FDA Orders 500 Unapproved Cold, Cough Medicines Off the Market

Furthering its goal to remove unapproved prescription drugs from the market, the FDA has ordered that drugmakers stop manufacturing hundreds of unapproved cough, cold and allergy medications.

CDER Compliance Director Deborah Autor cited safety and the unreliability of final product as the chief concerns for the agency’s move. “We don’t know what’s in them, how they work or how they were made,” she said in a teleconference Wednesday.

However, at least one drug maker ordered to stop manufacturing its unapproved drug say they were “surprised” by the FDA’s action, adding that the products’ efficacy and safety has been confirmed for years by physicians.

The agency ordered companies to stop making the drugs in 90 days and halt shipping the drugs in 180 days. The FDA lists on its

FDA Guidance Changes Distribution, REMS for Medication Guides

The FDA has published a new draft guidance on distribution requirements for medication guides and situations in which medication guides should be included in risk evaluation and mitigation strategies (REMS).

The guidance addresses questions that have arisen concerning distribution of medication guides for drugs that are dispensed to healthcare providers who directly administer the treatment, as opposed to self-administration by the patient.

The guidance also clarifies when REMS requires a medication guide and when the guide might be distributed on its own. Comments on the draft are due May 31.

Currently, 21 CFR Part 208 authorizes the FDA to require a medication guide be sent directly to patients if the agency determines that
Unapproved Drugs, from Page 1

website the impacted medications — more than 500 in total — that contain 27 active pharmaceutical ingredients (API).

Autor said the FDA has received a “handful” of adverse events regarding the unapproved cold and cough drugs the agency is removing from the market. “We believe the adverse events are under reported,” she noted.

For example, some products marketed as “time-release” drugs actually released 85 percent of their API in the first 30 minutes after ingestion rather than over 8 to 12 hours as labeled. Testing in young children is also insufficient, she said, and some drugs the FDA lists contain two antihistamines, which could lead to over dosage.

Some products Autor mentioned during the teleconference were Qualitest Pharmaceuticals’ Cardec DM (phenylephrine), ECR Pharmaceuticals’ Lodrane 24D (brompheniramine) and Meda Pharmaceuticals’ Organidin (guaifenesin).

Drugs Widely Used

Davis Caskey, vice president of pharmaceutical operations at ECR, said many of the drugs mentioned by the FDA have been “widely used with minimal if any safety issues associated with them.”

“Safety wise, I don’t know of any reasons to have any of these products recalled,” Caskey told WDL. He added ECR collects and reports adverse events on the unapproved products to the FDA the same as with approved drugs.

Caskey disputed Autor’s comments that the agency doesn’t know what’s in the unapproved products or how they are made because the company’s site is routinely inspected.

ECR had recently requested a hearing with the FDA regarding its unapproved products currently on the market after the agency placed a call for such hearings in January. “And no action has been taken on those hearings,” Caskey said.

However, the FDA also announced Wednesday it would withdraw all outstanding hearing requests, according to a notice in the Federal Register.

Recently, the FDA has taken dramatic steps to curb the manufacturing and sale of unapproved drugs. Wednesday’s move is the 17th action in the FDA’s Unapproved Drug Initiative, a safety program launched in June 2006 to remove unapproved drugs from the market.

Just last month, U.S. Marshals seized a prescription ear-infection treatment from a Deston, Fla., company, saying the drug was unapproved (WDL, Feb. 21).

A list of the drugs impacted by the FDA’s action is available at www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/SelectedEnforcementActionsonUnapprovedDrugs/ucm245106.htm. — David Pittman

Merck KGaA Gets Complete Response Letter for MS Drug Cladribine

The FDA has issued a complete response letter to Merck KGaA for its oral relapsing-remitting multiple sclerosis (MS) drug cladribine, requesting further analyses of safety risks from current data or additional studies.

Although the letter acknowledges that substantial evidence of cladribine’s effectiveness was provided by the CLARITY study, the FDA requested the company provide an improved understanding of safety risks and the overall benefit-risk profile.

Merck says it intends to request an end-of-review meeting with the FDA to see if data from completed and ongoing clinical studies will address the agency’s concerns.

The ongoing trials are fully enrolled, according to the German drugmaker, and will provide additional information on the drug’s efficacy and safety.

(See Cladribine, Page 4)
Obama Signs Funding Measure Averting Possible FDA Shutdown

The FDA has been spared from having to stop working because of a federal government shutdown now that President Barack Obama has signed a measure temporarily funding the agency and other federal programs through March 18.

