30	**Almirall and Forest Laboratories' aclidinium** inhaled therapy for chronic obstructive pulmonary disease (COPD)	PDUFA date
	August 2012	
August 4	**Regeneron Pharmaceuticals** and **Sanofi's Zaltrap** (aflibercept) for colon cancer	PDUFA date
August 12	**Talon Therapeutics' Marqibo** (vincristine sulfate liposomes injection) for Philadelphia chromosome-negative acute lymphoblastic leukemia (ALL)	PDUFA date (extended from May 13)
August 21	**Pfizer's tofacitinib**, an oral JAK2 inhibitor for rheumatoid arthritis	PDUFA date
August 27	**Gilead Sciences' Quad** (emtricitabine+tenofovir+elvitegravir+cobicistat) for HIV	PDUFA date
	Other 2012	
September tba	**Vivus' Qnexa** (topiramate + phentermine) for obesity	EMA oral hearing
September 5	**Salix Pharmaceuticals' Provir** (crofelemer) for HIV-related diarrhea	PDUFA date (extended from June 5)
September 8	**Ironwood Pharmaceuticals and Forest Laboratories' linaclotide** for irritable bowel syndrome	PDUFA date
September 10	**Navidea Biopharmaceuticals' Lymphoseek**, a radioactive agent for tracing lymph nodes in cancer patients	PDUFA date (extended from June 10)
September 14	**Gilead Sciences' Truvada PrEP** HIV therapy to help prevent the transmission of HIV to healthy people	PDUFA date (extended from June 15)
September 23	**Regeneron's Eylea** (aflibercept) for central retinal vein occlusion (CRVO)	PDUFA date
October 21	**Impax Laboratories' IPX-066** for Parkinson's disease	PDUFA date
October 29	**Cornerstone Therapeutics' CRTX-080** to treat hyponatremia	PDUFA date
October 29	**Novo Nordisk's Degludec and DegludecPlus** (human recombinant basal insulin)	PDUFA date (extended from July 29)
	2013	
January 29	**Sanofi/Genzyme and Isis Pharmaceuticals' Kynamro** (mipromersen) for homozygous familial hypercholesterolemia	PDUFA date