

FDA Week

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Opioid REMS Provider Education Blueprint May Offer Model For Other Drugs

FDA's provider education blueprint for a class-wide Risk Evaluation and Mitigation Strategy for long-acting and extended-release opioids may foreshadow a move to make continuing medical education a significant component of future REMS, an industry attorney and the head of a group that accredits continuing medical education said. But other sources raised concerns that the blueprint lacks detail and may not do much to curb abuse of these drugs.

The blueprint released earlier this month provides the basic parameters of FDA's opinion of what a continuing medical education program should look like and the accompanying federal regulatory notice suggests the kind of

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Hatch Crafting Drug Shortage Bill That Includes Reimbursement Changes

Sen. Orrin Hatch (R-UT) is working on a bill that could provide economic incentives for medically necessary drugs that are in shortage, including exclusion of some medications from the 340B drug discount and Medicaid rebate programs, and basing reimbursement for these drugs based on wholesale acquisition cost instead of average sales price, sources said. The Obama administration decided against including reimbursement changes in its recent executive order on drug shortages after factoring in the complexity involved in hospitals' purchasing of drugs.

The legislation could also expand on a Senate bill mandating drug firms notify FDA about any discontinuance or

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FDA Device Officials Defend Call For Higher Fees As Industry Resists

FDA officials are making the case for higher device user fees in response to congressional concerns about lagging review times and inconsistent reviews, with the device center director telling lawmakers this week that the drug user fee program faced a similar pivotal moment in previous iterations. An industry source said that resources remain a sticking point in the device user fee negotiations, with the medical device industry reluctant to increase its contribution on the grounds that doing so would make the agency more reliant on fees and give device companies less clout in future talks.

Higher reviewer turnover has been consistently cited by FDA officials as a challenge for the agency, which has been

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Govt. Defends Constitutionality Of Medicines Company PTE In Patent Reform

Congress recently granted The Medicines Company its years-long request that patent extension policies be clarified to account for its narrowly missed deadline, but lawmakers' authority to do so is now being debated in a federal appeals court. The government is defending Congress' power to mandate an extension of Medicines Company's patent, but a drug industry competitor argues that because the company's patent theoretically expired before the bill was passed it does not fall under the new patent reform provision.

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Senate Bill Targets Drug Patent Settlements By Allowing Shared Exclusivity

A bipartisan group of senators is pushing a legislative solution to curb so-called pay-for-delay settlements that would let generic drug firms that win a patent challenge share or possibly overtake the six-month exclusivity period of the first filing generic company, sources said, noting that the effort could complement other legislative efforts in this area that have been floated as debt reduction measures. The bill would likely help small generic companies that are generally in the second filing position and have been blocked from coming to market because of drug patent settlements,

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according to a Senate aide.

Drug patent settlements have been a contentious issue with bans floated during debate on the health reform law and in super committee lobbying. The Federal Trade Commission deems the pacts between generic and innovator drug companies anti-competitive while drug companies assert that they allow generics to come on the market ahead of patent expiration. While drug companies have come out against other bills banning the patent settlements, the new legislative approach potentially could pick up support from smaller generic drug companies that would stand to benefit from the measure.

Sens. Jeff Bingaman (D-NM), David Vitter (R-LA), Sherrod Brown (D-OH) and Jeff Merkley (D-OR) introduced Wednesday (Nov. 16) the Fair and Immediate Release of Generic Drugs Act, which would shift the incentives crafted under Hatch-Waxman drug patent law to bring generic drugs to market. An industry source said the incentives in the bill would encourage shorter settlement periods and give other generic companies incentive to pursue patent litigation after a settlement occurs.

Legislation backed by Sens. Herb Kohl (D-WI), chair of the aging committee, and Chuck Grassley (R-IA), ranking member on the judiciary panel, would deem such pacts presumptively illegal. Wells Wilkinson, a staff attorney at Community Catalyst, said the recently introduced legislation could work in tandem with other legislative efforts to curb drug patent settlements, as FTC litigation would be lengthy and other settlements would occur in the meantime.

“I think one of the outcomes of this would be that you kind of open the doors for more generic competitors to come in,” he said.

The Senate aide also said the bill complements the other legislative efforts and it would further benefit the smaller companies frustrated with the current process, where companies that are the first to file an abbreviated new drug application could enter a patent settlement with the name-brand company, blocking other companies from coming on the market until after 180 days of exclusivity, which starts under terms agreed to in the settlement.

“Some of the bigger generics are probably happy with the way things are,” the aide said.

The drug patent settlements often include acceleration clauses that allow the initial generic company to come to market earlier than agreed to if another generic firm successfully challenges the patent, thus opening up the market. Under the bill, those clauses would be “neutralized” and lock the company into the settlement date, the industry source said.

If the date in the patent settlement overlaps with the market date allowed through the court challenge, the second company would come to market first while the first filing company would market its products on the date agreed to in the settlement, sharing exclusivity for the remainder of the six months. If the dates do not overlap and the first filer agreed to come to market six months or longer after the date allowed under a successful patent challenge, the company would forgo their exclusivity period, the source said.

“It creates a tremendous incentive for anyone to fight to open the market earlier,” the source said.

While the bill does not weigh in on the anti-competitive issues that have been debated in conjunction with the settlements, it incentivizes companies to enter shorter agreements, if at all.

“(It) makes you think twice about it but doesn’t interfere with your right to do so in any way shape or form,” the source said.

The Generic Pharmaceutical Association declined to comment on the bill, saying it is reviewing the legislation.

— Alaina Busch

FDA Gets Increase For Food Safety, MCM; Pressed On Cold Monograph

Congressional conferees agreed to raise FDA's budget by \$50 million over last year's level and directed the agency to use the money to implement the food safety law and work on new medical countermeasures. The conferees also asked FDA to publish a proposed rule revising the monograph regulating the labeling of over-the-counter cough and cold products for children by Dec. 31.

FDA funding advocates praised the targeted increases, included in a fiscal 2012 conference report unveiled Monday (Nov. 14), but also raised concern that funding for the agency's centers and offices will remain flat compared with last fiscal year.