Obama signed the short-term extension on Wednesday, hours after the Senate approved the measure and a day after the House did the same.

The measure extends by two weeks the current continuing appropriations law that was set to expire Friday at midnight. That law has funded federal programs at fiscal 2010 levels since Oct. 1, 2010, because Congress did not pass any appropriations bills for fiscal 2011.

Prior to the Senate vote, Majority Leader Harry Reid (D-Nev.) commented that the temporary spending measure, unlike a continuing resolution to fund the government through the remainder of fiscal 2011 that is pending in the Senate, did not have drastic cuts. “H.R. 1 … did such bad things to so many programs, but not a single one is in this bill. And they’ve taken our numbers; these are our numbers, so we’ll pass this.”

Shutdown Threat Could Reemerge

Some senators had expressed a desire to convert the bill to a four-week extension, but House leaders were not interested in such an extension and both sides appeared to want to avoid a repeat of the federal shutdown that occurred in 1995-1996. Sen. Daniel Inouye (D-Hawaii), chairman of the Senate Appropriations Committee, said he would try to push a longer stopgap measure.

H.R. 1, passed by the House Feb. 19, would fund the FDA through fiscal 2011 at $3.31 billion — a $241 million cut from the agency’s fiscal 2010 appropriations — however, Senate Democrats want time to debate the measure, come up with their own cuts and negotiate with the House on a final spending resolution.

Drug industry opinion leaders have predicted that if H.R. 1 is passed, the FDA funding cuts could lead to layoffs and limit new hiring for the agency’s drug programs, which have seen an upsurge in funding since the FDA Amendments Act was passed in 2007 (WDL, Feb. 14).

If the House and Senate are still unable to come to a long-term agreement in the next two weeks, the threat of a government shutdown could reemerge.

For the moment, though, agency employees and drugmakers with applications pending can breathe easier knowing that lawmakers will likely have at least two more weeks to work out a long-term spending plan. — David Belian, Pamela Taulbee

Federal Court Absolves Abbott Of $1.7 Billion Patent Verdict

A federal appeals court has overturned a $1.7 billion patent-infringement verdict against Abbott Laboratories, saying the company did not infringe a Johnson & Johnson (J&J) patent on the blockbuster autoimmune disease treatment Humira.

In a decision issued Feb. 23, the U.S. Court of Appeals for the Federal Circuit found Abbott could not be held responsible for infringing J&J’s ’775 patent on Humira (adalimumab) because Centocor Ortho Biotech, a J&J subsidiary, had never provided a valid written description of its claims.

“Because the asserted claims of the ’775 patent lack written description … we need not reach Abbott’s other invalidity arguments, its infringement arguments or the question of damages,” the court says in its ruling. “We reverse the district court’s denial of [Abbott’s appeal] on this ground and hold the asserted claims invalid for failure to meet the statutory written description requirement.”

Humira is marketed by Abbott and directly competes with Centocor Ortho’s Remicade (infliximab) and Simponi (golimumab).

(See Abbott, Page 4)
**Cladribine, from Page 2**

The CLARITY study is a two-year Phase III trial comparing cladribine to placebo as a monotherapy in patients with MS. CLARITY EXTENSION is a two-year Phase III study that will provide data on long-term safety and efficacy of extended administration of cladribine for up to four years. Top-line results are expected by the end of the year.

Results from another two-year Phase III study, ORACLE MS, are also expected by year end. That study is evaluating the efficacy and safety of cladribine as a monotherapy in patients at risk of developing MS.

A Phase II study, called ONWARD, is designed to primarily evaluate the safety and tolerability of adding cladribine treatment to patients with relapsing forms of MS, who experienced breakthrough disease while on established interferon-beta therapy. Results are expected in the first half of 2012.

**Boost for Novartis’ Gilenya**

Despite ongoing trials, the complete response letter comes as no surprise, since Merck has been struggling to gain approval in the U.S. and EU. In a Feb. 22 note, Credit Suisse analyst Luisa Hector did not expect U.S. approval, adding that a negative FDA assessment “should trigger a significant review of costs at Merck Serono.”

The European Medicines Agency’s (EMA) Committee for Medicinal Products for Human Use gave a negative opinion on cladribine due to cancer reported in trial patients, but recommended approval for its competitor, Novartis’ Gilenya (fingolimod), which is the first oral MS drug available in the U.S.

