NEW DRUGS
Linzess for Irritable Bowel Syndrome With Constipation
Linaclotide (Linzess, Ironwood Pharmaceuticals) capsules have been approved to treat chronic idiopathic constipation and irritable bowel syndrome (IBS) with constipation (IBS-C) in adults. IBS-C is a subtype of IBS.

The product is available in strengths of 145 mg or 290 mg; however, the 290-mg dose is not approved for chronic constipation because it was found to be no more effective than the 145-mg dose.

Linaclotide is taken once daily on an empty stomach, at least 30 minutes before the first meal of the day. A boxed warning mentions that the drug should not be used in patients 17 years of age and younger.

Source: FDA, August 30, 2012

Xtandi for Prostate Cancer
Enzalutamide (Xtandi, Astellas/Medivation) was approved 3 months ahead of schedule to treat men with late-stage castration-resistant metastatic or recurrent prostate cancer who were previously treated with docetaxel (Taxotere/Sanoﬁ). In a study enrolling 1,199 patients, the median overall survival with the study drug was 18.4 months, compared with 13.6 months with placebo.

Xtandi is discussed in this month’s Pharmaceutical Approval Update column on page 557.

Source: FDA, August 31, 2012

Bosulif for Chronic Myelogenous Leukemia
The FDA has approved an orphan drug, bosutinib (Bosulif, Pfizer), for the treatment of chronic myelogenous leukemia (CML).

Most patients with CML have a genetic mutation that causes the bone marrow to produce tyrosine kinase. Bosutinib is intended for patients with chronic, accelerated or blast phase Philadelphia chromosome–positive CML who have resistant disease or who cannot tolerate other therapies, including imatinib (Gleevec, Novartis). Bosutinib blocks the signal of tyrosine kinase, which promotes the development of abnormal granulocytes.

Bosutinib was evaluated in a single clinical trial that enrolled 546 adults.

Dasatinib (Sprycel, Bristol-Myers Squibb) and nilotinib (Tasigna, Novartis) are also approved to treat CML.

Source: FDA, September 4, 2012

Stribild for HIV Infection
A once-daily combination tablet, Stribild (Gilead), is approved to treat HIV-1 infection in therapy-naive adults. Stribild contains emtricitabine (Emtriva) and tenofovir (Viread) plus two new drugs (elvitegravir and cobicistat). Elvitegravir is an HIV integrase strand-transfer inhibitor, which interferes with viral multiplication. Cobicistat, a pharmacokinetic enhancer, is used to prolong the effect of elvitegravir.

The combination of emtricitabine and tenofovir (Truvada) was approved in 2004 to block the action of another enzyme that HIV needs to replicate in the body.

Stribild was evaluated in two double-blind clinical trials. Patients were randomly assigned to receive Stribild or Atripla (Truvada plus efavirenz [Sustiva, Bristol-Myers Squibb]) once daily in the first trial; and Stribild or Truvada plus atazanavir (Rayataz, Bristol-Myers Squibb) and ritonavir (Norvir, Abbott) once daily in the second trial.

At 48 weeks, from 88% to 90% of the Stribild patients had an undetectable amount of serum HIV, compared with 84% of patients receiving Atripla and 87% receiving Truvada plus atazanavir and ritonavir.

A boxed warning for Stribild refers to a buildup of serum lactic acid and severe liver problems. Stribild is not approved for the treatment of chronic hepatitis B virus infection.

Source: FDA, August 27, 2012

Aubagio for Relapsing MS
Teriflunomide (Aubagio, Sanofi/Genzyme) is a new therapy for relapsing forms of multiple sclerosis (MS) in adults. In clinical trials, patients receiving teriflunomide had a relapse rate that was roughly 30% lower than placebo controls.

A boxed warning mentions a risk of liver problems, including death, and a risk of birth defects. Blood tests to check liver function should be performed before and periodically during treatment.