FDA Commissioner Margaret Hamburg said the small but significant increase, while other agencies have received cuts, will allow FDA to work in critical areas like food safety, along with drug and medical product issues. "I take it as a very encouraging sign," she said at a conference at George Washington University Tuesday (Nov. 15).

FDA is required to tell Congress within 30 days after the bill is enacted how it plans to allocate the increase. The budget includes \$39 million for food safety and \$20 million for advancing medical countermeasures, which sources said will likely go toward advancing regulatory science and review of these medicines.

The conferees encouraged FDA to work with the public and private sectors to gain a better understanding of the causes of food borne illness, which they said should contribute towards the development of new strategies, policies and prevention methods, while also doing a better job of identifying more effective food safety activities to reduce illness, hospitalizations and death associated with food borne illness.

The report also directs the agency to develop a clear strategy for prioritizing intervention methods to reduce illness and to tie the funding levels for food safety to increased levels of activities to the sources of illness, with FDA including this information in its fiscal 2013 budget request.

In addition, the committee's joint explanatory statement requires FDA to submit a report to Congress within 90 days on the average number of calendar days between drug, biologic and medical device application submissions to a decision on the product's approval, clearance or licensure. This language mirrors an amendment from Richard Burr (R-NC) that lawmakers approved during floor consideration last month.

The committee also directs FDA to develop a comprehensive program for inspecting imported seafood and supports the agency's mission to expand nanotechnology research.

The increased FDA funding level agreed to by the conferees is just slightly below the Senate-passed FDA appropriations bill's level but well above the House bill's allocation, and \$234 million below the president's budget request for the agency. FDA is allocated a total of \$2.5 billion as part of a small omnibus package of three spending measures: Agriculture, Commerce/Justice/Science (CJS), and Transportation/Housing and Urban Development (THUD). Total funding for FDA increases to \$3.8 billion when user fees are included, according to the conference report.

The conference report cleared both chambers on Thursday (Nov. 17).

Alliance for a Stronger FDA praised the increased funds. "We are grateful to the conferees for assuring that FDA has the funds to continue its mission," said Nancy Bradish Myers, president of the Alliance for a Stronger FDA and president of Catalyst Healthcare Consulting. "FDA must continue to be a national priority so that we can advance medical progress, improve patients' lives, and assure Americans have a safe food supply."

But the group noted that spending for the agency's centers and offices will remain flat compared with last fiscal year, even as the agency faces increased challenges from globalization of food and drug supplies and increased scientific

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complexity of regulatory filings.

“We are pleased with the Congress’ commitment to begin funding the new food safety law.” said Margaret Anderson, vice president of the Alliance and Executive Director of *FasterCures*. “We remain concerned that investment has not increased in the critical area of medical product development—the quality and safety of the drugs, vaccines and devices upon which patients rely.”

The conference report also includes a continuing resolution that funds other federal operations until Dec. 16 or until Congress completes the remaining nine appropriations bills. The report was approved by the conference committee with all but one of 38 House and Senate conferees signing off on the package, according to a release from the committee. — *Nanci Bompey*

FDA Funding Alliance Breaks Down Fiscal 2012 Appropriations By Center

The Alliance For a Stronger FDA, a group which advocates for FDA funding increases, has put together the following chart outlining how the congressional conference report on the agency’s fiscal 2012 appropriations, which boosts FDA’s overall budget by \$50 million, breaks down by center. Conferees granted the agency increases to begin implementation of the Food Safety Modernization Act and advance medical countermeasures, but funding for the agency’s centers otherwise generally remains flat.

Function Note: budget authority only, by center	FY10 Final	FY11 Final CR 4/12/11	FY 12 Final 11/15/11
Food	\$784 million	\$836 million	\$ 866 million
Human Drugs	\$465 million	\$477 million	\$478 million
Biologics	\$206 million	\$212 million	\$212 million
Animal Drugs/Feed	\$135 million	\$139 million	\$138 million
Devices & Radiological Health	\$315 million	\$322 million	\$323 million
Natl. Ctr. For Toxicological Research	\$59 million	\$61 million	\$60 million
HQ, Officer. of Commissioner & Other	\$144 million	\$150 million	\$154 million
Rent & Facilities Cost	\$237 million	\$250 million	\$266 million
SUBTOTAL, Salaries and Expenses	\$2.345 billion	\$2.447 billion	\$2.497 billion
Building and Facilities Repair	\$16 million	\$10 million	\$9 million
All BA appropriations Total (no user fees)	\$2.361 billion	\$2.457 billion	\$ 2.506 billion (\$ 49 million increase from FY 11)

- Does not include user fees.
- Some variation due to rounding.
- The FY 12 appropriation for FDA included:
 - \$39 million to begin implementation of the Food Safety Modernization Act,
 - \$20 million for advancing medical countermeasures, and
 - \$13 million for mandatory rental payments.

In addition, the conferees accepted the FDA proposed base reduction of \$22 million for administrative and contract savings.

Pain Meds Academic Detailing Program Eyed For California Workers' Comp

Harvard University researchers are in talks with the California State Compensation Insurance Fund (SCIF) about establishing an academic detailing program to improve the prescribing habits of opioid medicines and painkillers for injured workers, with the effort likely representing the first iteration of such an activity that could also serve as a template for other states. Meanwhile, a parallel initiative to create the first U.S. insurance industry-funded academic detailing program is making headway, according to the organizer of the payor consortium.

The National Resource Center for Academic Detailing (NaRCAD) — led by Harvard doctors Jerry Avorn and Michael Fischer — and the California SCIF are hoping to finalize the details of the program, which would use physicians to provide information on pain killing medicines to other doctors, with the goal of reducing dependency on the drugs, speeding recovery and improving care.

“The goal in this case is to treat these workplace problems more effectively so you get these people back to work sooner,” Fischer told *FDA Week*. “The message won’t be, ‘Never use pain medicines’ ... but how to use the medicines appropriately and how to more effectively treat pain.”