Merck recently withdrew its marketing authorization application for cladribine from the EMA, based on that negative opinion.

Cladribine is approved in Australia and Russia for MS under the brand name Movectro.
— Molly Cohen

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**Abbott, from Page 3**

The decision is a major boost to Abbott, who had vowed to appeal the case after a jury in the U.S. District Court for the Eastern District of Texas ruled against the company and ordered it to pay J&J $1.2 billion in lost profits and $504 million in royalties.

That ruling was made worse for Abbott later that year when the Texas court added more than $175 million in interest payments to the penalty.

With the appeals court’s reversal of the decision, however, it is now J&J who is deciding how it will proceed.

“We are disappointed by the decision,” Centocor President Rob Bazemore said. “We are considering whether to ask for reconsideration by the panel or by the court of appeals as a whole.”

Since it was approved in 2002, Humira has gained five additional indications and brought in a record $6.5 billion in worldwide sales in 2010.
— David Belian

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FDA Gives Protalix Gaucher Drug A Complete Response Letter

Protalix Biotherapeutics has received a complete response letter (CRL) from the FDA for its Gaucher disease candidate taliglucerase alfa, though the agency is not requiring additional clinical trials.

The FDA’s CRL, received Feb. 25, raised questions mainly related to clinical and chemistry, manufacturing and control (CMC), the company said. The agency also requested more information regarding testing specifications and assay validation as well as additional data from the company’s switchover trial and long-term extension trial. When the Israeli biotech submitted the NDA, full data from these trials was not yet available.

Protalix said the FDA inspected its manufacturing facilities and found them acceptable. The agency also did not identify any issues in its audit of clinical sites.

No Additional Studies Needed

“While we are disappointed with the delay, we are encouraged by the response from the FDA,” added David Aviezer, Protalix’s president and chief executive officer, during a Friday conference call. He noted that company does not foresee any issues that cannot be addressed in an appeal.

Aviezer said the switchover and extension trials were ongoing when the NDA was submitted and now the FDA is interested in additional data from those studies. “There’s no need for additional studies, but the data is available and they’re asking us to put it in a format they can evaluate and see as part of their approval process. We believe this is really where this is coming from,” he said.

Meanwhile, the CMC issues raised in the CRL focus on technical aspects, such as narrowing specifications of some classifications or assessing data in some elements in a different way, according to Aviezer. “We believe they are all addressable technically, scientifically,” he said.

Protalix says it will work with its commercial partner, Pfizer, to address the issues outlined in the CRL.

“We won’t go into specifics because Protalix and Pfizer need to meet with the FDA to discuss some requests. We will meet with the FDA as soon as possible and then will provide a timeline for resubmission,” Aviezer said.

Aviezer was not concerned that the FDA’s decision will affect regulatory approvals in other countries.

“I think the only agency that has a clear link to the FDA is the Israeli Ministry of Health … We do not expect approval in Israel before an FDA approval … We are still waiting to hear back from the [European Medicines Agency (EMA)],” he said. The EMA’s decision is expected in April.

‘Meaningful Delay to Approval’

While Protalix is optimistic on taliglucerase alfa’s future, Noble Financial analyst Raghuram Selvaraju noted, “the receipt of a CRL constitutes a meaningful delay to approval of the drug.”

The delay is good news for Shire and Genzyme, who both have competing Gaucher treatments.

The FDA approved Shire’s Vpriv (velaglucerase alfa) in March (WDL, March 8, 2010). Meanwhile, shortages of Cerezyme (imiglucerase) due to manufacturing issues had previously plagued Genzyme.

If taliglucerase alfa does receive FDA approval, it will have to gain patient preference over these strong competitors.

Currently, patient enrollment is open in Protalix’s pediatric trial of taliglucerase alfa. Patients enrolled in the switchover and extension studies will continue to receive the drug, which is also being provided to Gaucher patients in the U.S., France, Brazil and other countries around the world under expanded access protocols.

— Molly Cohen
the drug has serious risks patients should be aware of, the label could help prevent adverse events or patient adherence to directions for use is crucial to the treatment’s effectiveness.

However, the agency intends to “exercise enforcement discretion regarding Medication Guide distribution” for drugs dispensed by a healthcare professional in either inpatient settings or in outpatient settings where the drug will be used immediately. In these settings, a healthcare professional can provide any necessary information and answer patient questions, the guidance says.