Because animal studies suggest that the drug may cause fetal harm, women of childbearing age should not be pregnant before starting therapy.

Sources: FDA and MedPage Today, September 12, 2012

Choline C 11, an Imaging Agent For Prostate Cancer
Choline C 11 Injection, an agent used in imaging, has been approved for use in detecting recurrent prostate cancer. The injection, developed by the Mayo Clinic, must be produced in a specialized facility and used shortly after production.

The radioactive form of choline (a vitamin) has been used in positron emission tomography (PET) imaging for several years, but the Mayo Clinic is the first facility to receive approval for the manufacture and use of the injectable agent.

Choline C 11 is used in patients with blood prostate-specific antigen (PSA) levels that have increased after prior treatment of prostate cancer. The product can detect recurrence of cancer that might be missed with other imaging. Choline C 11 was evaluated in four studies.

Sources: http://prostatecancerinfo-link.net; MedPage Today, September 12, 2012

NEW INDICATION
Nucynta ER for Diabetic Peripheral Neuropathic Pain
Janssen Pharmaceuticals has announced the approval of its supplemen-
tal New Drug Application (sNDA) for tapentadol extended-release (Nucynta ER) tablets for the management of pain in adults with diabetic peripheral neuropathy (DPN). Tapentadol provides continuous, around-the-clock opioid analgesia as needed for an extended period of time.

This is the first opioid indicated for neuropathic pain associated with DPN. Tapentadol is also approved for around-the-clock relief of chronic pain in adults.

Approximately 60% to 70% of patients with diabetes have a form of neuropathy. DPN is the most common type.

Tapentadol ER, a centrally acting synthetic analgesic, was approved in August 2011 and is classified as a Schedule II agent. A boxed warning refers to the risk of opioid abuse.

The tablets are taken twice daily and are available in strengths of 50, 100, 150, 200, and 250 mg.

Source: Janssen, August 29, 2012

NEW FORMULATIONS
Tbo-Filgrastim for Neutropenia
Tbo-filgrastim (Sicor Biotech/Teva) is now approved to reduce the duration of severe neutropenia in patients receiving chemotherapy.

Tbo-filgrastim, a short-acting recombinant form of granulocyte colony-stimulating factor (G–CSF), is intended to treat non-myeloid malignancies in adults who have used chemotherapy drugs that caused a decreased production of neutrophils in bone marrow. Tbo-filgrastim stimulates the increased production of neutrophils. It is given as an injection beginning 24 hours after chemotherapy treatment.

In a study of 348 adults with advanced breast cancer, patients receiving tbo-filgrastim recovered from severe neutropenia in 1.1 days compared with 3.8 days in those receiving placebo.

This is the first new G–CSF agent to be approved in the U.S. in more than 10 years. Last year, Teva agreed to wait until November 2013 to launch its versions of Amgen’s Neupogen (filgrastim) and Neulasta (pegfilgrastim) in the U.S.

Source: FDA, August 29, 2012; http://newsfeedresearcher.com

Pediatric Afinitor
For Rare Brain Tumor
An oral suspension of everolimus tablets (Afinitor Disperz, Novartis) has been approved for children with a noncancerous subependymal giant-cell astrocytoma (SEGA). Afinitor is usually considered to be an anti-cancer medication.

An orphan drug, Afinitor Disperz is indicated for patients 1 year of age and older with tuberous sclerosis complex (TSC) and inoperable SEGA. Everolimus had been indicated for use only in patients 3 years of age and older. In 2010, everolimus was granted an accelerated approval to treat SEGA in patients with TSC.

A rare genetic disease, TSC causes tumors to grow in the brain and in other organs. SEGA can cause life-threatening complications by blocking the flow of fluid in the brain.

The suspension is available in dose increments smaller than those used in the adult dosage form, and it easily dissolves in a small volume of water. Everolimus inhibits the uncontrolled activity of the mTOR kinase, a protein that plays a role in the growth of SEGA tumors that occur in patients with TSC.