A National Institute For Occupational Safety Health expert welcomed efforts to address worker medication issues. “Increasingly, the overall health challenges workers face makes it more difficult for them to remain at work and to stay alert and safe. Over half of workers over age 55 report to work each day with joint pain from arthritis. One in five adults sleeps poorly because of chronic pain,” said Casey Chosewood, NIOSH senior medical officer for Total Worker Health.

“Prescription medication usage and overdose risks also continue to rise, largely due to increases in the chronic pain burden in the working aged population. Employers must face these concerns head on,” Chosewood said. “Prevention efforts, self-management programs, and earlier screenings and interventions in the workplace are critically important. Medical providers must also prescribe medications and other treatment plans with the workplace, work hazards and individual personal and occupational risks in mind.”

Opioids in particular have been the target of FDA activities due to the potential for patients to become addicted to the medicines. FDA established the first class-wide Risk Evaluation and Mitigation Strategies for these drugs and has carefully scrutinized opioids, including painkillers with varying release intervals.

Fischer said that physicians are “often suffering form a lack of clear information and guidance” on how to prescribe painkillers, and that “the current patterns of practice don’t line up with what we think the best practices are.”

“Knowing how to steer the ship of pharmacology among those different drugs can be challenging,” Avorn said. “[Doctors] have a tendency to reach too quickly to potentially addicting medications.”

Therefore, obtaining information from an academic researcher whose mission is not to sell the drug could help provide doctors with the resources they need to improve care and reduce the negative side effects from taking the medicines.

“This is exactly the kind of situation where academic detailing makes sense,” Fischer said, adding that the program would “teach physicians how to manage these decisions more effectively.”

The California SCIF, a state payor, handles the workers compensation claims, and by its very nature has a large population suffering from chronic pain. The new program would teach doctors about the different treatments available and possible side effects, such as when to use a non-steroidal anti-inflammatory or drugs for neuropathic pain, Avorn said.

California SCIF Medical Director Bernyce Peplowski noted in an email that chronic pain costs amount to \$635 billion per year, and that there are approximately 300 million opioid medicine prescriptions per year.

“More patients suffer from chronic pain than heart disease, diabetes and cancer combined,” Peplowski said, adding that the Centers for Disease Control and Prevention has estimated that in New Mexico — the state with the highest rates — 27 per 100,000 people die of opioid overdose. “Thus the need to educate our doctors about right prescribing,” she said.

While recommendations could include less prescribing of the medicines, the program will not seek to prevent patients from obtaining the drugs.

“Overall their hope is to see less of them prescribed. ... They’re looking to see [the pain medications] prescribed in a

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- FDA Gets \$50 Million Hike In Appropriations Conference Agreement
- Senators Float Exclusivity Changes To Avert Drug Patent Settlements
- Markey Lauds J&J Removal Of Formaldehyde From Baby Products, Pushes Cosmetics Bill

more clinical way,” Fischer said. “They’re going to be used hopefully in a more targeted and evidence based fashion. ... Many of these patients will probably take pain medicines as part of their treatments.”

Fischer said that the program is “at a preliminary stage,” but that the parties have “all agreed in principle” with details still needing to be worked out.

Once it does take off, though, the program could serve as a template for other states to also offer academic detailing for workers compensations issues.

“I think its got a huge amount of possibility to spread because pain management is such a natural fit for this approach,” Fischer said. “It really is one where helping a physician to get better pain management tools can improve practice.”

Academic detailing has recently emerged as a counterpart to drug industry detailing, which has been criticized as an effort to support the prescribing of medicines. Academic detailing has also been chastised, though, with accusations that these programs advocate policies of their supporters, which has included state and federal government payors. Advocates of academic detailing counter that these programs are conducted by researchers that are presenting the science and don’t have ulterior motives.

“Traditionally drug ‘detailers,’ sponsored by the pharmaceutical industry, visit doctors’ offices to advise of new medications developed by the specific vendor. Certainly those visits carry the bias of the manufacturer and the promotion of only those drugs manufactured by the specific vendor,” Peplowski said. “[The Harvard researchers] questioned, ‘Why not ‘detail’ with a neutral medical professional, who would teach the doctor about ‘right’ prescribing (i.e. consistent with Evidence Based Medicine), rather than being vendor driven? Thus the search and subsequent approval for a grant to study the effects of academic detailing.”

Peplowski said the six month program will be piloted with Kaiser north following a smaller pilot by Kaiser On The Job, which demonstrated a 30 percent reduction in narcotic prescriptions.

Meanwhile, Avorn is spearheading an effort to create the first U.S. insurance industry detailing program, with that effort making headway. With the exception of Kaiser, health insurance companies have been reluctant to conduct their own detailing programs because, among other reasons, many firms could benefit from the detailing of one company.

Under Avorn’s proposal, insurance companies and payors would create a consortium to conduct the detailing, thereby skirting any potential free loading (see *FDA Week*, May 20).

Avorn told *FDA Week* that he has “elicited a lot of interest from a number of payors and healthcare systems” and has had “discussions with some very large insurers and those are moving along quite well.”

He declined to comment on the those ongoing talks, but the program has received substantial interest. The Agency for Healthcare Research and Quality similarly launched its academic detailing program (see *FDA Week*, May 27). — *Ben Moscovitch*

Senate PAMPA Reauthorization Would Expand EUA, Animal Model

Senate legislation reauthorizing HHS medical countermeasures programs would expand emergency use authorization, establish a process for FDA to consider animal models, and ensure the agency is involved earlier in the development process for these medications, garnering praise from a key biotechnology industry group and other stakeholders.

The Pandemic and All-Hazards Preparedness Act Reauthorization — introduced Nov. 10 by Sens. Richard Burr (R-NC), Tom Harkin (D-IA), Mike Enzi (R-WY) and Bob Casey (D-PA) — draws on ideas from FDA, industry and stakeholders to better define FDA’s role in medical countermeasure development, and improves regulatory certainty to speed up development of medical countermeasures, according to sources. But, the measure does not include money for two key Obama administration initiatives, including one program that would aid start-up companies in developing medical countermeasures.