A medication guide still must be distributed when:

- The patient or patient’s agent requests a medication guide;
- The drug is dispensed in an outpatient setting for later use by the patient;
- A healthcare professional dispenses the drug in an outpatient setting for the first time; or
- The drug is dispensed for the first time after a medication guide is materially changed.

The guidance also clarifies that newly required medication guides are not necessarily included in a REMS. The FDA may approve a medication guide without requiring it be part of a REMS. Conversely, a REMS may not require a medication guide if the REMS does not “include elements to assure safe use.”

Drugmakers whose products have a REMS that contains only a medication guide, a communication plan and timetable for assessment can apply to have the REMS eliminated.

Applicants must submit a prior approval supplement proposing a REMS modification, accompanied by a REMS assessment consisting of updates on any postapproval studies or clinical trials investigating safety issues. A new assessment is not required if the REMS has been reviewed in the past 18 months.

If a medication guide is removed from a REMS or the REMS is eliminated, the medication guide continues to be part of the approved labeling for the drug, the guidance says.


— Wilson Peden

US Supreme Court Hears Arguments In Roche, Stanford Dispute

Skepticism from several U.S. Supreme Court justices over arguments made by Stanford University in a licensing dispute with Roche over HIV test kits could mean a popular source for innovative new medical products could remain intact.

The case centers on the scope of the 1980 Bayh-Dole Act, which specifies how ownership of federally funded inventions can be transferred to private hands, and which allows universities to retain the rights to research funded by federal grants.

In oral arguments before the high court Feb. 28, Donald Ayer, an attorney for Stanford, said Bayh-Dole should be interpreted as a vesting statute, in which ownership of federally sponsored inventions automatically vests according to the act’s hierarchy, which is government, then contractor, then inventor. In the case, Stanford is considered a contractor.

If this automatic vesting were to occur, it could mean that the rights to products initially developed at a university with federally backed research could remain with that institution, regardless of wording in other contracts signed by the inventor.

Roche has argued that this would this would “chill the very ‘collaboration between commercial concerns and nonprofit organizations, including universities’ that the Bayh-Dole Act sought to foster,” Roche says in its amicus brief. “Such a
FDA Sees No Association of Heart Risks With GSK’s Ziagen

GlaxoSmithKline’s HIV medication Ziagen has no statistical association with an increased risk of myocardial infarction (MI), according to the results of a meta-analysis conducted by the FDA.

The results come after conflicting reports about the safety of Ziagen (abacavir), a nucleotide reverse transcriptase inhibitor (NRTI) included in several HIV medications, with some observational studies and one randomized trial indicating an increased risk of MI associated with the drug.

In conducting the meta-analysis, the FDA looked at the results of 26 randomized clinical trials from 1996 to 2010 that evaluated abacavir. The studies comprised a total of 9,868 subjects — 5,028 randomized to an abacavir-containing regimen, and 4,840 to a non-abacavir regimen.

A total of 46 MI events were reported, with 24 events occurring in subjects taking abacavir and 22 in subjects taking placebo or other treatments. These results do not indicate a statistical association between MI and abacavir treatment, the FDA says.

“We take any new data seriously,” Rebecca Hunt, Director of Communications at Viiv Healthcare, told WDL. Viiv, an HIV-specialty company formed by Pfizer and GlaxoSmithKline, manufactures several abacavir-based treatments, including Ziagen, Trizivir and Epzicomb.

“We stand behind this medicine and know it brings good to HIV patients,” Hunt said, adding, “It’s really interesting data, and it adds to the body of evidence behind this therapy.”

The FDA advises physicians to continue prescribing abacavir according to its label, but warns that there is still conflicting data about the drug’s safety.

The FDA first warned of an increased risk of MI associated with abacavir and several other NRTIs in 2008.

An abstract of the FDA’s meta-analysis is available at www.retroconference.org/2011/Abstracts/42436.htm. — Wilson Peden

Judge Denies Cephalon Request For FTC Pay-for-Delay Docs

Brand-drug makers can breathe easier following a federal court ruling Feb. 28 that rejected Cephalon’s request that the FTC release all documents related to pay-for-delay cases it has reviewed in the past.

Cephalon wanted the documents to prepare its defense of an FTC lawsuit concerning deals with Watson and other generic manufacturers to preserve market exclusivity of its narcolepsy drug Provigil (modafinil) (WDL, Jan. 31). The agreements preclude any generic competition until 2012.