Everolimus tablets are also approved for adults with renal cell carcinoma; pancreatic neuroendocrine tumors; TSC; renal angiomylipomas; and postmenopausal hormone receptor–positive, HER-2–negative breast cancer in combination with exemestane (Aromasin, Pfizer).

Source: FDA, August 29, 2012

Higher-Dose Exelon Patch
In Alzheimer’s Disease
A 40% higher dose of the rivastigmine transdermal system (Exelon Patch, Novartis) is now approved for the treatment of patients with mild-to-moderate Alzheimer’s disease (AD). The new dosage is 13.3 mg every 24 hours.

The FDA’s approval of the patch was based on the 48-week double-blind phase of the OPTIMA study in patients who met criteria for functional and cognitive decline with the previously approved 9.5-mg/24-hour dose. Patients receiving the higher dose (13.3 mg) experienced improved overall function compared with the 9.5-mg/24-hour patch.

Discontinuations resulting from adverse events were less frequent with the higher-dose patch.

Rivastigmine is an acetylcholinesterase inhibitor that boosts activity in surviving cholinergic neurons, helping to compensate for the neurodegeneration caused by AD. The drug does not modify the underlying disease process.

Source: Novartis, September 4, 2012; MedPage Today, September 5, 2012

DRUG NEWS
Label Changes and Warnings
Eye Problems With Kalydeco
Cataracts developed in young rats that were treated with the cystic fibrosis drug ivacaftor (Kalydeco, Vertex), prompting the FDA to order a label change. After receiving a dose of ivacaftor about one-tenth the maximum recommended for humans, the young rodents developed cataracts. It is unclear whether the same risk applies to humans.

Adult rats treated with ivacaftor did not show ocular abnormalities. Vertex indicated that this problem had not been noted in its clinical trials, and the company received no reports of the problem in postmarketing surveillance.

Approved earlier this year, ivacaftor is the first drug for cystic fibrosis that addresses the underlying defect in chloride channels that causes the disease.

The FDA has asked Vertex to conduct a 2-year risk-assessment study. The continued on page 549
No Revatio for Children

The FDA has cautioned against the use of sildenafil (Revatio, Pfizer) to treat pulmonary arterial hypertension (PAH) in children 1 through 17 years of age. An unexpectedly high mortality rate was observed among children receiving the drug in high doses in a clinical trial. Revatio has never been approved for the treatment of PAH in children.

During 3 years of follow-up in a study that included 234 patients, most of the deaths resulted from heart failure or PAH, which are the typical causes of death in children with the disorder. In addition, the primary endpoint of the 16-week randomized, placebo-controlled phase of the trial (improvement in exercise capacity) was not met.

The drug was given three times per day in low, medium, or high doses according to the patient’s body weight.

Sildenafil is a phosphodiesterase-5 inhibitor approved for the treatment of PAH in adults at a maximum of 20 mg three times per day to delay disease worsening and to increase exercise ability. The drug’s labeling will be changed to recommend against an off-label use in children.

A different dosage of sildenafil is sold as Viagra to treat erectile dysfunction in adults. The new safety concerns do not apply to Viagra.

Sources: FDA, August 30, 2012; MedPage Today, August 31, 2012

Recall: Generic Nimodipine

One lot of a generic form of nimodipine, which is used to treat patients with subarachnoid hemorrhage, has been recalled by Sun Pharmaceutical Industries because of a possible problem with bioavailability. Nimodipine, a cerebral atrial spasm inhibitor, is also known by its brand name, Nimotop, made by Bayer.

A consumer reported seeing crystals in 30-mg capsules of the drug. It is possible that the crystallization of the nimodipine fill material in the capsule could have adverse effects on the product’s bioavailability, causing the drug to no longer be bioequivalent.