The bipartisan bill aligns well with its House counterpart and is likely to move quickly through the Senate, with many

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of the FDA provisions remaining intact and possibly few amendments, said one source, although adding that Sens. Joe Lieberman (I-CT) or Susan Collins (R-ME) — the chairman and ranking member of the homeland security and governmental affairs committee — may try to attach some provisions, although likely not directly FDA related, onto the PAHPA legislation.

The bill is a series of “modest improvements across the board,” the source said. “This is a bill that is likely to get through the Senate ... All in all it’s a pretty good package.”

The legislation would expand the agency’s ability to make medical countermeasures under review available in limited circumstances, basing the decision either on a declared emergency or an identified material threat. The new “authorized use” would allow FDA more flexibility to set the terms of when and how this authority would kick in, according to a Senate aide, adding that using this authority for prepositioning could help cut down on red tape that could slow the agency’s response in an emergency.

“Basically, (under the bill) it is more up to the judgment of the secretary what constitutes authorized use of countermeasures,” said Crystal Franco, of the Center for Biosecurity at the University of Pittsburgh Medical Center. “It gives the secretary a little more flexibility, which I think is good.”

The bill would also allow FDA to consider material threats when reviewing and approving products, allowing the agency to use a different risk benefit analysis for medical countermeasures, the aide said. In addition, the agency would be able to extend the expiration date for countermeasures in the national stockpile. These measures “really envision a much more robust role for FDA”, the aide said.

Like the House bill, the Senate measure also provides for more communication between FDA and sponsors of these products. The Senate bill would require FDA to develop a process for creating regulatory management plans, also a component of the House bill, but expands on this idea to include more products eligible for these plans, the aide said, with these plans being developed 45 days after an IND or IDE is approved. The bill also directs the agency to create a procedure for developing plans for products under review in 45 days, with management plans for these products completed no later than 274 days after the law is enacted, unless the sponsor notifies the agency within 30 days that it will not be creating a plan.

These plans would provide a formal process for feedback and interactions about development and regulatory review of a medical countermeasure, including setting data requirements, milestones and performance targets. The goal, the aide said, “is to, as much as possible, create that regulatory certainty.”

The legislation would also increase FDA’s involvement earlier in the development process. Coordination between FDA and the Biomedical Advanced Research and Development Authority was left out of the original bill and has caused some concerns, according to one source.

“I think in general it ensures FDA is much more involved in the process of advanced development and procurement and makes sure they are involved earlier in the process,” Franco said. “I think it has been a concern from all sides. It is tough to get a countermeasure from beginning to end and I think the easier the final steps with regulation can be and the more the drug sponsor knows about how to facilitate that process, it will make things easier and we will be able to obtain countermeasures in a faster time line.”

The Senate legislation, like the House bill, also addresses animal models. Under the Senate bill, FDA would have 180 days to develop a procedure detailing how sponsors could request a meeting with FDA on using animal models in development activities and prior to initiating pivotal animal studies. Clarity on the animal rule is intended, like other aspects of the bill, to increase regulatory certainty, the aide said.

In addition, the bill charges FDA with increasing its medical countermeasure expertise, including developing regulatory science tools to advance review and approval of these drugs. The legislation instructs the agency to provide an annual report to Congress about its regulatory science initiatives, priorities and scientific gaps, along with progress of regulatory management plans and application reviews.

The agency is also instructed to address the need for pediatric formulations of medical countermeasures and to evaluate the need for studies in pediatric populations, an area that has concerned some safety advocates although stakeholders said these measures need to be taken. These measures could help the agency and industry start thinking about how best to bring these pediatric products to fruition, the aide said.

“We need to talk more about this and this bill is starting the conversation,” Franco said.

The Biotechnology Industry Organization said reauthorization of PAHPA is a opportunity to streamline, strengthen and improve the current system for developing medical countermeasures.

“The bipartisan legislation also provides needed clarity for the regulatory process for medical countermeasures at the Food and Drug Administration and requires the agency to take material threat determinations into consideration when reviewing products,” BIO President and CEO Jim Greenwood said in a statement. “These provisions will help accelerate the development and approval of medical countermeasures, improving the nation’s preparedness in the face of a public health crisis or bioterrorism event.”

Along with PAHPA, BIO also supports the simultaneous reauthorization of the BioShield Special Reserve Fund, the

funding for private companies working to develop these products. The fund would receive \$2.8 billion for 2014 — 2018. BARDA would be funded at \$415 million annually for fiscal 2012 — 2016.

Along with legislation reauthorizing PAHPA, the senators also introduced the Medical Surge Capacity Act to enable the HHS secretary to better target and issue waivers under Section 1135 of the Social Security. — *Nanci Bompey*

Senate Finance Members Press Berwick On ‘Durable’ Device Standards

CMS officials briefed Senate Finance Committee staff days after the committee’s GOP members admonished the agency for using the final End-Stage Renal Disease payment regulation to determine that newly approved durable medical equipment must have at least a three-year life span in order to be eligible for Part B reimbursement, Inside Health Policy has learned. The senators relayed to Berwick that a number of medical device companies and other stakeholders have visited their offices citing concerns with the proposal and its potential to stifle innovation.

The senators Nov. 8 sent a strongly worded letter to CMS Administrator Don Berwick saying that while Medicare says that “durable” equipment must be able to withstand repeated use, CMS has never put forth a “length of life” standard, and suggested that doing so within the ESRD rule conflicts with the administration’s goal of transparency. Two days later, Finance Committee staff held a meeting with CMS officials to discuss the issue.

“The revised definition of DME will discourage the development of new DME items and enhancements to existing DME items that may fail to meet the proposed three-year minimum lifetime criterion,” they wrote. “We are concerned that this additional regulatory threshold will hurt medical innovation, increase development costs for the companies investing in innovative products, discourage hiring in industry, and have the effect of denying Medicare beneficiaries access to important treatments,” the letter states.

The medical device industry is also strongly opposed to the new definition. In August, the Advanced Medical Technology Association (AdvaMed) wrote a letter to CMS saying that the proposed definition would deter innovation, result in regulatory burden, lead to inconsistent coverage policy and create problems with multi-component devices.