In December, the company asked the U.S. District Court for the Eastern District of Pennsylvania to order the FTC to release the documents, arguing that the commission drew on them in public reports intended to bolster their case against certain types of patent settlement suits, such as those involving Cephalon.

According to the court, the FTC has maintained it has no plans to offer as evidence the two reports based on the confidential documents, and that it will disclose all data or facts considered by FTC experts testifying in the case. “Therefore, the Court will not order the disclosure of documents underlying the above studies at this time,” the decision says.

“While the Court did not grant us all of the relief we requested, we are pleased that the Court’s decision confirms that the FTC will not seek to offer the studies in question into evidence,” Cephalon spokeswoman Natalie de Vane told WDL.

Other companies had opposed Cephalon’s efforts, saying the documents were highly sensitive patent litigation settlements that would compromise business and legal interests if exposed. — Meg Bryant
Supreme Court, from Page 6

rule would discourage scientific cooperation with no countervailing public benefit, only a windfall for Stanford.” (WDL, Nov. 8, 2010).

“What you’re asking for, based on submissions to us [in] amicus briefs, means a very great change in how patents are held,” Justice Anthony Kennedy said. “Why can’t we resolve this case in a simple way?”

Justice Samuel Alito questioned if it was possible to allow automatic vesting considering how Bayh-Dole is currently written. The law now says small businesses and nonprofit organizations may “elect to retain title” to subject inventions, which the statute defines as inventions conceived or first actually reduced to practice under a government-funded agreement.

Assigning IP Rights

“It has long been the rule that inventors have title to their patents initially, even if they make those inventions while working for somebody else,” Alito said. “You are relying on a provision that says that the nonprofit organization may elect to ‘retain’ title, which means hold onto a title that the organization already has.”

“There’s just no accepted definition of the word ‘retain’ that corresponds to the meaning that you want to assign to that word. ‘Retain’ does not mean ‘obtain.’”

The case involves work done by Mark Holodniy, a medical professor at Stanford, who as a research fellow in 1988 signed an agreement turning over rights to future inventions.

A year after signing the agreement, Holodniy began conducting research at Cetus, a biotech company collaborating with Stanford on HIV research. Cetus was later bought by Roche. While there, he signed a separate agreement to relinquish intellectual property rights to his work.

Three patents were ultimately granted for products based on his work.

Stanford has argued that the Bayh-Dole supersedes any agreement between Cetus and Holodniy. Because the underlying research was funded in part by the federal government, the law barred Holodniy from assigning his rights to Cetus, Stanford said.

While a lower court agreed, a federal appeals court did not.

Moving forward, Roche may have grounds to be cautiously optimistic, Steve Chang, a patent attorney at Banner & Witcoff, says in a client note.

“The questions from the bench suggest that the Justices are hesitant to read the Bayh-Dole Act as a vesting statute,” he said. “However, this hesitance does not automatically mean a win for Roche, as the Justices may well change their mind, and also appeared willing to consider alternative grounds.”

The case is Board of Trustees of the Leland Stanford Junior University v. Roche Molecular Systems, Inc. et al. — Virgil Dickson
Elan Pays Feds Over $200 Million For Off-Label Marketing

Irish drugmaker Elan has pled guilty to a misdemeanor violation of the Food, Drug and Cosmetic Act for promoting its epilepsy drug Zonegran for off-label uses.

The plea, which was entered by the company Feb. 28 in the U.S. District Court for the District of Massachusetts, marks the final step in the drugmaker’s $203.5 million settlement of the case that was reached with the Justice Department late last year.

As part of its settlement, Elan agreed to pay $102 million to resolve civil False Claims allegations, as well as a $97 million criminal fine and will forfeit $3.6 million in assets.

The company also agreed to enter into a corporate integrity agreement with the HHS Office of Inspector General, which will create processes and reviews designed to help avoid or detect similar conduct.

Concerted Effort by Justice

Zonegran (zonisamide) is indicated as an adjunctive therapy for partial seizures in epilepsy for adults over the age of 16. But according to the U.S. Attorney’s Office for the District of Massachusetts, Elan promoted sales of the drug for off-label uses including psychiatric disorders, migraine headaches, eating disorders, weight loss, movement disorders and a variety of seizures in children under the age of 16.

The company’s actions also had an impact on Japanese drugmaker Eisai, which purchased Zonegran from Elan in 2004.