The lot in question was shipped from January to April by Caraco Pharmaceuticals and included blister packs of 30 and 100 capsules. Lot numbers were 3305.039A (100-capsule pack, NDC product No. 57664-135-65) and 3305.039B (30-capsule pack, NDC product No. 57664-135-64).

Sources: FDA, September 5, 2012; MedPage Today, September 6, 2012

TNF Blockers Decrease Heart Risk in Psoriasis Patients

Treating psoriasis patients with biologic drugs that inhibit tumor necrosis factor (TNF) may lower the risk of heart attacks more effectively compared with other treatments, observational results suggest. Patients who received TNF inhibitors were half as likely to have a myocardial infarction (MI) as those who received topical drugs. In the retrospective cohort study, oral drugs and phototherapy were also better than topical treatment in terms of MI risk, although rates tended to be even lower with the TNF inhibitors.

Researchers retrospectively analyzed the health plan databases of Kaiser Permanente Southern California. During a mean 4.3 years of follow-up, the TNF blockers were associated with a 21% lower risk of MI compared with other systemic drugs or phototherapy. The study did not compare individual TNF blockers, such as infliximab (Remicade), etanercept (Enbrel), and adalimumab (Humira).

Aggressive psoriasis therapy can lower inflammation, thereby reducing the risk of MI. Psoriasis, a systemic inflammatory disease, is linked to cardiovascular risks such as obesity, atherosclerosis, type-2 diabetes, stroke, MI, and cardiac death.

Sources: Arch Dermatol, 2012; MedPage Today, August 20, 2012

Inspra Not Living Up to Promise In Heart Failure

Eplerenone (Inspra, Pfizer) has been hailed as an effective drug for reducing hospitalizations and mortality rates in...
patients with mildly symptomatic heart failure and other cardiovascular conditions. It also produces fewer adverse effects than its older competitors, the aldosterone antagonists such as spironolactone (Aldactone, Pfizer). Because of eplerenone’s cost, however, researchers from Maimonides Medical Center, N.Y., and Texas Tech University Health Sciences Center in El Paso sought to determine whether the higher price was justified according to patient outcomes.

Eplerenone had been studied in only one randomized trial of mildly symptomatic heart failure, whereas spironolactone and canrenone (e.g., Contaren, Amirall) have been studied much more extensively. In the absence of head-to-head trials, the researchers looked for randomized studies of aldosterone antagonists and comparators, including placebo, angiotensin-converting enzyme (ACE) inhibitors, angiotensin-receptor blockers (ARBs), and beta blockers. The primary outcome was all-cause mortality at the follow-up evaluation. The secondary outcome was cardiovascular mortality. Sixteen studies met their criteria, with 3,016 subjects taking aldosterone antagonists other than eplerenone and 9,489 taking eplerenone.

All aldosterone antagonists significantly reduced mortality rates in patients with heart failure and post-myocardial infarction (MI) left ventricular dysfunction. However, the aldosterone antagonists (with a 26% mortality reduction) outperformed eplerenone by far (with a 15% reduction in mortality). Similarly, eplerenone was not as effective as the other aldosterone antagonists in reducing cardiovascular mortality rates (17% vs. 25%, respectively).

Eplerenone was tested in a generally healthier population, but outcomes were less positive, resulting in, for example, higher rates of hyperkalemia. Eplerenone-treated patients did have a lower rate of gynecomastia, compared with older aldosterone antagonists, but the reduced risk was not statistically significant.

The researchers concluded that eplerenone did not fulfill its touted benefits in terms of effectiveness and incidence of side effects. They advise a head-to-head comparison between the two agents to determine true differences in efficacy.


Was Vioxx Dangerous For Too Long?

When rofecoxib (Vioxx, Merck) was withdrawn from the market in 2004, the company cited new 3-year data showing unacceptably high cardiovascular risks—nearly doubling cardiovascular (CV) thrombotic events—in the placebo-controlled APPROVe (Adenomatous Polyp Prevention on Vioxx) study.