AdvaMed suggested that CMS convene a study panel to discuss the definition, and also asked the agency to consider ways to reduce the associated regulatory burden.

CMS officials told Finance Committee staff at the Nov. 10 briefing that they viewed the definition as codifying standard practice, and pointed out that the agency already asks for durability data when reviewing a product for coverage, a congressional staffer tells Inside Health Policy. Agency officials also argued that the change is pro-industry in that it creates a sense of regulatory certainty by preventing companies from developing a product and then discovering after the fact that it will not be covered, the staffer says.

CMS also took issue with the argument that innovative products would be harmed if they didn’t meet the durability test, telling Finance staff that most DME is not disposable, the staffer says. The agency did note that several products had been grandfathered in, but GOP staff asserted that the fact that some devices needed to be grandfathered suggests that there are products that should not be covered under the new definition. CMS, however, said that the number of products that could be impacted is small, the staffer says. — *Amy Lotven*

OIG Finds Hospital Oversight Concerns; AHA Says Final CoP Rule May Help

The HHS Office of the Inspector General warns that CMS and states have missed major opportunities to tackle hospital patient safety issues linked to alleged serious adverse events like surgical errors, abuse by hospital staff and patient suicide. A top hospital lobbyist said OIG raises important concerns, but adds that once CMS’ newly updated hospital Conditions of Participation (CoP) are fully in place the overall outlook should improve. She also called for standardization in state oversight regulations.

Nancy Foster, the American Hospital Association’s vice president of quality and patient safety policy, told Inside Health Policy that the 1980s CoPs are “out of step with medicine.” She called CMS’ recent interim rule updating the CoPs “a very big step in the right direction.” She also urged revisions in the standardization of interpreted guidelines for state oversight, arguing that the process would be smoother and more transparent if each state did not have its own regulations.

In its recent report titled “Adverse Events In Hospitals: Medicare’s Responses To Alleged Serious Events,” OIG’s survey of 78 complaint cases found that CMS told state agencies to assess CoP issues less than half the time, and state agencies asked hospitals to submit performance data only once out of 19 times required. Hospitals, said OIG, found state agency responses urgent but also disruptive. The report found that hospitals took some corrective action in each of 64 complaints studied, including training staff, firing staff or device and workspace changes.

“State agencies and CMS missed opportunities to incorporate patient safety principles in their responses,” OIG wrote. “State agencies performed little monitoring to verify that hospitals’ corrective actions resulted in sustained improvements.”

OIG recommended that CMS require all Immediate Jeopardy complaint surveys to examine compliance with CoP on performance improvement and quality assurance, direct states to closely track hospitals’ corrective actions, improve disclosure regarding alleged adverse event complaints and enhance federal communication with accreditors. CMS agreed

with OIG's recommendations and said it will take action.

"We fully agree on the value of clear, prompt and adequate communication between CMS and CMS-approved accrediting organization," responded CMS at the end of OIG's report. "Such correspondence includes communicating survey results and enforcement actions, if applicable. ... We will clarify the existing policy for the ROs [regional offices] and work with them to enhance compliance."

Foster said the report brought up key issues that hospital advocates have been raising. "Overall I think what we'd say is they raised some important issues that need to be addressed by CMS. We too have raised some questions about the inspections process following a complaint," she said. "There needs to be better communication with the hospital, so that the hospital can really do their own investigation."

However, Foster warned that stricter "enforcement in existing CoP" as a response to the OIG report "is not necessarily what we think will be in anyone's best interest. Until the proposed rule becomes final, we think there needs to be some judicious applications to the current CoP." She said hospitals "want further improvements to bring [regulations] in line with the current facets of medicine."

Once the new rule is set and the reforms have taken effect, Foster said, "I think you will see a decrease in the relative proportions of citations given to hospitals based on CoP standards."

CMS did not comment by press time, but Foster said she expects to see the final rule early next spring. — *Sahil Kapur*

Opioid Education Model Floated . . . begins on page one

process that would be used to implement such a CME program, said Howard Dorfman, a REMS expert and vice president and general counsel at Ferring Pharmaceuticals. Moving forward with the first class-wide REMS also reinforces that these tools are becoming mainstream by FDA and industry and the development of the educational piece shows the agency is taking a new approach with regard to REMS and class-wide REMS, he said.

Under the class-wide REMS — the first FDA has developed — manufacturers of long-acting and extended-release opioids are required to submit to the agency a risk management plan that includes voluntary prescriber training. The training will be provided by accredited, independent continuing education providers without cost to healthcare professionals, with sponsors offering unrestricted grants to CE providers to develop the education.

The training is not mandatory for prescribers, but sponsors will be required to establish goals and report to FDA the number of prescribers trained. FDA's draft blueprint, released earlier this month, provides a basic outline and core messages for continuing education providers to develop educational materials on training prescribers, including how to assess patients for treatment with extended-release and long-acting opioids; become familiar with how to initiate therapy; modify dose and discontinue; be knowledgeable about how to manage ongoing therapy; counsel patients and caregivers about safe use including storage and disposal; and be familiar with general and product-specific drug information about these drugs.

The REMS and the blueprint are basically telling industry to use accredited professional medical education as a tool to deliver risk information, which the agency has not specified before, said Murray Kopelow, chief executive for the Accreditation Council for Continuing Medical Education.

"It will be very interesting to see how the opioid REMS is viewed as a laboratory for the REMS process generally," Dorfman said.

Likewise, Kopelow said, "We are hoping that this opioid REMS will work and continuing education will rise to the challenge ... and accredited continuing medical education will be a part of future REMS."

Dorfman said there have been questions raised over the last several years that continuing medical education was influenced by industry, but the blueprint addresses this issue as well as concerns raised by various stakeholders about the initial class-wide REMS proposal.

"I think the CME concept has come a long way since the first proposal and I think if the educational component is launched successfully, it will go a long way toward giving FDA comfort to look beyond the opioid drug area and work toward implementing other class-wide REMS they feel are appropriate," Dorfman said.