In a deal reached with Justice in December, Eisai agreed to pay $11 million to resolve allegations that the company illegally promoted Zonegran through off-label marketing and benefited from previous off-label advertising conducted by Elan.

The settlements are the latest move in a concerted effort by Justice over the past year to increase its focus on healthcare fraud cases.

According to an HHS report to Congress last month, recoveries from civil false claims violations totaled more than $2.5 billion in 2010, with drugmakers providing a significant portion of that amount (WDL, Jan 31). — David Belian

Court Finalizes Forest $164 Million Fine Over Off-Label Marketing

A federal judge Wednesday ordered Forest Pharmaceuticals to pay $164 million to settle civil and criminal charges related to the illegal distribution and promotion of several of its drugs.

The payment caps a lengthy Department of Justice investigation into the company’s distribution of unapproved Levothroid (levothyroxine sodium) for hypothyroidism and Lexapro (escitalopram oxalate) for pediatric depression, as well as off-label promotion of its antidepressant Celexa (citalopram hydrobromide) for use in children.

Forest pleaded guilty to the charges and agreed to the payment in September. Wednesday’s sentence by the U.S. District Court for the District of Massachusetts includes $150 million in criminal fines and a $14 million forfeiture of company assets, and is part of a larger settlement totaling $313 million (WDL, Oct. 11, 2010).

The Levothroid charge stems from Forest’s continued distribution of the drug from August 2001 until August 2003, when it stopped production of the unapproved version. However, the company legally manufactures an oral formulation of the drug under the same name. Forest also attempted to hide serious equipment malfunctions related to the production of Levothroid during a November 2003 FDA inspection.

Forest’s off-label promotion of Celexa included, among other things, aggressively publicizing positive results from a company-sponsored clinical trial of Celexa in adolescents, while negative results from a similar European study were suppressed.

The settlement is the latest in Justice’s campaign to curb off-label marketing of drugs by levying huge fines against drugmakers that do so. — Meg Bryant
FDA Oversight at ‘High-Risk,’ For Mismanagement, GAO Says

The FDA’s oversight of medical products remains a “high-risk” area of government operation, according to a recent update to the Government Accountability Office’s (GAO) High-Risk Series, which points to ongoing issues with the agency’s inspection of overseas facilities and postmarket safety monitoring.

The series highlights federal government operations GAO determines to be at risk for “fraud, waste, abuse, and mismanagement” or that require “transformation to address economy, efficiency, or effectiveness challenges.”

Risk of Fraud, Mismanagement

The FDA was first added to GAO’s High-Risk List in 2009, after GAO determined the agency “needs to enhance its oversight of medical products to better protect public health” (WDL, Jan. 26, 2009). That update criticized the FDA’s inspections of foreign facilities as well as the agency’s monitoring of clinical trials and review of promotional materials.

Since then, the FDA has continued to struggle with foreign inspections (WDL, Nov. 1, 2010). While the agency has opened new offices overseas, it still lacks performance goals and a plan to address potential staffing challenges, according to the most recent update.

The FDA’s approach to choosing facilities for inspection is also inconsistent with the GAO’s recommendation that the agency inspect facilities with the highest public health risk potential at a comparable rate, regardless of whether they are in the U.S. or overseas.

In addition, the agency continues to struggle with postmarket safety monitoring, another weakness noted in the 2009 report. The 2011 update expresses concern that some FDA staffers consider premarket responsibilities a higher priority and that staffing and technological issues limit the agency’s capacity to conduct safety studies.

GAO is also concerned that the FDA is not routinely monitoring postmarket studies for drugs expedited under the accelerated approval program and notes the agency has not developed criteria for withdrawing drugs that fail to confirm clinical benefit under the program.

The report acknowledges some progress in this area though, pointing to FDA initiatives to improve reporting of adverse events and make tracking more efficient.

Despite these improvements, the FDA has a long way to go, GAO says. Before the high-risk designation can be removed, the agency must:

- Strengthen its resource management and strategic planning;
- Develop results-oriented performance measures;
- Create a workforce plan for the new overseas offices; and
- Implement a rigorous postmarket safety program.

— Wilson Peden
For 2011, the FDA has dramatically changed the rules for drug and biologics trials. The new rules will reduce unnecessary reporting of events that aren’t relevant to a drug, and force investigators and sponsors to do a better job identifying the events that are relevant. There’s no doubt that these new requirements will increase the regulatory burden on drug and biologics trial sponsors and investigators already laboring under a heavy load.

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