Merck said that the first 18 months of the APPROVe study did not show an increased risk, and this finding was similar in two previous placebo-controlled studies. However, researchers from Columbia University, University of New Mexico, Wake Forest University, Brigham and Women’s Hospital, and Harvard Medical School claim that Merck knew well before the withdrawal that there were problems.

According to their analysis of three randomized placebo-controlled trials of rofecoxib versus placebo, which were completed by April 2003, rofecoxib more than tripled the risk of confirmed CV thrombotic death. Moreover, the finding was statistically significant by June 2001.

Even before rofecoxib was approved, Merck’s scientists themselves were expressing concerns about the potential for thrombotic CV events. In 2000 the VIGOR (Vioxx Gastrointestinal Outcomes Research) study, which compared rofecoxib with naproxen (Naprosyn, Roche) found that rofecoxib-treated patients had a five-fold higher incidence of myocardial infarction. Nonetheless, Merck stated that the APPROVe trial provided the first evidence of a heightened risk of rofecoxib compared with placebo.

While rofecoxib remained on the market (from 1999 to 2004), approximately 106.7 million prescriptions were dispensed in the U.S. alone. During that time, the drug was associated with 88,000 to 140,000 iatrogenic cases of serious coronary heart disease. Conservatively, the researchers say, between 50,000 and 79,000 of those cases might have been prevented had the drug been withdrawn 39 months earlier.

The FDA relied heavily on Merck’s trials of rofecoxib in patients with Alzheimer’s disease (AD); according to Merck, those results did not indicate an excess of CV thrombotic events. However, the current researchers say that an intention-to-treat (ITT) analysis of the three AD studies would have revealed, as early as September 2000, eight confirmed deaths in the rofecoxib arm, compared with two deaths in the placebo group.

By March 2001, the ITT analyses confirmed 10 CV thrombotic deaths with rofecoxib, in contrast to four deaths with placebo. In 2002, when new labeling was approved, the ratio was 17 deaths versus six for placebo. Yet the difference in mortality risk was not included in the new labeling.

The researchers recommend making ITT analyses routine with supervision by an independent data safety and monitoring board. None of the AD trials were overseen by this board, which might have raised concerns about the trials as they progressed.

Source: Am Heart J 2012;164:186–193

Antibiotics and E. coli–Induced Hemolytic Uremic Syndrome

It may be time to rethink recommendations for adults with hemolytic uremic syndrome (HUS). Findings from a multihospital study of patients involved in an outbreak of Escherichia coli contradicted some assumptions and reaffirmed others.

In the largest outbreak to date in 2011, more than 3,800 people in northern Ger-
The large number of patients and the differences in treatments allowed researchers an opportunity to compare the main treatments (plasmapheresis, glucocorticoids, antibiotics, and eculizumab (Soliris, Alexion). They evaluated the effectiveness of the treatments in 298 patients. In most cases, diarrhea worsened within 1 day and lasted a median of 6 days. Most patients were admitted to hospital within 7 days after the onset of diarrhea. The median length of hospital stay was 19 days.

More than half of the patients temporarily needed dialysis; three needed long-term treatment; 37 had seizures; 54 required mechanical ventilation; and 12 died. Plasmapheresis, the primary choice, was used to treat 251 patients. Most of the centers also used high-dose prednisone or prednisolone as premedication before giving fresh frozen plasma. However, 80 patients from seven centers did not receive glucocorticoids.

Antibiotic use in these cases is controversial; theoretically, it could cause an intestinal Jarisch–Hерxheimer reaction, releasing shiga toxin through bacterial death. Still, a combination of at least two antibiotics was administered at one university hospital.

Sixty-seven patients received eculizumab, a monoclonal antibody that has been successful in patients with paroxysmal nocturnal hemoglobinuria (PNH) and atypical HUS. At the start of the German outbreak, eculizumab seemed to be beneficial in three infants with severe shiga toxin–associated HUS, and it had been used as compassionate treatment for HUS thereafter.