Dorfman said that the blueprint provides greater detail that FDA had not previously provided. It also addresses one of the significant issues raised by industry with the original opioid class REMS proposal, that the significant differences between opioid drugs were not addressed by having the characteristics depicted in a chart addressing drug-specific information that would focus the REMS CME requirement.

But he said it remains to be seen whether the educational component of the REMS will be the centerpiece of the risk benefit analysis and what role other components will play. There is also the question about what role pharmaceutical manufacturers will play in developing patient education, Dorfman added.

Jen Bolen, an attorney who educates prescribers about regulatory compliance, said the blueprint is a "step in the right direction" but is "missing a lot of the how-to." She said the document lacks a lot of the detail physicians need

and is not very different from what is already out there.

“I think that fundamental how-to component, how FDA plans to implement this, seems to be missing from this,” Bolen said. “I think they should give a best practices statement how they expect manufacturers to carry this out.”

“For the amount of time they’ve taken to get this far, I would have expected to see a little more,” she said.

Brian Malkin, an attorney at Frommer, Lawrence & Haug, said the REMS and blueprint don’t seem to go far enough in their recommendations. For example, the document only appears to apply to long-acting and extended release products and says that prescribers should be aware of the existence of - but are not required to use - patient provider agreements.

Malkin also questioned why FDA has so far not made the training mandatory, although he said the agency might have been concerned about cost issues raised by industry. FDA has said it has the authority to mandate the training but that it would be a less onerous process to combine it with Drug Enforcement Agency registration, a measure included in legislation pending in both houses of Congress.

Instead of making training mandatory for all doctors, Malkin suggested that FDA consider making it mandatory at least for physicians whose patients have had problems with misuse or abuse. He said that under the current proposal it is possible, for example, that the prescribers who will attend the voluntary training are not the ones who need the training most.

“The recommendations are a good start,” he said. “They seem appropriate and correct but it is unclear why FDA did not go choose to go further given the recent health reports documenting increased opioid painkiller misuse and abuse leading to increasing nonmedical uses and overdoses .”

Lynn Webster, of the American Academy of Pain Medicine, said the blueprint is a practical outline of what needs to be covered but it may not be adequate for physicians who are going to be prescribing these medications, including addressing why an individual may be misusing the drugs or problems with non-medical users obtaining and abusing opioids.

But Webster acknowledged that some of these issues may not be under FDA’s authority, and it will be up to the physician community to address some of the larger problems, including abuse of other types of opioids and medications.

He said he is also concerned that the minimalist approach by industry to education may not be sufficient for what FDA is trying to achieve with the REMS.

“If we only do what the FDA has set out in its guidelines, I think that we will fall short of our expectations,” Webster said. But he added that the agency has “lit a fire” for addressing these issues. “It is a fire that I hope will grow and we will use it as the first step toward reversing the trend of all the scheduled drug problems in the country.” — *Nanci Bompey*

Hatch Pursues Shortage Solution . . . begins on page one

interruption in prescription drug manufacturing, although Hatch’s bill may include privacy protections for drug firms, and monetary and criminal penalties for intentionally creating a shortage, sources said.

Hatch is working to define which “medically necessary” drugs would be eligible for incentives, how many of these incentives manufacturers would be eligible for and other details, a source said. While there may be only one or two manufacturers for generic drugs, the same situation exists among brand-name pharmaceuticals, the source said, adding that the difference is how generics are reimbursed. One source said the exclusion from the 340B drug discount and Medicaid rebate programs would be temporary, possibly for three years.

The senator is working with stakeholders — including manufacturers, doctors and pharmacists — to come up with a comprehensive solution to the drug shortage problem, with legislation expected to be introduced after the Thanksgiving recess, a source said, adding that the bill could come as independent legislation or attached to the Prescription Drug User Fee Act.

Drug shortages have reached record high levels this year, prompting President Obama in October to issue an executive order expanding FDA’s efforts to combat the drug dearths, including increasing drug shortage staff, speeding up reviews of medicine applications and urging manufacturers to notify the agency of impending shortages, while also launching an investigation into the gray market.

HHS — in a report released in conjunction with the executive order — said that demand has outstripped supply among sterile injectable drugs, where the majority of the shortages have occurred, and that drug prices are likely in part to blame for shortages.

Along with the early warning system legislation introduced in the Senate, a group of Democratic senators last week called for a hearing on drug shortages. A bill pending in the House would also create an early warning system similar to the Senate legislation.

Hatch’s bill would expand on these efforts and create a more comprehensive approach to addressing the problem, a source said, adding that an early warning system alone may not address the root cause of the shortages, which some say

are a result of economic factors, including reimbursement for these drugs. Some experts have also said that early warning systems could cause panic in the marketplace, resulting in hoarding or gray market problems, the source said.

“I think it is a much more balanced approach than what the current bills that are out there would do,” the source said.

A report released Monday by the IMS Institute for Healthcare Informatics said policymakers should focus solutions to the drug shortage problem on the market and supply chain that is most disrupted, and advocates for FDA or industry to create an early warning system for drug shortages.

The IMS study found that the problem of drug shortages is much more complex, yet narrower, than expected, with the problem highly concentrated among generic injectables. While these drugs represent a small part of the overall medicines market, affected products include critical drugs used to treat cancer, infection, cardiovascular disease, central nervous system conditions and pain, according to the report.

Meanwhile, the American Medical Association House of Delegates planned to vote Monday on resolutions to address drug shortages, with the organization advocating for FDA or Congress to establish incentives for drugs where production is not economically feasible and for manufacturers to have contingency plans for supply of vital and life-sustaining drugs, with drug makers possibly subject to fines and loss of patent protection if they fail to supply medically necessary drugs within 30 days.

Generic drug manufacturers have said they are working together to examine and adjust their manufacturing schedules for life-saving drugs that could be susceptible to shortages, and drug makers are adding capacity and redundancy to deal with future problems. One group purchasing organization has been meeting with manufacturers, other GPOs and distributors to identify market-based approaches to deal with drug shortages.