The researchers found no clear benefit from plasmapheresis, with or without glucocorticoids, nor did eculizumab show any short-term benefit. New complications, such as seizures and the need for mechanical ventilation, still occurred. In more than 40% of the cases, plasmapheresis was continued after eculizumab had been started. However, the effect of eculizumab might have been confounded by the fact that the patients may have been sicker. Furthermore, nearly all patients receiving eculizumab were also receiving azithromycin (Zithromax, Pfizer) for meningococcal prophylaxis.

However, aggressive antibiotic treatment (with at least two antibiotics) had encouraging results. Enterohemorrhagic E. coli was eradicated about 8 days sooner compared with the use of other treatments, and patients had significantly fewer seizures (2% vs. 10% for plasmapheresis), required no abdominal surgery, and showed no signs of toxic shock. None of the antibiotic-treated patients died, compared with eight patients who died after receiving plasmapheresis and three who received eculizumab. The researchers suggest that antibiotics might be beneficial in the later stages of the disease when the prodromal phase with diarrhea has nearly subsided.

Source: BMJ 2012;345:e4565 (online)

**RESEARCH NEWS**

**New Gene Variants Raise Risk Of Pediatric Brain Cancer**

Researchers at Children’s Hospital of Philadelphia have discovered two gene variants that increase the risk of the pediatric cancer neuroblastoma. Using automated technology to perform genome-wide association studies on DNA from thousands of subjects, the study may broaden our understanding of how genetic changes may increase the susceptibility to this early childhood cancer as well as cause tumor progression.

Common variants in the HACE1 and LIN28B genes have been shown to increase the risk of neuroblastoma. For LIN28B, these variants also appear to contribute to the tumor’s progression once it forms. HACE1 and LIN28B are both cancer-related genes, but this was the first study to link them to neuroblastoma.

Neuroblastoma affects the peripheral nervous system and usually appears as a solid tumor in the chest or abdomen. It accounts for 7% of all childhood cancers and from 10% to 15% of all cancer deaths in children.

The researchers compared DNA from 2,800 neuroblastoma patients with DNA from nearly 7,500 healthy children. They found that HACE1 functions as a tumor-suppressor gene, whereas LIN28B is an oncogene. Low expression of HACE1 and high expression of LIN28B correlated with worse survival.

Sources: Nat Genet; Children’s Hospital, www.chop.edu, September 4, 2012

**DEVICE NEWS**

**Recall: Tissue Support Tool**

Covidien has recalled all production lots for the Duet Tissue Abdominal Tissue Reinforcing System (TRS) Universal Straight and Articulating Single-Use Loading Units and has stopped making the device. The tissue-reinforcement material was reported to be linked to an injury after abdominal surgery.

The product has the potential to injure adjacent anatomical structures. This recall follows a voluntary recall in January 2012 that was related to a contraindication of the product’s use in the thoracic cavity.


**Approvals**

**Surgical Stapling System**

Covidien’s iDrive Ultra is a reusable, battery-operated endoscopic surgical stapler. The device can be used with one hand and features push-button operation and full articulation of the stapling tool. The surgeon does not have to power-squeeze the trigger to apply the staples,
and there is less stress on tissue during compression and clamping.

Sources: Medgadget, August 29, 2012; FDA, August 30, 2012

Ultrasound System For Dense Breast Tissue

The somo-v Automated Breast Ultrasound System (ABUS, U-Systems Inc.) is the first ultrasound device approved for use with standard mammography in women with dense breast tissue who have a negative mammogram and no symptoms of breast cancer. Approximately 40% of women undergoing screening mammography have dense breast tissue. Detection of cancer in these patients often occurs at a more advanced stage, because dense tissue may obscure smaller tumors, potentially delaying detection of cancer.

In a clinical study, there was a statistically significant increase in breast cancer detection when ABUS images were reviewed in conjunction with mammograms, compared with detection by mammograms alone.

The device is approved for women who have not had previous breast surgery or biopsy, which might alter the appearance of tissue in an ultrasound image.

Source: FDA, September 18, 2012

Device Identifies Fake Drugs

The FDA has developed a battery-operated, hand-held device that helps to identify adulterated and unapproved drugs, cosmetics, food, devices, and packaging. Counterfeit Detection Device No. 3 (CD3) sprays 10 different wavelengths of visible and invisible light on tablets, capsules, and powders being inspected. It can also detect products that have been tampered with, relabeled, or reglued.

When a light is aimed over tablets, boxes, and package inserts, the fake products show up in a different color or shade.

Approximately 50 devices are now being used in the field. CD3 has been in use since 2010, but its future could be in jeopardy because of budgetary constraints. Each device costs $1,000. The FDA and other federal agencies face as much as an 8% cut in funding on January 2, 2013, unless Congress comes up with more than $1 trillion in savings over the next decade.


NEW MEDICAL DEVICES

Marvin M. Goldenberg PhD, RPh, MS

Name: WiTouch and WiTouch Pro
Manufacturer: Core Products International, Chattanooga, Tenn.
Approval Date: August 27, 2012
Purpose: The Hollywog WiTouch is a wireless, drug-free, remote-controlled device that incorporates transcutaneous electrical nerve stimulation (TENS) technology to relieve lower back pain.

Description: The device is worn under clothing, adapts to most body shapes, and fits the contours of the back. More than 150 30-minute treatment sessions are provided for each battery’s life.

Benefit: The lightweight WiTouch can be worn discretely to provide pain relief for hours as needed. It contains no wires, bulky back wraps, belts, or complicated programs or settings to adjust. The output is 20% higher in intensity compared with typical portable devices, and the covered treatment area is 2.5 times larger. Replaceable gel pads are available.

WiTouch is sold over the counter, and the WiTouch Pro is available by prescription.

Sources: www.coreproducts.com; http://hollywog.com/witouch/#video

Name: Noninvasive Prostate Health Index

Manufacturer: Beckman Coulter, Inc., Brea, Calif.
Approval Date: June 25, 2012
Purpose: The Prostate Health Index (phi) is a noninvasive blood test that is more specific in detecting prostate cancer compared with prostate-specific antigen (PSA) screening. The test is intended to reduce the number of biopsies when PSA values are 4 to 10 ng/mL (just above the upper limit of normal).

Description: The test combines data...
from three automated blood tests of total PSA, free PSA, and a PSA precursor protein, [-2]pro-PSA.

**Benefit:** Physicians usually recommend that men with a PSA of 4 to 10 ng/mL consider a prostate biopsy, but an elevated PSA level can also represent benign conditions. The *phi* test can help to distinguish prostate cancer from benign conditions. A clinical study showed a 31% reduction in unnecessary biopsies, but it was not clear whether this test can differentiate between prostate cancer that needs to be treated and prostate cancer that can simply be monitored. The firm says that the assay was 2.5 times more specific than the PSA test in detecting prostate cancer in a subset of patients.

Available in Europe since 2010, the *phi* test must be performed in laboratories equipped with the company’s analyzers.


**Recall**

A Class I recall was issued for Care-Fusion EnVe Ventilators, made and distributed from 2010 to 2012. A leak may occur in the patient breathing circuit or the system, resulting in the inability of the ventilator to maintain positive end expiratory pressure (PEEP) either intermittently or continuously.

If ventilation resumes after an intermittent leak and the audible alarm stops, the user should clear the alarm indicator on the ventilator display by entering the “Alarm Messages” tab and pushing the alarm reset to clear the display. If the ventilator has a continuous leak and normal ventilation does not resume, users should provide another method of ventilation. Patients should be constantly monitored to ensure that if a malfunction occurs, another method of ventilation can be provided.

**Source:** FDA, July 20, 2012