As of the end of October, 232 drugs have experienced shortages, surpassing last year’s high of 211, according to the University of Utah Drug Information Service, which tracks the shortages. — *Nanci Bompey*

Device Levels Debated . . . begins on page one

confronted with questions from lawmakers and industry about lagging review times and changing data requirements. GOP lawmakers recently introduced a series of device bills aimed at addressing those issues. Device center Director Jeffrey Shuren told Senate health panel members this week that putting more money into the device program would, in part, assuage those concerns.

“I empathize with industry by the way,” Shuren told lawmakers. “They’re paying more money. They’re not seeing the kind of performance they want to see, but quite frankly what we never tackled is making sure we have enough resources not only to handle the workload, but to actually get over this hump of too much workload for the individual people and not having enough managers. If we can break that cycle, we will have a program where people stay.”

Shuren has pointed to the drug center, which receives a higher level of user fees compared to the device center, as an example of why more device fees are needed. In previous iterations of prescription drug user fees, industry and FDA were faced with similar problems that were resolved with more fees, he said.

However, an industry source noted that device companies are concerned about the precedent set by drug user fees. Once the agency and industry become reliant on higher user fees, it becomes more difficult for companies to negotiate from a position of strength, the source said.

“We know that the ultimate threat of walking away can’t happen,” the source said. It’s more than just the fee amount because FDA knows industry could not leave the program in the future, the source added.

However, in this round of negotiations, industry has more data on product approvals in other markets such as Europe that have allowed companies a different comparison point.

“Bottom line, the market has moved over there,” the source said. A recent survey of venture capitalists found that investments are moving overseas, a finding that has prompted key lawmakers to pursue reforms. However, FDA officials have raised concerns about the safety of device approvals in Europe.

The debate surrounding resources also occurs as a key Senate lawmaker is floating safety initiatives that could be funded by user fees (see related story).

As user fee negotiations continue, FDA and industry are hammering out the details of the agreement, such as a switch to total time reviews, which count the time an application is with the product sponsor as well as the agency. The agency noted in meeting minutes that the discussions are moving toward an improved program, as long as the resources are provided.

“FDA noted that one challenge the group will face is that preliminary estimates put the cost of this package above that which FDA proposed in April and May,” according to meeting minutes. “Industry had indicated that FDA’s April proposal package was not acceptable.”

When probed by Sen. Richard Burr (R-NC) about requests from the agency to significantly increase fees, Shuren compared user fees to research and development

“Quite frankly if you put a little bit in research and development you may not get enough out of it,” Shuren said.

“You just have to put enough into it to get enough of a return. It’s the same for our program.

Shuren said almost half of device reviewers have four years or less of experience. Because turnover rates are so high, he said it takes three hires to get a net increase of one employee. He noted that money alone would not solve the problem and the agency is tackling it from other angles such as working with industry to improve the quality of submissions. — *Alaina Busch*

Harkin Floats Predicate Limits, Device Fees For Post-Market Surveillance

Sen. Tom Harkin (D-IA) recently floated the idea of allocating medical device user fees toward post-market surveillance activities and limiting the number of predicates that can be used for a 510(k) clearance submission. An industry source said predicates are a likely area to be targeted in medical device reforms, especially regarding pre-amendment devices.

Harkin’s suggestions came during a Senate health committee hearing on the subject, as lawmakers further probed FDA officials about improvements they are making to the clearance pathway and experts about their suggestion to scrap the process altogether.

“Perhaps we have reached a point in time, after 35-36 years, that we need to take a more intense look at this whole realm of the approval process, post-market surveillance, especially for certain higher risk devices,” said Harkin, chair of the Senate health panel, at the Tuesday (Nov. 15) hearing.

Harkin also floated the idea of limiting the number of times an initial device could be cited as a predicate “so that you don’t get devices to the nth degree out there that bear very little resemblance to what was initially approved.” He said he was thinking about the predicate issue in light of safety concerns addressed by the Institute of Medicine’s evaluation of the 510(k) clearance process.

Medical device reform has been pegged as an area ripe for legislation heading into user fee reauthorizations next year, with House lawmakers recently proposing a slew of bills targeting de novo reform, approval processes and conflict of interest changes. Senators are mirroring the reform efforts.

An industry source said predicate limits are a likely area to be targeted in policy riders, particularly restrictions on using pre-amendment devices, which are more than 30 years old and were grandfathered into the current regulatory structure.

“I think there will be an attempt here,” the source said. The Government Accountability Office has been critical of FDA in this area and some in industry have been supportive of the change, the source added. If devices are on their 22nd or 23rd iteration and still use a predicate from the 1970s, “maybe we’re not executing the best public health policy,” the source said.

Regarding post-market surveillance, there is a limited amount of user fees that go toward those activities, but they do not focus on the systems proposed by Harkin, an FDA official said. Further, industry has been reluctant to give FDA an increase in fees that agency officials say would help address resource problems in the device center.

Harkin said he is reluctant to embrace the idea of user fees and he has fought against using them for meat inspections, but they should be changed to focus on post market and safety issues alongside industry issues of predictability and transparency. He further suggested that a “simple reauthorization” is not what the program needs. — *Alaina Busch*

Patent Extension Debated . . . begins on page one

The case is pending before the U.S. Court of Appeals for the Federal Circuit and oral arguments were scheduled this week. In light of passage of the patent reform act, supplemental briefs were filed last month, with the government weighing in favor of Medicines Company, which had originally initiated the case against the Patent and Trademark Office for not granting an extension for the company’s anti-coagulant Angiomax.

The company received court-ordered interim extensions as the case moved through the lower courts, but APP Pharmaceuticals contends in its briefs that the patent was set to expire in March 2010 and the interim extensions are invalid.

“[B]ecause (Medicines Company’s) patent term extension (‘PTE’) was untimely, the patent ran its original term and the subject matter of the patent entered the public domain,” according to the brief. “Congress cannot constitutionally revive it. The Supreme Court has never held otherwise.”

The issue stems from an incident in 2000 when Medicines Company lawyers missed the filing deadline for a patent extension to account for regulatory delays. Other large pharmaceutical companies have since also raised issues with confusion surrounding the deadline.

Generic drug lobbyists fought hard against the patent filing provision but were unable to convince lawmakers to ax it from the patent reform bill. Some lawmakers also opposed it, saying the matter should be left to the courts, but the bill’s primary sponsor argued that because PTO did not challenge the district court decision in favor of Medicines Company, the issue should be resolved through the legislative measure, despite the controversy surrounding it.

In a court brief, government intervenors argue that the district court has authority through the Administrative Proce-

dures Act to grant the interim extensions, therefore the patent never expired as APP Pharmaceuticals asserted. The patent was set to expire March 23, 2010, but starting March 18, 2010, the court issued a continuous chain of extensions, according to court documents.

“APP claims that Congress lacks the power to extend the term of a patent after the patent’s original term has lapsed,” according to the government brief. “As we show presently, that claim has no basis in the Constitution. But even if it were correct as a matter of constitutional law, it would have no bearing on the constitutionality of section 37 as applied in this case, for the simple reason that the ‘404 patent has never lapsed.”

Medicines Company argues that the congressional record further demonstrates that the provision was intended to apply in their specific case as lawmakers on both sides of the argument repeatedly referred to the company throughout debate. Further, because of the extensions, other companies were barred from bringing the product to market, the company said.

“APP relies on legal fiction that the ‘404 patent ‘expired’ and ‘entered the public domain’ over 18 months ago,” according to the company’s brief. “But APP cites no support for its imaginary public domain theory. No case has ever suggested that Congress lacks the authority to extend an existing patent.” — *Alaina Busch*

FDA To Collaborate With Foreign Regulators On Tobacco

A group of tobacco regulators from 22 countries met this week to discuss opportunities for collaboration and information sharing, according to FDA. “The industry sees the entire world as a potential market,” said FDA Commissioner Margaret Hamburg. “It is only natural that like-minded leaders band together to combat this global threat in unison.”

The International Tobacco Regulators’ Conference was hosted by FDA and the World Health Organization Tobacco Free Initiative. Conference participants committed to an ongoing international discussion about tobacco regulation, according to FDA.

FDA gained the power to regulate tobacco in 2009 and recently faced a setback to a key regulation mandated under that law, when a district court judge blocked FDA’s ability to implement graphic warning labels while First Amendment issues are evaluated. — *Alaina Busch*

Bipartisan, Bicameral Bill Hikes Counterfeit Drug Penalties

A bipartisan group of lawmakers from both chambers Thursday (Nov. 17) introduced legislation to increase criminal penalties for counterfeiting drugs, saying the current penalties do not go far enough to curb the problem and are equivalent to penalties for trafficking electronics and clothing. The effort was lauded by the drug industry.

Sens. Patrick Leahy (D-VT), Chuck Grassley (R-IA), Michael Bennet (D-CO) and Richard Blumenthal (D-CT) as well as Reps. Patrick Meehan (R-PA) and Linda Sanchez (D-CA) introduced the Counterfeit Drug Penalty Enhancement Act, which includes penalties of up to \$4 million and prison sentences of up to 20 years. The fine could be doubled for multiple offenses and also include up to 20 years in prison.

“While the manufacture and sale of any counterfeit product is a serious crime, counterfeit medication poses a grave danger to public health that warrants a harsher punishment,” Leahy said. “This legislation will raise those penalties to a level that meets the severity of the offense. Deterring this epidemic problem is a bipartisan effort.”

Pharmaceutical Research and Manufacturers of America President and CEO John Castellani applauded the effort, echoing the argument that the penalties should be more in line with the crime.

“In most cases, criminals selling illicit drugs face tougher jail sentences than those selling dangerous counterfeit medicines, which provide no therapeutic benefit and cause great harm to patients suffering from disease. Make no mistake: criminals are not only targeting ‘lifestyle’ drugs, but also vital medicines that treat cancer, diabetes, malaria and high blood pressure,” Castellani said.

A recently introduced online piracy bill backed by House Judiciary Committee members also includes counterfeit drug penalties and would impose fines of up to \$2 million and prison sentences of up to 10 years for illegal trafficking.—*Alaina Busch*

FDA Challenges Court Ruling That Limited Agency’s Compounding Oversight

FDA is challenging a recent federal district court decision that said the agency went too far in targeting animal drug compounding pharmacists and has prompted calls for clarity on FDA’s policies in this area. The move comes as FDA shifts its stance regarding enforcement discretion of pharmacists compounding Makena for pricing issues, saying recently that it will begin looking at quality discrepancies between the manufactured and compounded injections.

The agency Nov. 11 appealed to the U.S. Court of Appeals for the 11th Circuit, challenging the previous decision from the U.S. District Court for the Middle District of Florida in favor of Franck’s Lab, an Ocala-based compounding pharmacy.

The September ruling said FDA was trying to expand its power beyond its mandate in preventing the facility from compounding animal drugs from bulk chemicals and that its compounding policies have been codified in compliance guides as opposed to regulation, thus limiting the agency’s ability to take action in this area (see *FDA Week*, Sept. 15).

Pharmacists lauded the decision for affirming that state boards of pharmacy have jurisdiction in this area, while animal and veterinary industry groups have been trying to rope in widespread animal drug compounding that ventures into the realm of drug manufacturing.

Compounding policies have also been central to the pricing controversy regarding the pre-term labor drug Makena, which was widely available through compounding before FDA approved the higher-priced injection. FDA exercised enforcement discretion as the pricing issue played out with payers, advocacy groups and lawmakers, but recently signaled that it will test the compounded drugs for safety issues (see *FDA Week*, Nov. 11).

Franck’s Lab had been implicated in a 2009 incident where 21 polo horses died from compounded drugs that were too potent. The Florida Board of Pharmacy investigated and resolved the case, while FDA reinspected and issued a warning letter to the facility. For the first time, the agency enjoined a state-licensed pharmacist from compounding animal drugs from bulk chemicals in 2010, the action central to the pending case. — *Alaina Busch*